RESEARCH ARTICLE

Factors Contributing to Institutionalization in Patients with Huntington's Disease

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ABSTRACT: The objective of this study was to determine which factors are predictive of institutionalization in Huntington's disease. Seven hundred and ninety-nine subjects with 4313 examinations from the Baltimore Huntington's Disease Center were included in the data set; 88 of these patients with an average follow-up time of 9.2 years went from living at home to being institutionalized while being observed in our clinic. We examined demographic, genetic, and clinical variables for a relationship with institutionalization using linear regressions, a Cox proportional hazards model, and χ^2 or *t* tests in certain cases. In our linear models, scores on the Quantified Neurologic Examination ($R^2 = 0.203$, $P < .001$), Huntington's disease Activities of Daily Living Scale ($R^2 = 0.259$, $P < .001$), and Motor Impairment Score ($R^2 = 0.173$, $P < .001$) were found to have the strongest correlation with time until institutionalization. In addition, CAG repeat length ($R^2 = 0.248$, $P < .001$) was significantly associated with disease duration at institutionalization, when controlling for age at onset. In the Cox proportional hazards model, scores on the Activities of Daily Living Scale, Mini–Mental State Examination, Quantified Neurologic Examination, and Motor Impairment Score all significantly predicted placement in long-term care. Finally, institutionalized patients were shown to have a higher CAG number and a lower level of educational attainment than patients who avoided institutionalization for at least 15 years after disease onset. Neurologic findings, functional capacity, cognitive impairment, and CAG repeat length are all likely determinants of institutionalization. In contrast with other dementing conditions like Parkinson's and Alzheimer's, psychiatric symptoms were not shown to predict institutionalization in Huntington's disease. This may illustrate the especially debilitating nature of the movement disorder of Huntington's disease in comparison with the other dementias.

Key Words: Huntington's disease; institutionalization; progression

Huntington's disease (HD) is an inherited neurodegenerative condition resulting from an expanded CAG triplet repeat on chromosome 4.[1,2] Progression is inexorable, and the resulting movement disorder, cognitive decline, and behavioral difficulties lead to worsening functional impairment, so that affected individuals may eventually become entirely dependent on others. As a result, a significant number of HD patients require permanent institutionalization. This may impose a severe burden on patients and families, particularly because HD patients are often no older than middle-aged at the time of institutionalization and consequently lack the savings, adult children, and government-sponsored health benefits of older patients with common forms of dementia such as Alzheimer's disease.

Although institutionalization represents a significant event in the course of illness of HD, literature on this topic is relatively scarce. A 1996 retrospective study conducted by Nance and colleagues of 97 HD patients in long-term care found that the average newly institutionalized patient was approximately 45 years old, of either sex, not currently married, a high school graduate, and affected with HD for 10 years.[3] In this study, HD patients were likely to remain in long-term care until their death. In 2003, Wheelock et al specifically examined factors contributing to institutionalization and found that motor symptoms, but not

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psychiatric or behavioral symptoms, were predictive of institutionalization.[4]

In this retrospective study we examined a cohort of 799 HD patients, 88 of whose transitions from living at home to being institutionalized were observed while being followed in our clinic. We investigated both clinical (activities of daily living, neurologic score, etc.) and fixed demographic and genetic variables (sex, CAG number, etc.) to determine which, if any, were predictive of institutionalization. We hypothesized that a higher CAG number would be associated with a shorter time to institutionalization and that cognitive impairment, motor symptoms, and psychiatric problems would be associated with time to institutionalization. To test these hypotheses, we conducted 3 types of analysis. Linear models were employed on our institutionalized cohort to identify variables correlated with time until institutionalization. Next, a survival analysis was performed on the entire cohort using a Cox proportional hazards model. Finally, a subset of community-dwelling patients with disease durations of 15 or more years (well beyond the median time to institutionalization of 12 years) was compared with the institutionalized cohort on various demographic variables.

Patients and Methods

The Baltimore Huntington's Disease Center has been following a large number of HD patients prospectively since 1977, using standard neurologic, cognitive, functional, and psychiatric measures. At the time of analysis, the electronic database included 5297 examinations of 1434 individuals. For our analyses, a data set was created by querying the electronic database for a subset of patients who had been examined in the clinic and then had subsequent examinations recorded in a long-term care facility or who had both home and long-term care addresses recorded in the database. Paper charts were then reviewed to make sure that the transitions to long-term care did in fact take place while the patients were being followed in our program and to ascertain the date of institutionalization precisely to within 1 month and the type of institutional setting. Eighty-eight patients with 625 exam records met these criteria, and 1 was excluded because institutionalization took place for psychiatric reasons before the onset of motor symptoms. Seven hundred and twelve contemporaneous patients with 3688 exam records and having no record of being institutionalized served as a comparison group.

For the first, linear analysis, only the institutionalized cohort was examined. Using the program PASW Statistics (SPSS) 18, a series of baseline demographic and genetic variables were regressed linearly onto disease duration at time of institutionalization, that is, the time elapsed between disease onset and institutionalization. These variables included CAG number, age at onset, and age at institutionalization. A *t* test was used to determine whether these measures varied significantly with race and sex.

A series of cross-sectional clinical variables were also regressed linearly on the remaining time to institutionalization from the point of the examination. These variables included the Quantified Neurological Examination (QNE) score,[5] the Mini–Mental State Examination (MMSE) score,[6] the HD Activities of Daily Living Scale,[7] the Hamilton Depression Scale,[8] the HD Irritability and Apathy scales used in our clinic (unpublished), weight loss in the previous 6 months, age at time of exam, and frequency of swallowing difficulties on a scale of 0–4 (hereafter referred to as choke). A *t* test was used to measure the significance of the occurrence of falls in the 6 months prior to examination. The QNE is an instrument for quantifying the number and severity of neurologic findings in HD. Factor analysis of the QNE items has revealed 3 subscales of internally correlated items: an eye movement subscale, a measurement of chorea, and a scale that contains largely measures of voluntary movements such as fine motor control and gait, called the Motor Impairment Score (MIS).[5] The MIS, in particular, has been shown to be highly correlated with functional impairment and with the degree of neuropathological degradation at autopsy,[7,9] and it was also included in our analyses. Unlike MIS, chorea is a poor indicator of disease severity,[10] but it was included in our analyses because severe chorea may increase the difficulty of at-home caregiving and because motor symptoms have been shown to promote institutionalization in previous studies.[4] The HD Activities of Daily Living Scale (ADL) scale resembles the widely used Total Functional Capacity scale of Shoulson and Fahn,[11] now incorporated into the Unified Huntington's Disease Rating Scale.[12] It consists of 18 items scored from 0 (no impairment) to 3 (severe impairment), for a maximum total score of 54. The ADL score was determined by a questionnaire completed by each subject's caregiver, spouse, or close relative. Only data from exams after disease onset but prior to institutionalization were used.

For the survival analysis, a Cox proportional hazards model was performed on the entire cohort. Variables included in this analysis were QNE, MIS, ADL, and MMSE. The Cox model was also used to simultaneously examine QNE, ADL, and MMSE in a stepwise manner.

Finally, we sought to identify special characteristics of individuals who managed to avoid institutionalization. Noninstitutionalized patients with exam records at disease durations of at least 15 years (hereafter referred to as long-survivors) were compared with our

TABLE 1. Institutionalized cohort

Characteristic	n (%) or mean (SD)
Number of patients	88
Sex	
Male	46 (52%)
Female	42 (48%)
Race	
Black	20 (23%)
White	68 (77%)
Type of facility	
Nursing home	59 (67%)
Psychiatric	8 (9%)
VA hospital	3 (3%)
Assisted living	5 (6%)
Multiple types	13 (15%)
Age at onset	35.4 (14.5)
Age at institutionalization	47.8 (14.7)
Disease duration at institutionalization	12.6 (7.2)
Length of follow-up	9.2 (6.0)
CAG number	49.1 (7.3)

institutionalized cohort on the basis of sex, race, educational attainment, number of children, CAG number, age at onset, and average age at time of examination. The χ^2 test was used to determine whether sex and race varied significantly between the 2 groups, and *t* tests were used to examine the differences between groups in educational attainment, number of children, CAG number, and age at onset. Using exam data, MIS scores of the 2 groups were compared using the exam closest to 6 years of disease duration (approximately half the mean disease duration at time of institutionalization). Patients with no records within 2 years of this disease duration were excluded from this analysis.

Results

Table 1 shows the composition of our institutionalized cohort. Among the institutionalized cohort, sex was not significantly associated with either CAG number, age at onset, or disease duration at time of institutionalization. Blacks had a lower mean age at onset than whites, 27.70 (SD 2.25) versus 37.63 (SD 1.181), and this was statistically significant ($P = .002$). Blacks also had a higher mean CAG repeat length than whites (51.10 vs 48.51) but a higher mean disease duration at time of institutionalization (15.30 vs 11.81), although neither difference was statistically significant. There was also some indication that blacks had more severe symptoms at baseline and at time of institutionalization than whites. At baseline (disease duration of 0–2 years), blacks had higher mean MIS (mean difference = 2.49, $P = .019$), QNE (mean difference = 8.20, $P = .03$), and ADL (mean difference = 6.62, $P = .003$) scores than whites. When comparing test scores within 1 year of institutionalization, blacks had higher mean QNE scores (mean difference = 10.44, $P = .045$). Other clinical variables were on the margin of statistical significance.

TABLE 2. Linear models of clinical correlates with time to institutionalization from exam

Variable	*R*	R^2	*df*	*F*	*P* value
QNE	−0.451	0.203	299	76.1	<.001
Chorea	−0.375	0.141	341	55.7	<.001
MIS	−0.416	0.173	338	70.6	<.001
ADL	−0.509	0.259	242	84.1	<.001
MMSE	0.202	0.041	318	13.4	<.001
Hamilton Depression	−0.121	0.015	170	2.5	0.113
Irritability	0.008	0.000	180	0.011	.915
Apathy	−0.195	0.038	181	7.1	0.008
Weight loss	0.029	0.001	281	0.228	.634
Choke	−0.175	0.031	247	7.8	.006
Age at exam	−0.130	0.017	390	6.7	.010

Neither age at onset ($R = -0.196$, $P = .067$) nor CAG number ($R = -0.206$, $P = .055$) alone were significantly correlated with disease duration at time of institutionalization. However, when controlling for age at onset, CAG number was significantly associated with disease duration at time of institutionalization ($R = -0.498$, $P < .001$).

Table 2 details the results of linear analyses performed on our institutionalized cohort. Figure 1 shows a scatter plot of ADL versus time until institutionalization from exam with a best-fit line. A *t* test on the recent occurrence of falls was suggestive ($P = .052$), but not conclusive, of an association with time until institutionalization.

Results of the survival analysis are shown in Table 3. The hazard ratio represents the change in hazard per unit increase of covariate. For example, with a 1-unit increase in QNE, a patient's risk of institutionalization went up by 1.033, or 3.3%, for a given disease duration. In a stepwise model of QNE, ADL, and MMSE,

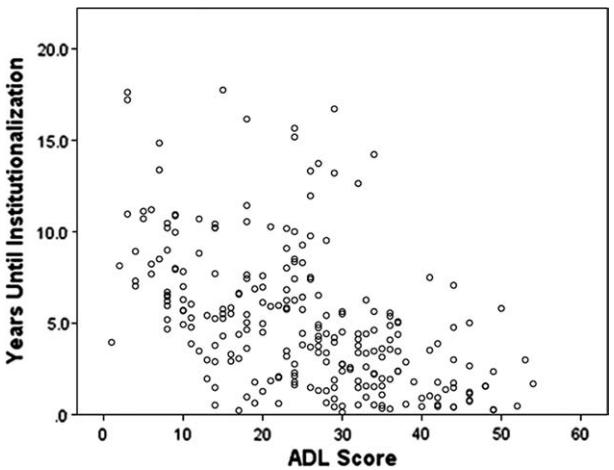

FIG. 1. Correlation of Activities of Daily Living score with time until institutionalization from date of exam.

TABLE 3. Predictors of institutionalization (Cox proportional hazards model)

Variable	Hazard ratio	Significance
QNE	1.033	<.001
MIS	1.046	<.001
ADL	1.084	<.001
MMSE	0.960	<.001

only ADL was left in the model, with a hazard ratio of 1.095 ($P < .001$).

Table 4 presents the results of the comparison between long-survivors and the institutionalized cohort. The institutionalized cohort was found to have a lower mean education attainment (11.4 vs 13.0, $P = .002$) and a higher mean CAG number (49.1 vs 45.0, $P < .001$) than the long-survivors. The data also suggested that the institutionalized cohort had a higher composition of blacks than did the long-survivors (23% vs 14%, $P = .063$). We obtained nearly identical results when excluding subjects in psychiatric facilities from this last analysis (as well as the linear models).

Discussion

Our results hint at the effects of the aging process itself on outcomes in HD, which has become apparent in recent studies.[13] By itself, CAG repeat length was not associated with disease duration at time of institutionalization; however, when controlling for age at onset, CAG repeat length was found to explain 21% of the variation in disease duration at time of institutionalization. This probably reflects the competing effects of aging and CAG number; although a low CAG number leads to slower disease progression, the corresponding delayed age at onset and the natural effects of aging unrelated to HD are likely to promote institutionalization. This is consistent with previous studies on CAG repeat length and disease progression,[14] as well as similar but still unpublished findings of our own.

We also uncovered some notable racial differences. In our institutionalized cohort, blacks had a lower age at onset and a higher CAG number than did whites; however, blacks also had a higher mean disease duration at time of institutionalization. We believe this is because of cultural or socioeconomic factors that make blacks less likely to become institutionalized. It is also conceivable that this is a result of younger age masking the effects of a higher CAG repeat length, as discussed previously. Blacks also displayed more severe symptoms both at disease onset and at time of institutionalization. Because previous studies have not shown any phenotypic differences between blacks and whites in HD, this suggests that socioeconomic and cultural factors may lead to delayed diagnosis and also later institutionalization in blacks.

In our linear models and Cox proportional hazards model, QNE, ADL, and MIS scores were shown to be the greatest statistical determinants of institutionalization; MMSE and chorea scores offered additional predictive value. Our findings about QNE, MIS, and chorea, which all measure motor dysfunction, are consistent with the Wheelock study, which demonstrated that motor symptoms were predictors of nursing home placement. The links between functional capacity (ADL) or cognitive impairment (MMSE) and institutionalization have not previously been systematically examined in HD; however, our findings are echoed by literature on institutionalization in the general elderly population.[14,15]

The absence of an association between institutionalization and Hamilton Depression, Irritability, and Apathy scores is consistent with Wheelock's findings that psychiatric symptoms did not predict nursing home placement in persons with HD. This result differs from findings that psychiatric symptoms promote institutionalization in other dementing conditions like Alzheimer's disease (AD) and Parkinson's disease.[16,17] This finding may reflect a shortage of data or the debilitating nature of the movement disorder of HD.

TABLE 4. Institutionalized cohort versus long-survivors

Characteristic	Institutionalized cohort	Long-survivors	Method	*P* value
Sex			χ^2	.491
Male, n (%)	42 (48%)	95 (52%)		
Female, n (%)	46 (52%)	87 (48%)		
Race			χ^2	.063
Black, n (%)	20 (23%)	25 (14%)		
White, n (%)	68 (77%)	157 (86%)		
CAG number, mean (SD)	49.1 (7.3)	45.0 (4.2)	*t* test	<.001
Age at onset, mean (SD)	35.4 (14.5)	38.3 (12.0)	*t* test	.087
Education, mean (SD, n)	11.4 (3.4, 76)	13.0 (3.7, 152)	*t* test	.002
Children, mean (SD, n)	0.5 (0.6, 4)	2.07 (1.7, 29)	*t* test	.075
Age at exam, mean (SD, n)	46.9 (14.4, 626)	52.0 (13.5, 1508)	*t* test	<.001
MIS, mean (SD, n)	12.5 (4.3, 41)	6.9 (4.3, 54)	*t* test	<.001

In a stepwise Cox model of ADL, QNE, and MMSE, only ADL was left in the equation. This suggests that the variation in time to institutionalization explained by QNE and MMSE is also explained by ADL. This conclusion is supported by previous findings of ours that demonstrate a high degree of colinearity between these variables.[9] ADL has moderately enhanced predictive value in this stepwise model (1.095 vs 1.081), which probably reflects the exclusion of cases with missing variables.

In our comparison of long-survivors to institutionalized individuals, we found that individuals in long-term care had on average fewer years of education and a higher CAG number than did long-survivors. Educational differences may indicate socioeconomic factors such as the ability of a spouse to take a leave of absence from work to care for the affected individual or the means to afford household care. The difference in CAG repeat length is supported by analysis in the present study showing that CAG promoted institutionalization when controlling for age at onset. The discrepancy in MIS supports the results of our linear and Cox proportional hazards models and suggests that motor impairment may predict institutionalization several years before the actual event.

Some important differences between the Wheelock study and ours should be noted. The average length of follow-up in our study was longer than that in the Wheelock study (9.2 $\pm$ 6.0 vs 1.89 $\pm$ 1.2 years), and our cohort included individuals in nursing homes, VA hospitals, psychiatric facilities, or some combination of these rather than exclusively skilled nursing facilities. However, our data on psychiatric symptoms were less comprehensive than those of Wheelock.

There are a number of limitations of this study. Our data set contained no information on caregivers. In previous studies of other dementing conditions, caregiver stress has been shown to be predictive of placement in long-term care.[18] Further, the retrospective nature of this study, based on chart review, might have caused us to miss cases in a systematic way. For example, high caregiver stress may have been associated with a high dropout of follow-up because patients are dependent on caregivers to bring them to the clinic. Our data set also suffered from a lack of detailed information at the precise time of institutionalization. Finally, of 799 subjects, 287 were lost to follow-up as dropouts and 92 individuals were lost due to early death (death before disease duration of 15 years). Subjects lost to follow-up did not differ significantly from the rest of the cohort in CAG repeat length, age at onset, or sex distribution. However, there was a higher proportion of whites among subjects lost to follow-up (90% white vs 10% black, $P = 0.037$). This may have been a result of the strong ties that our clinic has maintained with a few very large pedigrees of black participants.

To the best of our knowledge, only 1 previous study was undertaken that specifically analyzed predictors of institutionalization in HD. We have confirmed its findings that motor symptoms predict placement in long-term care. We have also established CAG repeat length, cognitive impairment, and functional ability as predictors of institutionalization. These represent novel findings. Although at present only symptomatic therapies are available for HD, targeted treatment strategies intended to delay institutionalization may be of value to HD patients, their families, and health care practitioners. Our study adds to the limited body of knowledge about institutionalization in HD and may help direct such treatment strategies.

In contrast to the dementias, in HD physical factors seem to be the main contributor to institutionalization. This could reflect that HD creates more severe physical symptoms than other more purely dementing conditions like AD or that HD patients, who commonly have behavioral issues, do not show enough variation in behavior for this to be the main determinant of institutionalization. In the present study, we compared HD patients with each other, but behavioral symptoms might be highly correlated with institutionalization when comparing HD patients with AD patients for example. To improve contemporaneous data at the time of institutionalization, a future study might involve a survey or questionnaire asking about the current condition of the patient and the reasons for the move to be filled out at the time a patient enters long-term care. ■

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