Clinical characteristics of African Americans vs Caucasian Americans with multiple sclerosis

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Abstract—*Background:* African American (AA) individuals are thought to develop multiple sclerosis (MS) less frequently than Caucasian American (CA) individuals. *Objective:* To compare the clinical characteristics of AA and CA patients with MS. *Methods:* The clinical features of MS were compared in a large retrospective cohort of AA (n = 375) and CA (n = 427) subjects. *Results:* The proportion of women to men was similar in AA and CA subjects (81% [AA] vs 77% [CA]; $p = 0.122$). There were no differences in the proportions of subjects with relapsing–remitting, secondary progressive, primary progressive, and progressive relapsing MS. The median time to diagnosis was 1 year after symptom onset in AA subjects and 2 years after symptom onset in CA subjects ($p = 0.0013$). The age at onset was approximately 2.5 years later in AA than CA subjects (33.7 vs 31.1 years; $p = 0.0001$). AA subjects presented with multisite signs and symptoms at disease onset more often than CA subjects ($p = 0.018$). Clinical involvement restricted to the optic nerves and spinal cord (opticospinal MS) occurred in 16.8% of AA patients compared with 7.9% of CA patients ($p < 0.001$). Transverse myelitis also occurred more frequently in AA subjects (28 vs 18%; $p = 0.001$). Survival analysis revealed that AA subjects were at higher risk for development of ambulatory disability than CA subjects. After adjusting for baseline variations and differences in therapeutic interventions, AAs were at 1.67-fold greater risk for requiring a cane to ambulate than CA patients ($p < 0.001$). There was a trend suggesting that AAs were also at greater risk for development of wheelchair dependency ($p = 0.099$). Adjusted Cox proportional hazard models showed that this effect was in part attributable to the older age at onset in AAs ($p < 0.001$). *Conclusions:* Compared with multiple sclerosis (MS) in Caucasian Americans, African American patients with MS have a greater likelihood of developing opticospinal MS and transverse myelitis and have a more aggressive disease course.

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African Americans (AAs) develop multiple sclerosis (MS) less frequently than Caucasian Americans (CAs).[1-4] A recent study found that AAs had a relative risk of 0.64 for developing MS compared with CA.[5] Because AAs represent a population with variable Caucasian and African ancestry, this observations suggests that African ethnicity may be responsible for partial protection against MS. Indeed, MS appears to be extremely rare in black Africans, with few documented cases.[6-10] This observation could be due to an inherent genetic resistance or to a low prevalence of environmental risk factors. Similarly, the increased prevalence of MS in AAs compared with black Africans could be due to genetic admixture of a resistant African population with a susceptible Caucasian population or to environmental risk factors operative within the United States.

It is unclear whether MS in AAs is clinically distinctive. Some observers reported a more aggressive disease course in AAs.[11-14] A recently reported matched case-control series found that AA patients with motor symptoms at disease onset have greater disability over time than CA patients.[15] In addition to motor disability, AAs may experience more optic nerve impairment than CAs. In a small series, 7 of 12 (58%) AA subjects with MS had neurologic deficits confined to the optic nerves and spinal cord.[16] The same study reported that AAs with a single episode of demyelinating optic neuritis had more severe loss of visual acuity in comparison with CAs. Interestingly, neuromyelitis optica (NMO), the co-occurrence of acute transverse myelitis with optic neuritis, is reported to be more common than MS in African and African Caribbean individuals.[17,18] A study of South African patients presenting with optic neuritis found that black South Africans were more likely to have bilateral involvement and worse recovery of vision than white South Africans.[19] Taken together, these observations suggest that demyelinating disease in persons of African ancestry preferentially affects the optic nerves and spinal cord and results in a more

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severe clinical course than in persons of Northern European ancestry.

This retrospective cohort study compares the clinical characteristics of AA and CA subjects. Although there are many similarities between these groups, AAs are at higher risk for ambulatory disability and have a higher prevalence of symptoms restricted to the optic nerves and spinal cord.

Methods. *Subjects.* Subjects were recruited through an ongoing multicenter consortium (Multiple Sclerosis Genetics Group).[20] In addition to the clinical information, DNA and serum were collected from all subjects as well as, whenever possible, from both parents, unaffected siblings, friends, and spouses. The study received institutional review board approval, and written informed consent was obtained from all participants.

We systematically reviewed medical records of each subject. Subjects whose records were incomplete, did not confirm a diagnosis of clinically definite MS,[21] or were consistent with other diagnoses such as neurosarcoidosis or systemic lupus erythematosus were excluded. The final dataset consisted of 375 AA and 427 CA subjects from simplex pedigrees (only one member affected with MS per generation). Figure 1 illustrates the geographic distribution by current state of residence for all subjects. Ethnicity was self-reported; however, the extent of admixture of Northern European chromosomes in the AA population was estimated to be 21%.[22] All clinical and demographic data were entered into a specifically designed relational database (Microsoft Access, Redmond, WA).

Opticospinal MS was defined clinically by a history of relapses or clinical signs restricted to the optic nerves and spinal cord. A minimum of 5 years of follow-up time after onset of the first demyelinating event was required to give subjects the opportunity to manifest symptoms in other anatomic areas. Subjects with clinical involvement of the cerebrum, cerebellum, or brainstem at any time during their disease course were considered to have nonopticospinal, that is, typical, disease. The results of brain MRI studies were not considered in making the distinction between opticospinal and typical MS. Transverse myelitis is defined as bilateral paresis with a sensory level and sphincter impairment. In this study, cases of paraparesis as well as paraplegia were categorized as transverse myelitis even if the sensory level was incomplete.[23] During the course of the disease, if transverse myelitis occurred only once, it was characterized as nonrecurrent transverse myelitis. If transverse myelitis occurred more than once, it was characterized as recurrent transverse myelitis.

Statistical analysis. Statistical analysis was conducted using STATA 7.0 (College Station, TX). Categorical variables were compared using the χ^2 test. Continuous variables were compared using the Student t-test or the Wilcoxon test, as appropriate. Survival analysis was used to assess time-dependent variables. The disease duration was defined as the time from disease onset to the last documented neurologic examination. Outcome variables were time from disease onset to important markers of disability: ambulation with a cane and wheelchair dependency. Time to ambulation with a cane was defined as time from disease onset to the time when the subject was unable to ambulate without unilateral assistance (6 on the Expanded Disability Status Scale [EDSS]). Time to wheelchair dependency was defined as time from disease onset to the time when the subject was no longer able to ambulate with bilateral assistance for more than a few steps (EDSS = 7). Analysis of secondary progressive (SP) disease (SPMS) was restricted to the subgroup of subjects who initially had a relapsing–remitting (RR) course. We identified the onset of SPMS as the point in time when the clinical history documented insidious progression of disease without relapses. Kaplan–Meier curves were used to explore and describe survivor functions across groups and were compared using the log-rank test for equality of survivor functions. The Cox proportional hazard model was used to assess the effect of predictors of event times using the likelihood ratio test.

To control for differences in type and duration of treatment between AA and CA groups, we constructed time-dependent covariates for both Food and Drug Administration (FDA)–approved as well as non-FDA-approved therapies that are commonly used to treat MS. The time-dependent covariate method is able to account for the actual periods during which therapy was received. To simplify analysis, we defined four treatment groups: interferon, glatiramer acetate, cytotoxic, and other. The "interferon" category grouped together treatment with any of the interferon preparations (Betaseron [Berlex, Wayne, NJ], Avonex [Biogen-Idec, Cambridge, MA], and Rebif [Serono, Inc., Rockland, MA]). Similarly, "cytotoxic" grouped together treatment with any cytotoxic agent (e.g., mitoxantrone, cyclophosphamide, azathioprine, methotrexate, and cladribine). We defined the "other" category to include monthly pulsed dosed glucocorticoids, IV immunoglobulin, and experimental protocols. Treatments that were administered to subjects for durations of <2 months were not considered to be of sufficient duration to alter the course of the disease and were not included in our analysis.

Other baseline covariates such as age at onset, site of onset, gender, and disease phenotype (i.e., opticospinal disease) were initially included in the Cox proportional hazard models, and nonsignificant variables were removed step-wise from the final models. Tests for interaction were examined but were not found.

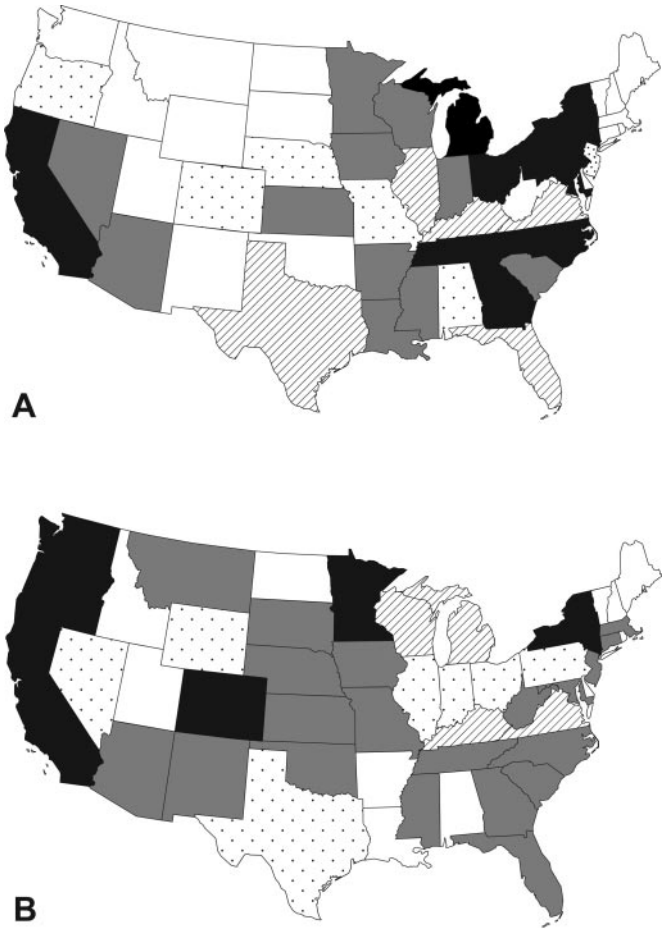

Figure 1. Geographic distribution of subjects by state of residence at time of enrollment. (A) Three hundred seventy-five African American subjects were recruited from 33 states. (B) Four hundred twenty-seven Caucasian American subjects were recruited from 37 states. The number of subjects residing in each state at the time of recruitment is indicated. Because the study is not population based, the locations of collaborating multiple sclerosis centers strongly influence the recruitment patterns. White areas = 0; gray areas = 1 to 2; dotted areas = 3 to 4; hatched areas = 5 to 9; black areas = ≥10 subjects.

Results. The clinical profiles of the subjects showed similarities between the two groups but also revealed several

Table 1 *Demographic/clinical analysis of MS dataset*

Clinical/demographic information	Caucasian American, n = 427	African American, n = 375	*p* Value
Female/male ratio	3.3:1	4.4:1	0.122
Mean (SD) age at onset, y	31.1 ± 8.9	33.7 ± 9.8	0.0001
Mean (SD) disease duration, y	11.4 ± 8.4	9.8 ± 7.2	0.0043
Proportion relapsing–remitting, %	66.8	65.1	0.600
Proportion secondary progressive, %	24.8	25.1	0.922
Proportion primary progressive, %	6.5	6.7	0.943
Proportion progressive relapsing, %	1.4	1.9	0.603
Median time from onset to diagnosis, y	2	1	0.013
Median time from onset to treatment, y	5.3	3.9	0.0048
Mean (SD) time from onset to treatment, y	8.0 ± 7.7	6.0 ± 6.0	0.0005
Median time to EDSS ≥ 6, y	22	16	<0.0001
Median time to EDSS ≥ 7, y	38	30	0.05
Median time to SPMS, y	21	18	0.051

MS = multiple sclerosis; EDSS = Expanded Disability Status Scale; SPMS = secondary progressive MS.

important differences (table 1). There was no difference in the proportions of RRMS, SPMS, primary progressive MS (PPMS), and progressive relapsing MS (PRMS) subjects (figure 2). The proportion of affected women was similar in the AA and CA cohorts (81 vs 77%; $p = 0.12$). The mean age at onset of first symptoms of MS in AA subjects was 2.6 years older than in CA subjects (33.7 vs 31.1 years; $p = 0.0001$). The median time from disease onset to diagnosis was 2 years in the CA and 1 year in the AA group ($p = 0.013$), and the median time from onset to treatment was shorter in the AA group ($p = 0.0048$). The median time to ambulation with a cane was 6 years shorter in AA than in

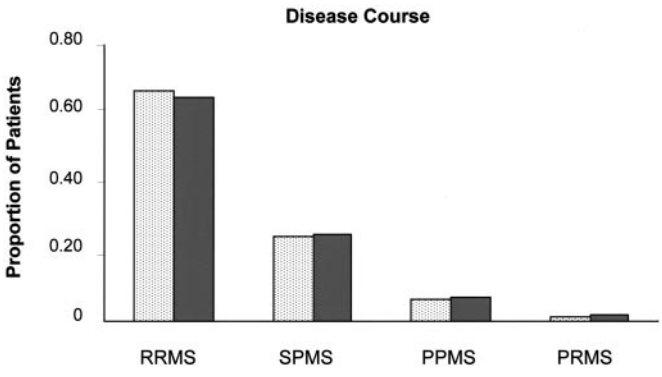

Figure 2. Proportion of subjects with relapsing–remitting (RRMS), secondary progressive (SPMS), primary progressive (PPMS), and progressive relapsing (PRMS) multiple sclerosis in African American (dotted columns) and Caucasian American (filled columns) groups (p = *0.719).*

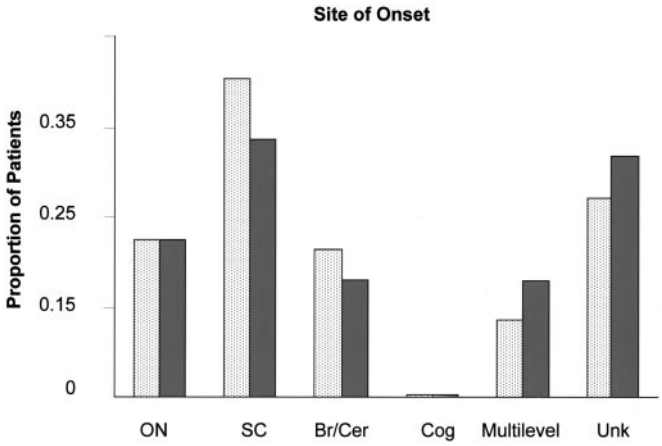

Figure 3. Anatomic site of disease onset deduced from initial clinical presentation. ON = optic neuritis; SC = spinal cord; Br/Cer = brainstem/cerebellar; Cog = cognitive; Unk = unknown. Dotted columns = Caucasian Americans; filled columns = African Americans.

CA subjects (16 vs 22 years; $p < 0.0001$). The median time to wheelchair dependency (EDSS = 7) was 8 years shorter in the AA than in CA group (30 vs 38 years; $p = 0.05$). There was also a trend to a shorter median time to SPMS in AA compared with CA subjects (18 vs 21 years; $p = 0.051$).

The initial demyelinating event was categorized by the probable site of onset and grouped into the following categories: optic nerve, spinal cord, brainstem or cerebellar, cognitive, multisite (more than one site of onset affected simultaneously, e.g., optic neuritis and cerebellar ataxia), and unknown (could not clearly be deduced based on the medical records). The overall distribution of site of onset was similar between the two groups (figure 3), although AAs more often presented with multisite involvement ($p = 0.018$).

Opticospinal MS. Optic nerve and spinal cord involvement is frequent in MS; however, some populations are more likely to develop involvement restricted to this distribution. In CAs, a pattern of opticospinal involvement was found to segregate in some MS-prone families.[24] In Japanese and other Asian ethnic groups, clinical attacks are especially likely to be restricted to the optic nerve and spinal cord.[25] Based on prior observations,[17,18] we speculated that optic nerve and spinal cord involvement may be more prevalent in AA MS subjects. Opticospinal MS was more prevalent in the AA population (16.8% [AA] vs 7.9% [CA]; $p < 0.001$). Our criteria potentially allowed subjects with NMO, the co-occurrence of optic neuritis and acute transverse myelitis with a normal brain MRI scan, to be included in this category. Because NMO is associated with more severe disease and poorer clinical outcomes than other forms of demyelinating disease, an overrepresentation in one of the ethnic groups might bias the results.[26] Three AA and one CA subjects in the dataset met proposed diagnostic criteria for NMO.[27] A sensitivity analysis showed that these subjects did not influence the reported observations (data not shown).

Transverse myelitis. Although spinal cord involvement, manifested as partial myelitis, is a typical clinical feature of MS, transverse myelitis, defined as bilateral

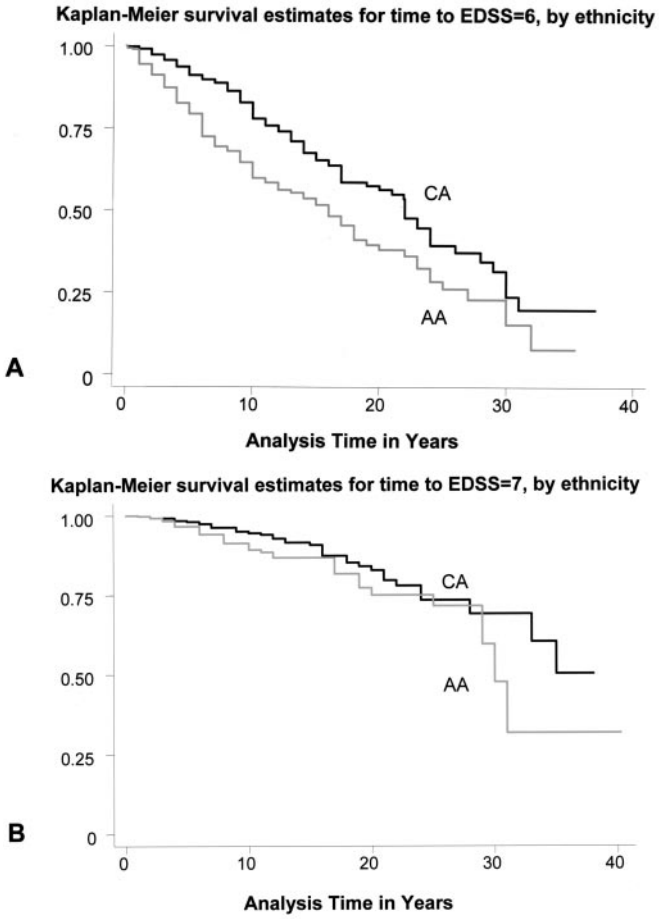

Figure 4. Kaplan–Meier curve for time to ambulatory disability. (A) Time to Expanded Disability Status Scale (EDSS) score = 6 (ambulation with unilateral assistance); (B) time to EDSS = 7 (wheelchair dependency). CA = Caucasian American; AA = African American.

paresis with a sensory level and sphincter impairment, occurs less frequently and is rarely recurrent.[28-30] In this study, transverse myelitis occurred during the course of illness in 28% of AA and 18% of CA subjects ($p = 0.0011$). Nonrecurrent transverse myelitis occurred in 16.5% of AA and 11.4% of CA subjects ($p < 0.0001$). Recurrent transverse myelitis was similarly more prevalent in AAs (11.2 vs 6.5%; $p = 0.0009$).

Optic neuritis. Optic neuritis occurred frequently in both cohorts. There was no difference in the prevalence of unilateral optic neuritis, bilateral optic neuritis, or bilateral simultaneous optic neuritis between the two groups ($p = 0.23$). A trend suggested that optic neuritis more often affects both eyes in AAs than CAs (17.6 vs 14.2%; $p = 0.10$).

Survival analysis. The mean times to markers of disability reported in table 1 show that the AA cohort more rapidly develops ambulatory disability than the CA cohort. In figure 4, Kaplan–Meier survival curves for time to EDSS = 6 (ambulation with unilateral assistance) and time to EDSS = 7 (wheelchair dependency) are presented. AAs have a higher probability of more rapidly requiring a cane to ambulate ($p < 0.0001$) and becoming wheelchair dependent ($p = 0.05$) than CAs.

Access to care and disease-modifying therapies. A more severe disease course in AA than CA MS patients might reflect an intrinsic difference in disease severity, a difference in access to healthcare, or baseline variation between these groups. All subjects in the cohort were actively followed by neurologists. As one measure of quality of care, the time from disease onset to diagnosis of MS was assessed. The median time to diagnosis was 1 year shorter in AA subjects (1 vs 2 years; $p = 0.013$), indicating that there was not a significant delay from onset of symptoms to diagnosis in either group. Treatments received were also analyzed as another measure of quality of care. AA and CA groups were equally likely to receive disease-modifying treatments for MS (77 vs 79%; $p = 0.43$), and the median time from diagnosis of MS to initiation of treatment was also similar (1.6 [AA] vs 1.5 [CA] years; $p = 0.12$). It is possible that care provided by neurologists, other than timely diagnosis and initiation of disease-modifying treatment, might influence disease severity. These subtle differences are difficult to quantify and were not assessed in this study. Uncontrolled-for differences in the quality of care between the two groups could be a source of bias.

However, there were differences between the AA and CA groups with regard to the duration of treatment and numbers of treatments given to each subject. For example, 13 CA patients received treatment with monthly pulsed glucocorticoids, whereas no AA patients were treated in this fashion. In addition, therapies were more often switched in the CA group (data not shown). To adjust for different durations of time, different treatments at different times, more than one treatment at a given time, and lapses in treatment, we used time-dependent covariates in Cox proportional hazard models. In this analysis, time-dependent treatment covariates are confounded by the indication to treat (subjects who are sicker are more likely to receive treatment than subjects with benign disease), thereby limiting interpretations regarding treatment efficacy.

Table 2 shows the results of the Cox proportional hazard models adjusting for ethnicity, gender, age at onset, and the duration or combination of the four treatment groups (interferon, glatiramer acetate, cytotoxic agents, and other). Even when adjusting for these covariates, AA subjects have a higher probability of developing a need for ambulation with a cane more rapidly than CA subjects ($p < 0.001$). There was a trend suggesting that African ethnicity was also a predictor of wheelchair dependency ($p = 0.099$). However, in the adjusted analysis, the effect of African ethnicity on the hazard ratio for wheelchair dependence was largely accounted for by the older age at onset in this group. In both models, there was a trend suggesting that male gender was predictive of disability. A history of transverse myelitis at any time during the duration of follow-up was also predictive of disability in both models ($p = 0.003$ [time to EDSS = 6] and $p = 0.03$ [time to EDSS = 7]); in contrast, a history of unilateral optic neuritis was protective ($p = 0.038$ [time to EDSS = 6] and $p = 0.044$ [time to EDSS = 7]). Because these covariates did not necessarily occur at baseline, they were not included in the Cox models. Nevertheless, a sensitivity analysis showed that adjustment for these covariates did not influence the Cox models (data not shown). Controlling for center of recruitment did not alter these models.

Subgroup analysis. The proportion of PP and PR subjects in this cohort was <10% of all subjects, and there was

Table 2 *Cox proportional hazard models for time to ambulatory disability*

	Cox proportional hazard model for ambulation with cane			Cox proportional hazard model for wheelchair dependency		
	Hazard ratio	95% CI	*p* Value	Hazard ratio	95% CI	*p* Value
Unadjusted analysis						
African ethnicity	1.84	1.43–2.36	<0.001	1.46	0.93–2.33	0.099
Adjusted analysis						
African ethnicity	1.67	1.29–2.15	<0.001	1.32	0.83–2.11	0.238
Age at onset by decade	1.58	1.37–1.82	<0.001	1.62	1.25–2.09	<0.001
Male gender	1.22	0.91–1.63	0.177	1.52	0.92–2.50	0.101

no difference in the proportion of these phenotypes by ethnicity. Nevertheless, survival analysis segregating RR and SP subjects from PP and PR subjects was undertaken. The RR and SP subgroups showed similar characteristics to that of the entire cohort (data not shown).

We also examined subjects with progressive disease from onset (PP and PR subjects grouped together). Although the number of subjects in this subgroup was small (n = 66), a trend suggested that African ethnicity was predictive of ambulating with a cane (hazard ratio = 1.58, $p = 0.144$). Cox models did not identify other significant risk factors for disability.

Discussion. The Cox proportional hazard models revealed several insights about the development of disability in MS. First, African ethnicity is a highly significant predictor of requiring a cane to ambulate sooner in an analysis that adjusted for age at onset, gender, and types and durations of medications commonly used to treat MS. Second, the age at onset was a strong predictive factor for ambulatory disability. Indeed, when age at onset was taken into account in our analysis, the effect of African ethnicity became less apparent. This suggests that AA patients are at higher risk for disability in part because of their older age at onset. Similar effects on disability for the predictor variables age at onset and optic neuritis were previously reported in other MS cohorts.[31-35] Third, differences in type, duration, and combinations of treatment, when rigorously controlled for by time-dependent covariates, did not influence the models.

The risk of developing ambulatory disability appears to be independent of access to health care because all study subjects received ongoing care from a neurologist. Moreover, AA subjects received earlier diagnosis and treatment than did their CA counterparts. It is possible that AA patients were diagnosed more rapidly because they more often present with multilevel symptoms that are highly suggestive of demyelinating disease.

We found that the progression of disability in AA subjects was in part due to the older age at onset in this group. Older age at onset is well recognized as a prognostic factor for disability in MS.[31,32,34,35] An older age at onset may be an intrinsic feature of the epidemiology of MS in AAs. The average age at onset for CA subjects (31.2 years) in our study was identical to that reported in an earlier population-based study.[31] Interestingly, an older age at onset in AAs was recently reported in a matched case-control study.[15] In that study, the mean age at onset was 2.2 years later in AAs than CAs, closely paralleling our observations (see table 1). We cannot exclude the possibility that AAs may have a longer period of subclinical disease activity prior to the heralding demyelinating event. If true, the burden of disease might be greater in AAs than in CAs at the onset of clinical symptoms. In this regard, one case series comparing 25 AA and 25 CA MS patients suggested that a greater burden of disease on brain MRI may be present in the AA group.[12] Further brain MRI studies that quantitatively compare patterns of disease between these ethnic groups are needed.

Transverse myelitis was also found to occur more frequently in AA than CA subjects. Because transverse myelitis is a predictor of ambulatory disability, AA patients with MS are at higher risk for disability in part due to the increased frequency of transverse myelitis in this group.

The prevalence of opticospinal MS was increased in AAs. Clinical involvement confined to the optic nerves and spinal cord is a known characteristic of some Asian patient cohorts[25] and has been described in small series of African and Caribbean individuals.[17,18] MRI in Asian patients with MS showed a relative paucity of intracranial lesions in comparison with typical Western patients with MS.[36,37] Although we were unable to quantitatively analyze brain MRI in our cohort, the majority of AA and CA subjects with opticospinal MS had abnormal brain MRI studies (data not shown), suggesting that the opticospinal phenotype observed in this cohort may be different from descriptions of Asian MS.

Higher proportions of Asian patients also have the more aggressive disease course of NMO.[38-40] In a nationwide survey of MS in Japan, 7% of patients with demyelinating disease had NMO.[39] In the current cohort, only four subjects met diagnostic criteria for NMO (three AAs and one CA). The number of subjects with NMO in this cohort is too small to draw any conclusions about the frequency of NMO in AAs. However, the low frequency of NMO in our cohort

suggests a scarcity of this phenotype in AA MS patients in contrast to the high numbers of NMO patients observed by the study of MS in Martinique.[18] In our Cox proportional hazard models, the opticospinal phenotype was not shown to be a significant risk factor for ambulatory disability. Thus, although AA patients with MS appear to have opticospinal MS more frequently than CA MS patients, this phenotype does not seem to influence disease severity.

We actively recruited CA and AA subjects through a network of collaborating centers as well as through advertisements. These efforts allowed us to generate the largest cohort of MS subjects with AA ethnicity studied to date. This cohort is not population based and therefore might be biased. However, the direction of potential bias is not obvious. The average time from disease onset to ambulation with a cane in our CA cohort was similar to that reported in a large population of European subjects.[35] This indicates that our CA cohort is not biased by inclusion of an excessive proportion of subjects with benign MS. Another study reported more rapid progression in populations of Northern European descent; however, treatments with disease-modifying therapies were not available for that cohort.[41] Ours is the first study of the development of disability in a cohort in which the majority of MS patients received treatment with disease-modifying therapies (78%). Therefore, because of the potential impact of treatments on disability, any direct comparison with natural history studies in other MS cohorts is problematic.

Conversely, it is possible that our recruiting efforts produced an AA cohort comprising individuals with more severe disease because these individuals were especially motivated to participate in the study. However, severely disabled MS subjects are often confined to nursing homes, which might produce a bias in the opposite direction. Other potential confounders are environmental factors. The assessment of exposures to environmental factors that might influence MS was not possible because of inherent limitations of the retrospective study design. Only information that could be reliably ascertained by review of medical records was analyzed. Consequently, this study does not control specifically for environmental factors such as diet,[42] use of multivitamins,[43] or exposure to tobacco[44]; however, it is unclear how the sampling methods would have resulted in a bias due to such factors.

Exposure to environmental factors that may influence the clinical characteristics of MS, as well as other potential confounders such as socioeconomic status that were not controlled, potentially could be assessed by a prospective design. Although a prospectively gathered MS cohort is problematic because of the slow evolution of disability, a prospective study to validate and expand on the observations of this study is being planned.

It is likely that the clinical differences observed between the two groups are explained at least in part by genetic variation. A preliminary whole-genome admixture analysis using polymorphic markers that are highly differentiated in frequency between Europeans and West Africans, and therefore can distinguish chromosomal segments of African from European origin, has been completed in this population.[20,22] Here, we defined African ancestry as the proportion of a person's genome that derived from West African ancestors. African ethnicity was quantified by genotyping markers that are highly informative about ancestry, that is, markers whose frequencies significantly differ between Europeans and West Africans. When applied to this cohort, the results suggest that approximately 79% of the composite ancestry in the AA cohort is African and 21% is European in origin. In addition, the human leukocyte antigen (HLA) allele *DRB1*1501*, long known to be associated with CA MS, was also associated with AA MS in this cohort, as was the closely related African HLA gene termed *DRB1*1503*.[20] The presence of the *DRB1*1501* allele in AA suggests that admixture with Northern European chromosomes contributes to MS susceptibility; however, the finding of a second MS susceptibility allele (*DRB*1503*), uniquely African in origin, indicates that MS susceptibility in this population is not entirely due to admixture with Northern European chromosomes. Genetic admixture studies represent a novel approach for the discovery of genes that contribute to disease susceptibility or modify its expression, especially for diseases such as MS in which ethnically determined differences in prevalence exist.[20,22] For example, it is possible that MS susceptibility genes can be identified on chromosomal regions in AA subjects that are Caucasian in origin, whereas modifiers that worsen disease severity or produce opticospinal symptoms might conversely be located within chromosomal regions of African origin.

It is important to recognize that the clinical manifestations of MS in AA patients differ somewhat from those in CAs and that these differences are likely to be biologically based. AA patients with MS are at high risk for disability; thus, early initiation of treatment seems prudent. However, the benefits of disease-modifying therapies may also differ between AA and CA populations. In this regard, an exploratory analysis suggested that AA MS patients did not respond to interferon β-1a as well as their CA counterparts.[45] Interestingly, the response to α-interferon may also be less robust in AA patients treated for chronic hepatitis C infection.[46] These data support the need for additional studies to define treatment responses to interferon as well as other approved therapies in AA MS patients. Differences in treatment response between ethnic groups might be explained by genetic variation at relevant loci, such as the type 1 interferon receptor or downstream targets.

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