Title

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MEDICARE EXPENDITURE CORRELATES OF ATROPHY AND CEREBROVASCULAR DISEASE IN OLDER ADULTS

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Abstract

Background/Study Context—Magnetic resonance imaging (MRI) markers of cerebrovascular disease and atrophy are common in older adults and are associated with cognitive and medical burden. However, the extent to which they are related to health care expenditures has not been examined. We studied whether increased Medicare expenditures were associated with brain markers of atrophy and cerebrovascular disease in older adults.

Methods—A subset of participants ($n = 592$; mean age = 80 years; 66% women) from the Washington Heights Inwood Columbia Aging Project (WHICAP), a community-based observational study of aging in upper Manhattan, received high-resolution MRI and had Medicare expenditure data on file. We examined the relationship of common markers of cerebrovascular disease (i.e., white hyperintensities and presence of infarcts) and atrophy (i.e., whole brain and hippocampal volume) with Medicare expenditure data averaged over a 10-year period. Main outcome measures were (a) mean Medicare payment per year across the 10-year interval; (b) mean payment for outpatient care per year; and (c) mean payment for inpatient care per year of visit. In addition, we calculated the ratio of mean inpatient spending to mean outpatient spending as well as the ratio of mean inpatient spending to mean total Medicare spending.

Results—Increased Medicare spending was associated with higher white matter hyperintensity volume, presence of cerebral infarcts, and smaller total brain volume. When examining specific components of Medicare expenditures, we found that inpatient spending was strongly associated with white matter hyperintensity volume and that increased ratios of inpatient to outpatient and inpatient to total spending were associated with infarcts.

Conclusion—Medicare costs are related to common markers of "silent" cerebrovascular disease and atrophy.

Structural changes are ubiquitous in the aging brain. Using high-resolution structural magnetic resonance imaging (MRI), these changes can be quantified and classified as markers of atrophy and of small- and large-vessel cerebrovascular disease. Atrophic changes include widespread decreases in volume and ventricular expansion (Fox & Schott, 2004; Good et al., 2001), thought to reflect nonspecific tissue loss due to the aging process (Nugent et al., 2014). Atrophy in medial temporal lobe regions, including the hippocampal formation and entorhinal cortex, are more specifically related to neurodegenerative changes due to Alzheimer's disease (AD)(Jack et al., 1997). White matter hyper-intensities (WMHs), or increased signal on T2-weighted MRI scans, and focal infarction reflect small- and large-vessel cerebrovascular disease, respectively.

It is well documented that MRI-derived age-associated atrophic and cerebrovascular markers are strongly related to several clinical outcomes. For example, global atrophy correlates with cognitive decline (Raz & Rodrigue, 2006); atrophy in medial temporal lobe structures is associated with increased risk for AD and the severity of symptoms in AD, increasing proportionately with the progression of the disease (Dukart et al., 2013; Jack et al., 1997). Small- and large-vessel cerebrovascular disease is related to cognitive, emotional, and motoric functions (Alexopoulos et al., 1997; Meier et al., 2014; Prins & Scheltens, 2015; Silbert, Nelson, Howieson, Moore, & Kaye, 2008; Willey et al., 2013) and to risk for stroke,

mild cognitive impairment (MCI), dementia including AD, and death (Breteler, 2000; Brickman et al., 2012; Debette et al., 2010; Helzner et al., 2009; Zhu et al., 2014).

Despite the known clinical and functional correlates of MRI-derived markers of brain aging, their financial costs are poorly understood. The examination of health care–related expenditures is one critical way in which the economic burden can be defined operationally. Previous studies, for example, examined the extent to which Alzheimer's disease and related dementias (ADRDs) incur Medicare costs for patients in late life (Bynum et al., 2004; Gilden, Kubisiak, Sarsour, & Hunter, 2015) and found that Medicare expenditures for dementia patients are as much as 3 times more than for nondemented patients. Other studies suggested that these costs are comparable to the financial burden of heart disease and cancer in the United States (Hurd, Martorell, Delavande, Mullen, & Langa, 2013). To our knowledge, the relationship of Medicare expenditures with common MRI markers of age-associated atrophic and cerebrovascular changes has not been examined systematically.

The purpose of this study was to better understand the costs associated with cerebral aging. We acquired high-resolution MRI scans among a large group of community-dwelling adults who were all Medicare beneficiaries and examined the extent to which atrophic and cerebrovascular markers relate to Medicare costs averaged over a 10-year period. We hypothesized that common age-related markers of atrophy and of small- and large-vessel cerebrovascular disease would be related to Medicare health care costs.

MATERIALS AND METHODS

Subjects

Participants came from the Washington Heights-Inwood Columbia Aging Project (WHICAP), a longitudinal study of a multiethnic cohort of Medicare-eligible residents from northern Manhattan. Recruitment and assessment procedures have been described previously (Tang et al., 2001). Briefly, lists of all Medicare or Medicaid recipients in the northern Manhattan catchment area were obtained from the Centers for Medicare & Medicaid Services (CMS), previously known as the Health Care Financing Administration (HCFA) until 2001. Recruitment efforts focused on equal representation of the three primary racial/ethnic groups that populate the catchment area, including non-Hispanic white, non-Hispanic black, and Hispanic (primarily from the Caribbean). Participants in the current study were recruited in two waves, beginning in 1992 and 1999. Longitudinal follow-up evaluations occur every 18 to 24 months and include comprehensive demographic, historical, medical, and neuropsychological assessments (Tang et al., 2001).

Magnetic Resonance Imaging

Between 2005 and 2007, high-resolution structural MRI data were acquired in 769 active participants (see Brickman et al., 2008, for detail). Recruitment strategy for the MRI substudy focused on nondemented participants, although 52 individuals meeting criteria for dementia at the follow-up visit closest to the MRI scan were included in the MRI substudy. Participants were scanned on a 1.5-T Philips Intera scanner (Brickman et al., 2008). T1-weighted (TR = 20 ms, TE = 2.1 ms, field of view [FOV] 240 cm, 256×160 matrix, 1.3 mm

slice thickness) and T2-weighted fluid attenuated inversion recovery (FLAIR; TR = 11,000 ms, TE = 144.0 ms, inversion time = 2800, FOV 25 cm, 2 nex, 256 × 192 matrix with 3 mm slice thickness) images were acquired in the axial orientation. Markers of regional atrophy were derived with FreeSurfer Version 5.1 (http://surfer.nmr.mgh.harvard.edu); we focused on total hippocampal volume and total brain volume. Cerebrovascular markers included presence of brain infarction and total volume. Lesions (signal void) greater than or equal to 3 mm on T2-weighted images with accompanying cerebrospinal fluid density on the T1-weighted image were considered infarcts, as previously described in greater detail (Blum et al., 2012). White matter hyperintensities were derived with in-house-developed software (Brickman et al., 2012, 2011). Briefly, a Gaussian curve was fit to map the voxel intensity values on the FLAIR images and a study-specific intensity threshold was derived to label voxels appearing as hyperintense. Labeled voxel values were multiplied by voxel dimensions and summed to yield total volumes in cm^3. White matter hyperintensity volumes were log transformed for statistical analysis.

Medicare Expenditures

Data from participants in the WHICAP study were matched to a Medicare Beneficiary Summary file from 1 January 1999 to 31 December 2010, using participant social security numbers and Medicare beneficiary ID. Detailed information about Medicare expenditure was obtained from Medicare claims, as described previously (Zhu et al., 2014). We focused on the following Medicare expenditure variables: (a) mean Medicare payment per year across the 10-year interval; (b) mean payment for outpatient care per year; and (c) mean payment for inpatient care per year of visit. Years in which participants were enrolled in Medicare fee-for-service for fewer than 6 months were excluded from the analyses (Zhu et al., 2014). Other costs, for example, costs related to skilled nursing home health, durable medical equipment, and hospice, were not considered separately but did contribute to mean total Medicare expenditures per year. We considered inpatient and outpatient spending separately because of the greater costs associated with hospital (i.e., inpatient) stays and the possibility that increased inpatient resource utilization may reflect greater overall morbidity that might manifest in more severe cerebrovascular and atrophic markers. As such, we calculated the ratio of mean inpatient spending to mean outpatient spending as well as the ratio of mean inpatient spending to mean total Medicare spending. The purpose of calculating these ratios was to examine the proportion of total Medicare spending that was devoted to inpatient resources.

Other Relevant Variables

Participant sex, age, education, and race/ethnicity volume were considered in all the analyses. Race/ethnicity was determined by self-reported responses using 1990 US Census format and grouped into non-Hispanic white, non-Hispanic black, and Hispanic; for statistical analyses, these variables were "dummy coded" with non-Hispanic white as the reference. Total intracranial volume and the presence or absence of diagnosis of dementia at the time of the MRI scan were also considered.

For secondary analyses, we also considered comorbid medical conditions by calculating a modified Charlson index of comorbidity at the time of the scan (Charlson et al., 2008). By

including the Charlson index as an additional covariate in the follow-up analyses, we could assess the extent to which our primary observations were mediated by or independent of major medical morbidity. The comorbidities were calculated based on assessments conducted at the clinical follow-up visit closest to the MRI scan and included myocardial infarct, congestive heart failure (CHF), peripheral vascular disease, hypertension, chronic obstructive pulmonary disease (COPD), arthritis, gastrointestinal disease, mild liver disease, diabetes, and renal disease. These medical conditions were ascertained via self-report during a medical interview, which surveyed participants on diagnostic histories and medication prescriptions (Manly et al., 2005). All items received weights of 1 if present and 0 if not, with the exception of chronic renal disease, which was given a weight of 2. The variables were summed to yield a single Charlson index score reflecting the overall burden of medical comorbidity.

Statistical Analyses

Separate linear regression analyses were performed to examine the relationship between the MRI variables and Medicare expenditure data, including mean total spending, mean inpatient spending, mean outpatient spending, ratio of inpatient to outpatient spending, and ratio of inpatient to total spending. We performed separate analyses for cerebrovascular and atrophic imaging independent variables. White matter hyperintensity volume and presence of infarct were considered cerebrovascular predictors, whereas total brain volume and total hippocampal volume represented atrophy predictors. Age, sex, education, race/ethnicity, intracranial volume, and diagnosis of dementia were additional predictors in all models. The analyses were repeated with the Charlson index score as an additional covariate. We also limited the expenditure data to the year closest to the MRI scan and repeated the analyses for total Medicare spending. For example, if the MRI scan was obtained on 7 July 2007, we selected the Medicare data corresponding to 2007. If Medicare data were not available for the same year of scanning, we selected the closest year before or after the year of MRI scan. In 82% of the cases, Medicare data from the same year of MRI scan were selected. In 8% of cases, Medicare data were selected from years before the MRI scan (median of 2 years), and in 10% of cases, Medicare data were selected from years after the MRI scan (median of 2 years). Finally, because the distribution of inpatient expenditure data was positively skewed, we examined explicitly whether the general linear model statistical assumption of homoscedasticity was met and confirmed our significant observations with Spearman rank order correlations.

RESULTS

Medicare spending data were available for 592 participants in the MRI substudy; these participants did not differ in terms of age, education, sex, and race/ethnicity from the overall sample with available MRI data ($n = 769$). Demographic characteristics are shown in Table 1. Results from the multiple regression analyses are presented in Tables 2– and 3.

Cerebrovascular Disease

Higher WMH volume was associated with increased total Medicare spending averaged over the 10-year interval and greater average inpatient spending (see Table 2). Individuals with an

infarct had significantly greater total spending. Cerebral infarction did not appear to be differentially associated with inpatient versus outpatient expenditures when the two were considered separately. However, when considering the calculated ratios, individuals with infarcts had greater inpatient expenditures relative to outpatient and relative to total expenditures. Men had greater expenditures for inpatient resources than women. Expenditures for inpatient versus outpatient services were greater for African-Americans than for non-Hispanic whites. A diagnosis of dementia at the time of scan was associated with greater total and inpatient spending. Based on visual inspection of residual variance, the regression models for inpatient spending met the statistical assumption of homoscedasticity, and our primary findings involving inpatient spending were confirmed with Spearman correlation analysis (data not shown).

When we included the Charlson index as a covariate, many of the associations between cerebrovascular disease markers and spending remained significant. Although WMH volume was no longer associated with total Medicare expenditures ($\beta = .079$, $p = .088$), it remained associated with greater inpatient expenditures ($\beta = .098$, $p = .036$). The associations between cerebral infarct and Medicare expenditures remained the same ($\beta = .087$, $p = .043$ for total spending; $\beta = .094$, $p = .044$ for the ratio of inpatient to outpatient spending; and $\beta = .113$, $p = .012$ for the ratio of inpatient to total spending). In terms of the Charlson index itself, higher scores, indicating greater medical burden at the time of MRI scanning, were associated with greater total ($\beta = .285$, $p < .001$), inpatient ($\beta = .230$, $p < .001$), outpatient ($\beta = .207$, $p < .001$) expenditures, and with a greater ratio of inpatient to total spending ($\beta = .192$, $p < .001$). Of note, of the 193 participants with brain infarction detected on MRI scans, only 43 had self-reported history (Reitz et al., 2009) of clinical stroke.

Medicare spending reliably increased over the 10-year follow-up period (data not shown). When we selected total Medicare spending data from the year closest to the date of MRI scan and reran the primary analyses with this value as an outcome measure, as opposed to the averaged spending over the entire interval, the findings were commensurate. That is, WMH volume remained significantly associated with total spending in the year closest to the scan date at a very similar magnitude ($\beta = .102$, $p = .03$) to the mean total spending data over the 10-year interval. In this analysis, the presence of a cerebral infarct and spending was attenuated to nonsignificance but the magnitude of the effect was similar ($\beta = .051$).

Atrophic Factors

Smaller total brain volume, but not hippocampal volume, was associated with increased total Medicare spending and more in outpatient spending (see Table 3). As with our analysis of cerebrovascular factors, men had higher expenditures for inpatient resources and blacks had higher inpatient to outpatient and inpatient to total spending ratios. A diagnosis of dementia was associated with greater total Medicare spending and greater inpatient spending. When we incorporated the Charlson index into our analyses, the significance between total brain volume and total spending of Medicare resources dissipated ($\beta = -.109$, $p = .120$), but the association with outpatient spending remained significant ($\beta = -.150$, $p = .037$). The Charlson index score was associated with greater costs of total ($\beta = .287$, $p < .001$), inpatient ($\beta = .235$, $p < .001$), outpatient ($\beta = .198$, $p < .001$), and inpatient-to-total ($\beta = .$

203, $p < .001$) spending. When we examined the association of our atrophy measures with Medicare spending in the year closest to the scan, total brain volume remained significantly associated with total Medicare spending at a similar magnitude ($\beta = -.033$, $p = .025$).

DISCUSSION

Although previous studies demonstrated the escalating Medicare costs associated with dementia, the extent to which cerebral aging is related to health care spending has been unexamined. This study examined this relationship in a community-dwelling cohort of Medicare beneficiaries who underwent structural MRI. We focused our MRI analysis on two parameters—atrophic and cerebrovascular markers—and related them to Medicare expenditures.

Higher health care expenditures were related to markers of both atrophy and cerebrovascular disease: the presence of infarcts, WMH severity, and decreased total brain volume. Among individuals with infarcts, Medicare expenditures were, on average, $2183 higher per year, than among those without infarcts (unstandardized $\beta = 2183.51$); for every log cm^3 in WMH volume, there was an associated $815 average increase in average annual spending (unstandardized $\beta = 815.78$); and with every cm^3 decrease of total brain volume, there was an associated $18 average increase in total Medicare spending per year. When we delineated how these total expenditures were utilized, greater expenditures on inpatient resources in particular were related to WMHs. Moreover, inpatient costs increased in relation to outpatient spending, and composed a greater share of total Medicare costs, among individuals with infarcts compared with those without infarcts. It should be noted that the correlational nature of the study limits the ability to determine causality or temporal ordering of the observed associations.

Although previous reports have linked clinical strokes with increased medical expenditure (Demaerschalk, Hwang, & Leung, 2010; Taylor et al., 1996), our findings are noteworthy because we examined the association of radiologically determined vascular events and health care expenditure. These radiological phenomena are often considered clinically "silent" because they are not associated with acute and lasting neurological signs and symptoms; indeed, only 22% of participants with radiological infarcts in our sample reported a history of clinical stroke. However, despite not meeting clinically relevant thresholds, radiological abnormalities are in fact associated with health care expenditures, even after controlling for medical burden and diagnosis of dementia. This is the first analysis, to our knowledge, that has related radiologically determined vascular events to medical expenditure data. It sheds light on the relevance of brain injuries, which may not meet clinical thresholds but do seem to be captured by Medicare spending.

Our study examined common markers of cerebral aging and their relationship to Medicare. We wanted to establish that this relationship exists independently of common medical comorbidities, well-established drivers of health care expenditures (Charlson et al., 2008). When we accounted for medical comorbidity, we found some, but not all, of the associations between MRI markers and spending dissipate. The findings suggest that the relationship of cerebrovascular and atrophic markers of brain aging with Medicare expenditure is not fully

mediated by medical morbidity. We speculate that these common markers of brain aging are "quiet" rather than "silent"—they are not fully accounted for by obvious medical morbidity, but they likely still contribute to individual differences in health status and resource utilization. Certainly, the nature of these relationships is difficult to disentangle without longitudinal neuroimaging data and a more mechanistic understanding of disease pathways.

Although there has been scientific inquiry devoted to understanding the mechanisms mediating structural brain changes with the purpose of developing prevention strategies, there has been little done in the way of policy to encourage beneficial behaviors that have impact on brain health. Healthy lifestyle factors can prevent stroke even for individuals who are at high risk (Larsson, Akesson, & Wolk, 2015); physical exercise and a healthy diet confer greater white matter integrity and are associated with reduced WMHs (Gardener et al., 2012; Tseng et al., 2013; Voss et al., 2013); healthy lifestyle contributes to greater hippocampal size (Woodard et al., 2012); and aerobic exercise has been shown to spare total brain atrophy (Colcombe et al., 2006; Erickson, Weinstein, & Lopez, 2012). Making public health a priority on a systemic level is tantamount to avoiding the prohibitive costs of an aging nation.

Of note, several demographic characteristics were associated with higher spending costs. Men had higher inpatient expenditures than women. This observation is counter to consistent findings in the literature that women spend more than men on health care costs in nearly all domains of utilization (Bertakis, Azari, Helms, Callahan, & Robbins, 2000; Owens, 2008). A deeper investigation of this countervailing finding is of interest for future research. Also of note, black participants in our sample utilized a greater share of their total Medicare expenditures on inpatient costs, in particular, when examined in relation to their outpatient spending. It is likely that blacks in our sample are similarly affected by the many systemic forces mediating health disparities between blacks and whites in this country, including geographic segregation, lower socioeconomic position, depleted financial resources, lack of access to and lower quality of health services, and occupational opportunities, and higher allostatic load due to discrimination (Geronimus, Hicken, Keene, & Bound, 2006; Glymour & Manly, 2008). However, more factors would be worth exploring for a comprehensive understanding of what might account for this difference between groups. At the very least, this observation suggests that sociodemographic factors contribute to the determination of how health care spending is allocated.

In sum, our findings suggest that increased health care system costs are associated with measures of vascular brain injury and atrophy in this ethnically diverse community sample. As the size of the older adult population continues to increase, future work should focus on strategies to prevent or delay these age-associated cerebral changes.

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Table 1

Demographic data

Demographic characteristics	Sample of study
N	592
Number of years with Medicare expenditure data, mean (SD)	9.94 (3.01)
Age (at time of scan), mean (SD)	80.56 (5.64)
Sex, % women	66.6
Race/ethnicity (%)[a]	
White/other	30.7
Black	28.7
Hispanic	40.5
WMH volume, mean (SD) (cm^3)[b]	3.85 (6.14)
Infarct, %	32.6
Total brain volume, mean (SD) (cm^3)[c]	870.15 (101.77)
Hippocampus volume, mean (SD) (cm^3)[d]	6.69 (0.95)
Total cranial volume, mean (SD) (cm^3)[e]	1310.14 (156.79)
Charlson index score, mean (SD)[f]	2.69 (1.60)
Average yearly total Medicare spending, mean (SD) (USD)	9282.49 (12340.45)
Average yearly outpatient spending, mean (SD) (USD)	895.55 (1658.22)
Average yearly inpatient spending, mean (SD) (USD)	4475.96 (8603.43)
Any diagnosis of ADRD over the follow-up period, %	31.9

[a,b]Available for $n = 585$.

[c]Available for $n = 565$.

[d,e]Available for $n = 558$.

[f]Available for $n = 572$.

Table 2

Cerebrovascular factors

Predictor	Total spendingβ	Inpatient spendingβ	Outpatient spendingβ	Ratio inpatient/outpatientβ	Ratio inpatient/total spendingβ
WMH volume	.095*	.110*	−.001	.045	.064
Infarct (0 = absent, 1 = present)	.088*	.077	−.003	.091*	.118**
Sex (0 = Male, 1 = Female)	−.083	−.107*	−.063	−.059	−.058
Age at scan	.037	−.006	−.034	−.002	.048
Hispanic	−.114	−.092	−.035	−.021	−.026
Black	−.053	−.033	−.019	.152**	.090
Years of education	−.016	−.025	−.024	.034	−.014
Intracranial volume	−.054	−.052	−.055	.032	.077
Dementia diagnosis	.111*	.124**	.074	−.002	.067

Note. β values are standardized coefficients.

*
p < .05;

**
p < .01.

Table 3

Atrophic factors

Predictor	Total spendingβ	Inpatient spendingβ	Outpatient spendingβ	Ratio inpatient/outpatient spendingβ	Ratio inpatient/total spendingβ
Total brain volume	−.152*	−.089	−.189**	−.116	−.063
Total hippocampus volume	−.003	.004	.014	.016	−.017
Sex (0 = Male, 1 = Female)	−.087	−.108*	−.072	−.056	−.066
Age at scan	.044	.016	−.059	.005	.060
Hispanic	−.108	−.083	−.037	.018	−.025
Black	−.024	.004	−.018	.156**	.104*
Years of education	−.023	−.035	−.016	.032	−.019
Intracranial volume	−.082	.044	.188**	.122	.139
Dementia diagnosis	.097*	.116**	.065	−.003	.061

Note. βvalues are standardized coefficients.

*
$p < .05$;

**
$p < .01$.