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Prevalence of incidental brain MRI findings of clinical relevance in a diverse Hispanic/Latino population

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Abstract

Background and Purpose: There is limited literature on the prevalence of incidental brain MRI findings in the Hispanic/Latino population, despite their increased prevalence of vascular disease and undertreatment of chronic conditions. The purpose of our study was to determine the prevalence of clinically relevant incidental findings on brain MRI examinations obtained as a part of the Study of Latinos–Investigation of NeuroCognitive Aging MRI (SOL-INCA-MRI) study.

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CONFLICTS OF INTEREST

The authors report no conflicts of interest.

Methods: Brain MRI examinations were obtained on 1389 participants in the SOL-INCA-MRI study, a cross-sectional ancillary study of the Hispanic Community Health Study, Study of Latinos, which is a longitudinal, community-based study. Study design of SOL-INCA-MRI involves imaging cognitively normal and participants with mild cognitive impairment. Brain MRI findings were categorized as Level 1 (normal), Level 1.5 (findings of unclear medical significance), Level 2 (potential medical concern), or Level 3 (medically urgent). This article focuses on Level 2 and Level 3 findings.

Results: The average age of the sample was 60.8 years (+/− 10.3 years), 66.1% were females. Level 2 and 3 findings were identified in 117 participants, (8.4%), of which 109 (7.8%) were recommended for medical follow-up (Level 2), and 8 (0.6%) were recommended for immediate medical attention (Level 3). Brain MRI findings consisted of chronic infarction in 33 (2.4%), vascular abnormality in 27 (1.9%), intracranial mass in 20 (1.4%), other intracranial findings in 28 (2.0%), and skull base/extracranial findings in 26 (1.9%) patients.

Conclusion: Incidental findings of clinical relevance were common among SOL-INCA-MRI participants, but rarely required urgent medical intervention.

Keywords

brain MRI; community population study; Hispanic; incidental findings

INTRODUCTION

Incidental imaging findings are defined as an incidentally discovered mass or lesion detected by CT, magnetic resonance imaging (MRI), or other imaging modality performed for an unrelated reason.[1,2] Population-based studies of asymptomatic individuals have shown prevalence of incidental findings on brain MRI between 1.7% and 3.2%, with 0.2–0.5% requiring medical treatment or surgery.[3–9] Two large meta-analyses of incidental findings on brain MRI examinations found prevalence of potentially significant findings between 1.4% and 1.7%.[10,11]

There is limited literature on the prevalence of incidental brain MRI findings in the Hispanic/Latino population, despite their increased prevalence of vascular disease,[12] which would be expected to result in higher incidence of MRI abnormalities. The Hispanic Community Health Study/Study of Latinos (HCHS/SOL) is the most comprehensive study of Hispanic/Latino health and disease in the United States. The Study of Latinos-Investigation of Neuro-Cognitive Aging (SOL-INCA) is an ancillary study to the HCHS/SOL examining neurocognitive performance among HCHS/SOL's middle aged and older Latino subsample (> = 45 years at HCHS/SOL visit 1; 2008–2011).[13]

Characterizing the prevalence and severity of incidental brain imaging findings in the HCHS/SOL population is important not only because of cardiovascular disease (CVD) risk,[14–16] but also due to undertreatment of chronic conditions among Hispanic/Latino individuals.[17–19] In addition, the findings are important for planning of future ancillary studies, to refine consent documents and to plan for participant referrals to clinical care. The

purpose of our study is to determine the prevalence of clinically relevant incidental findings on brain MRI using the existing SOL INCA MRI imaging database obtained to date.

METHODS

Study population

Brain MRI examinations were acquired from a subset of individuals participating in the HCHS/SOL. HCHC/SOL, an ongoing community-based cohort study of self-identifying Hispanic/Latino population, consists of four field centers in or near San Diego, CA; Chicago, IL; the Bronx, NY; and Miami, FL. There is also a coordinating center located at the University of North Carolina, Chapel Hill. HCHS/SOL enrolled n = 16,451 individuals 18–74 years of age at recruitment between 2008 and 2011. Importantly, the HCHS/SOL included a complex design with stratification, clustering, and probability weighting whereby the sampling scheme of the HCHS/SOL allows for generalization of study findings to the target populations of diverse Hispanic/Latinos from these areas. Detailed descriptions of the goals, scope, target population, and sampling design of the HCHS/SOL are published elsewhere.[20,21] The primary goals of the HCHS/SOL are to characterize the prevalence of selected chronic diseases, including CVD, stroke, asthma, chronic obstructive pulmonary disease; the risk and/or protective factors associated with these conditions; and the relationship between initial health profiles and future health events in a cohort of Hispanics and Latinos from diverse heritage groups living in the United States. In addition to the main study, the Study of Latinos, Investigation of Neurocognitive Aging was funded in September of 2015 as an ancillary study to HCHS/SOL. The aims of this HCHS/SOL ancillary study are to evaluate the cognitive performance of individuals ages 50 years and older at HCHS/SOL visit 1 (n = 6377) who also underwent cognitive assessment at visit 1 and returned for a second main study visit (2016–2018). As with the main study, a weighting scheme was also generated for SOL-INCA to ensure that study estimates generalize appropriately to the target of diverse Hispanics/Latinos. A detailed discussion of the SOL-INCA study and its design are published elsewhere.[13] These individuals served as the main source of participants for the SOL-INCA-MRI substudy. Study design of SOL-INCA MRI involves imaging 1200 participants with mild cognitive impairment (MCI) with an additional 1200 cognitively normal participants selected from sex and study site matched nonimpaired sample strata to ensure appropriate representation of males and females and diverse Hispanic/Latino groups relative to the main study. Finally, an additional cohort of 400 younger (≤40 of age at visit 2) participants in HCHS/SOL will also be imaged. As of March 17, 2020, n = 1389 participants had completed MRI and are included in this study.

Cognitive status evaluation

Evaluation of the cognitive status and criteria used to establish MCI are described in our previous publications.[22,23] To summarize, baseline cognitive testing at HCHS/SOL visit 1 (baseline) included only middle-aged and older (45−74 years) participants who were oversampled (n = 9714) in the cohort. The Neurocognitive Reading Center trained and supervised bicultural/bilingual technicians who administered the brief cognitive battery, which included four tests: (1) six-item screener (SIS; mental status);[24] (2) Brief-Spanish English verbal learning test (B-SEVLT; verbal episodic learning and memory); (3) word

fluency (WF);[25] and (4) digit symbol subtest (DSS; processing speed, executive function).[26] SOL-INCA cognitive tests were administered to HCHS/SOL participants who returned for visit 2, which occurred on an average of 7 years after visit 1. We expanded the cognitive battery to derive an MCI research diagnosis based on the National Institute on Aging-Alzheimer's Association (NIA-AA) criteria.[27] In addition to visit 1 tests, we included the Trail Making Test (TMT, parts A&B, executive function) and NIH Toolbox Picture Vocabulary Test (PVT; general premorbid cognitive function), self-reported cognitive decline (Everyday Cognition-12; eCog12), and instrumental activities of daily living (a measure of functional impairment).[28,29] The PVT was used to assess premorbid cognitive function because these scores remain stable with age and in later neurodegenerative stages, and to control for potential educational quality test biases.[30] MCI diagnostic criteria in SOL-INCA were operationalized and implemented to generate four NIA-AA criteria: (1) any cognitive score in the mildly impaired range (i.e., from −1 to −2 SD) compared with SOL-INCA internal robust norms adjusted for age, education, sex, and PVT scores; (2) significant cognitive decline (≥−0.055 SD/year) from visit 1; (3) self-reported cognitive decline (eCog12); and (4) no or minimum functional (instrumental activities of daily living) impairment.[27] Alzheimer's disease (AD) biomarkers (e.g., amyloid β [A β]) were unavailable in the SOL-INCA. We included both cognitive impairment and significant cognitive decline to reduce false positive bias. Participants with severe cognitive impairment (below −2 SD relative to SOL-INCA robust norms and with significant functional impairment) were not included in these MCI prevalence estimates.

Imaging

3T MRI was performed at four Field Centers using GE 3T 750 (three sites) and Philips 3T Achieva TX (one site). MRI sequences included 3D volumetric (high-resolution images, 1 mm isotropic acquisition) T1, fluid-attenuated inversion-recovery, T2, T2*, and arterial spin labeling (ASL) sequences.

Image interpretation

As part of the study design, SOL-INCA MRI examinations were interpreted at each of the four primary sites by a neuroradiologist and categorized as: Level 1 (normal); Level 1.5 (findings of unclear medical significance, e.g., mild cerebral atrophy, mild to moderate nonspecific white matter disease); Level 2 (potential medical concern, e.g., remote stroke, aneurysm, meningioma without local mass effect, and severe parenchymal atrophy on a subjective assessment); and Level 3 (urgent findings, e.g., intracranial mass with local mass effect or midline shift, acute hemorrhage). All image interpretations were electronically transferred to the SOL-INCA-MRI coordinating center at UC Davis where they were reviewed by a neuroradiologist (VI) and a neurologist (CD) to ensure consistency across the sites. Any discrepancies were resolved by consensus of the two reviewers at the coordinating center. Once the site and coordinating center had reviewed the imaging, participants with Level 2 and 3 findings were identified, appropriately informed, and referred for clinical correlation and medical care if needed. In the case of urgent findings either at the site level or the coordinating center, this communication with the site physician and the participant would occur within 24 h. Level 2 and 3 incidental findings are included in the analyses for this study as we felt these represented findings of potential

clinical relevance, based on internally derived guidelines and in line with the published literature.[2–4,6,7,9,31,32] All Level 2 and 3 findings were categorized into the following groups: chronic infarction (e.g., territorial or lacunar infarcts); vascular abnormality (e.g., intracranial aneurysm, arteriovenous malformation [AVM], cavernous venous malformation, and vascular occlusion); intracranial mass (e.g., meningioma, pituitary mass, and brain parenchymal mass); other intracranial findings (all other intracranial findings not listed above); and skull base/extracranial findings. We decided to provide the interim analysis for our study because of the unusually high number of alerts for Level 2 and 3 incidental findings in this relatively young community-based cohort.

Statistical analysis

First, we provide the distribution of Hispanic/Latino groups by sex and report the average age within each background group (Table 1). Second, we calculate and plot the counts and prevalence rates of Level 2 and 3 incidental findings by subtype (Figure 1). Third, we estimate and plot the age distributions of participants with and without Level 2 and 3 incidental findings and calculate and plot the prevalence of females, Hispanic/Latino background groups (Figure 2). We then test differences in mean age (using *t*-test), sex (using Chi-squared test), and background, (using Fisher's exact test). Fourth, we calculate and plot the age distributions and female prevalence for each of the detected incidental finding subtypes (Figure 3). For steps 3 and 4 above, we present age distributions using scatter and box plots, and prevalence estimates using balloon plots. Tabular representation of all estimates is also included in Tables 2 and 3. We collapsed Levels 1 and Level 1.5 findings into one group Level 1. We used a generalized linear model, with a binomial family distribution, to examine the association between level of incidental findings (Level 1, Level 2, and Level 3) and cognitive status adjusting for age and gender. Statistical significance was assessed using two-tailed *p*-values from a Wald test. We used *p*-values less than 0.05 to define statistical significance.

RESULTS

Sample characteristics

One thousand three hundred and eighty-nine participants (66.1% females) with an average age of 60.8 years (+/− 10.3 years) underwent brain MRI. Females were on average older than males (62.6 vs. 60.1; $p<0.01$). Participant demographic characteristics by self-identified Hispanic/Latino background (Table 2) were: 9.6% Dominican, 12.2% Central American, 17.1% Cuban, 32.6% Mexican, 17.1% Puerto Rican, 9% South American, and 2.4% reported other Hispanic/Latino or more than one Hispanic/Latino background.

Level 2 and 3 incidental finding prevalence

A total of 117 participants (8.4%) had at least one incidental finding. Among those, 109 individuals (7.8%) had a Level 2 and 8 (0.6%) had a Level 3 finding. Overall, 116 (8.3%) participants had intracranial, and 26 (1.9%) skull base/extracranial abnormality (Figure 1 and Table 2).

Chronic infarct was present in 33 (2.4%) participants, including 23 (1.7%) with cortical infarct, and 15 (1.1%) with lacunar infarct. Vascular abnormality was identified in 27 (1.9%) participants, including intracranial aneurysm in 14 (1.0%), cavernous venous malformation in 7 (0.5%), decreased/absent large vessel arterial vascular flow voids in 2 (0.1%), and AVM in 1 (0.07%). Intracranial mass was seen in 20 (1.4%) participants, including meningioma in 12 (0.9%), pituitary mass in 8 (0.6%), prepontine mass in 1 (0.07%), and focal cortical dysplasia versus low-grade glioma in 1 (0.07%). Other intracranial findings were identified in 28 (2.0%) participants, including severe Fazekas 3 white matter hyper-intensities in 9 (0.6%), possible demyelination in 7 (0.5%), chronic post-traumatic encephalomalacia in 3 (0.2%), hydrocephalus in 3 (0.2%), severe parenchymal atrophy in 3 (0.2%), and 1 (0.07%) participant each with chronic cerebellar bleed, extensive microbleeds, chronic subdural hygroma, acute on chronic subdural hematoma, and low cerebellar blood flow on ASL.

Skull base/extracranial findings were present in 26 (1.9%) participants, including 6 (0.4%) with severe cervical spine degenerative changes with some cord flattening, 3 (0.2%) with Chiari I malformaion, 3 (0.2%) with parotid mass, 2 (0.1%) with chronic odontoid fracture, 3 (0.2%) with nasopharyngeal lesion, and 1 (0.07%) participant each with cord expansion, cystic skull base lesion, vertebral body lesion, masticator space mass, enlarged lacrimal glands, parapharyngeal mass, chronic ocular bleed, paranasal sinus fungus or mass, and extensive mastoid/middle ear opacification.

Level 3 (urgent) findings included two meningiomas with mass effect on underlying cortex, and one each of the following: brain parenchymal AVM, large intracranial aneurysm (>1.0 cm), pituitary mass with optic pathway compression, acute hemorrhage within a pre-existing chronic subdural hematoma, subacute blood products within a cortical infarct, extensive T2 signal abnormalities at the brainstem and cervical cord.

Age, sex, and background distribution of Level 2 and 3 incidental findings

There was a statistically significant difference in the sex distribution of participants with and without Level 2 or 3 findings. Female participants were more prevalent in the group without (65.6%) compared to those with MRI Level 2 or 3 abnormality (44.4%; $p = 0.012$). Differences in female prevalence (64.6% vs. 45.4%) remained unchanged after age correction. Age difference between the two groups ($\Delta = 1.98$ years), with and without Level 2 and 3 findings, was borderline significant ($p = 0.0466$). Mean age differences remained consistent ($\Delta = 2.27$ years) after correcting for sex. The age distribution of participants by sex and Level 2 and 3 incidental findings are presented in Figure 2. Hispanic/Latino background did not differ between those with and those without Level 2 or 3 findings ($p = 0.14$) (Figure 2 and Table 3).

Age and sex distributions by specific Level 2 or Level 3 findings

Summaries of the age and sex distributions by subtypes of incidental findings are provided in Figure 3. As of the writing of this manuscript, we present sample statistics and avoid inferential comparisons between groups given the evolving nature of the data collection. Descriptively, participants with chronic infarcts and those with intracranial findings were, on average, older than other participants with any other Level 2 or 3 finding. Female

participants were more prevalent in the vascular abnormality subtype. The age distributions by subtypes of incidental findings are provided for males and females in Figure 4.

Level 2 or Level 3 findings according to the degree of cognitive ability

We conducted preliminary analyses to compare the prevalence of incidental findings among 3 levels of cognitive ability: (1) cognitively normal, (2) questionably impaired, and (3) MCI as well as collapsing cognitive ability into normal and possibly impaired. After adjusting for age and gender, we found no differences in prevalence of level 2 or level 3 findings with any comparison. Further, the prevalence of chronic infarcts (likely to be associated with reduced cognitive ability) also did not show a difference between impaired and cognitively normal individuals.

Follow-up

Although $n = 117$ had Level 2 and 3 findings, no participant required hospital admission or immediate intervention.

DISCUSSION

Incidental findings of clinical relevance were common among SOL-INCA-MRI participants, but rarely required urgent medical intervention. There is a wide range of reported prevalence of incidental findings on brain MRI. Prevalence varies with the definition of what constitutes an abnormality, ranging from reporting any finding on brain MRI to reporting only findings that are of potential clinical concern. Choice of MRI scanning protocol also influences the rate of reported abnormalities, with higher rates of abnormalities detected using higher resolution, newer techniques, 4.3% versus 1.7%.[11] The age of the studied individuals similarly affects prevalence and distribution of incidental findings, with studies including older individuals demonstrating higher rates of detected incidental abnormalities.[3,5,31–33] Other factors influencing variability include study design, presence of vascular risk factors in the study population, and whether the study is evaluating asymptomatic versus symptomatic participants. 8.4% of our study population had potentially significant incidental findings, which is higher than what is reported in the published literature, while keeping in mind above mentioned technical heterogeneities between the studies. A large, recent community-based study of non-Latino participants (mean age 64.9 years, older than our population) reported 9.5% overall rate of incidental findings (similar to our rate), and 3.2% rate of referral to further medical evaluation; however, criteria for reporting an abnormality were a bit broader compared to our study (entities not meeting our inclusion criteria, such as arachnoid cyst, intracranial lipoma, fibrous dysplasia, and orbital dermoid cyst, accounted for 18% of the positives).[3] It is important to note that the above studies were predominantly conducted in non-Latino White adults.

Looking at the prevalence of specific abnormalities within Level 2 or Level 3 findings might offer a more accurate comparison between our study and the relevant literature conducted in a predominantly non-Latino White and relatively older age cohorts. Within this context, the rates of incidental findings in our Hispanic/Latino population are within or at the upper range of what was previously reported: 2.4% prevalence of chronic infarcts in our

study population, compared to 1.2–12.0%;[6,7,9,34,35] 1.0% intracranial aneurysms, compared to 0.1–2.3%;[3,4,6–11,31,34,36] 0.9% meningiomas, compared to 0.29–2.5%;[3,4,6–9,11,34,37,38] 0.5% cavernous venous malformations, compared to 0.1–2.4%;[3–7,9,11,31,34,36] 0.6% pituitary masses, compared to 0.1–0.8%;[3–7,9,11,34,36] 0.5% possible demyelination, compared to 0.04–0.4%;[5,11,31,36] 0.2% chronic post-traumatic encephalomalacia, compared to 0.1–0.2%;[31,34,36] 0.2% hydrocephalus, compared to 0.04–0.3%;[5,9,11,34] 0.2% Chiari 1, compared to 0.4–1.0%;[6,11,34] and 1.9% skull base/extracranial lesions, compared to 0.07–1.2%[3,4,34,36] in the literature. Our cohort's rate of potentially significant abnormalities on brain MRI was similar to the rates found in older populations; our participant's average age was 60.8 years, compared with 58–75 years old in the relevant literature.[3,4,6–8,32,34,36–38]

There is variability in the published literature on what is reported as potentially significant incidental findings on brain MRI, suggesting that the list of incidental abnormalities that are reported to participants in research studies and referred for further clinical care could be further refined. For example, in a study on the natural history of asymptomatic, unruptured aneurysms showed a 5-year risk of rupture of 0% for anterior circulation aneurysms <7 mm.[39] In the population-based Rotterdam study, asymptomatic anterior circulation aneurysms <7 mm were not referred for follow-up or medical treatment.[6] Likewise, small, calcified meningiomas at the cerebral convexity in asymptomatic elderly patients might not need any follow-up given their natural history.[40] Second interpretations of head and neck MRI and CT examinations by the experienced radiologists in the Tumor Board setting in tertiary academic setting were shown to change patient management in 38−40% of patients, when compared to the original interpretations by non-specialized general radiologists or neuroradiologists.[41,42] Therefore, a formal review of all extracranial and skull base abnormalities by a dedicated head and neck radiologist might offer value in distinguishing benign from concerning lesions and potentially avoid unnecessary follow-ups. Additionally, findings of chronic post-traumatic encephalomalacia, cavernous venous malformations without evidence of recent hemorrhage, borderline Chiari 1 findings, or cervical spine degenerative changes causing minimal cord flattening in asymptomatic patients, which are often reported as potentially significant incidental findings in the published literature, might not warrant further care or follow-up imaging. We are actively investigating the natural history of these findings in our own work.

To date, SOL-INCA MRI indicates an 8.3% prevalence of potentially significant incidental findings on brain MRI, sufficient to require participant notification of medical importance, in a representative population of Hispanic/Latino individuals. Our cohort's rate of potentially significant abnormalities on brain MRI was similar to the rates found in older populations. Although no MRI report resulted in immediate medical intervention, we believe our review approach and communication procedures benefited participant health by identifying unsuspected medical disorders that could be mitigated. While the prevalence of abnormal findings varies by the population studied as well as the criteria used, the higher prevalence of vascular risk factors, such as diabetes in Hispanic/Latino populations, suggests a consequential increase in asymptomatic cerebrovascular disease.[12]

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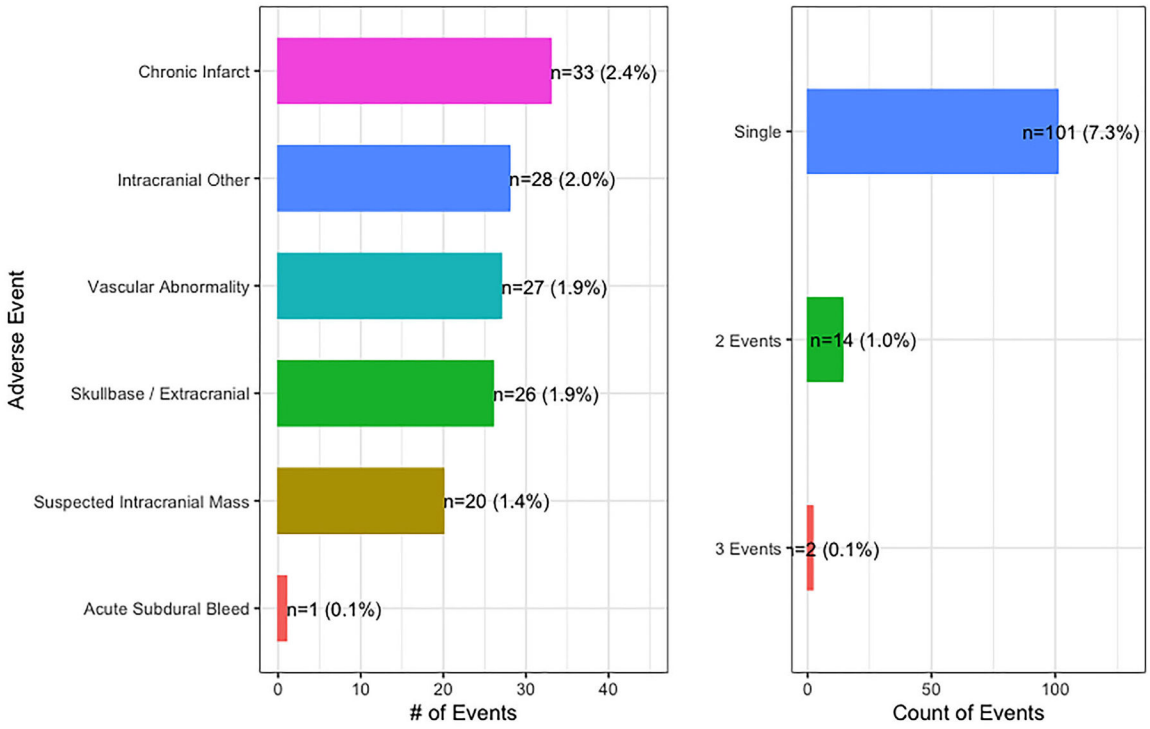

FIGURE 1.

Summary of prevalence rates and counts for Level 2 and Level 3 findings. Abbreviation, *n*, number

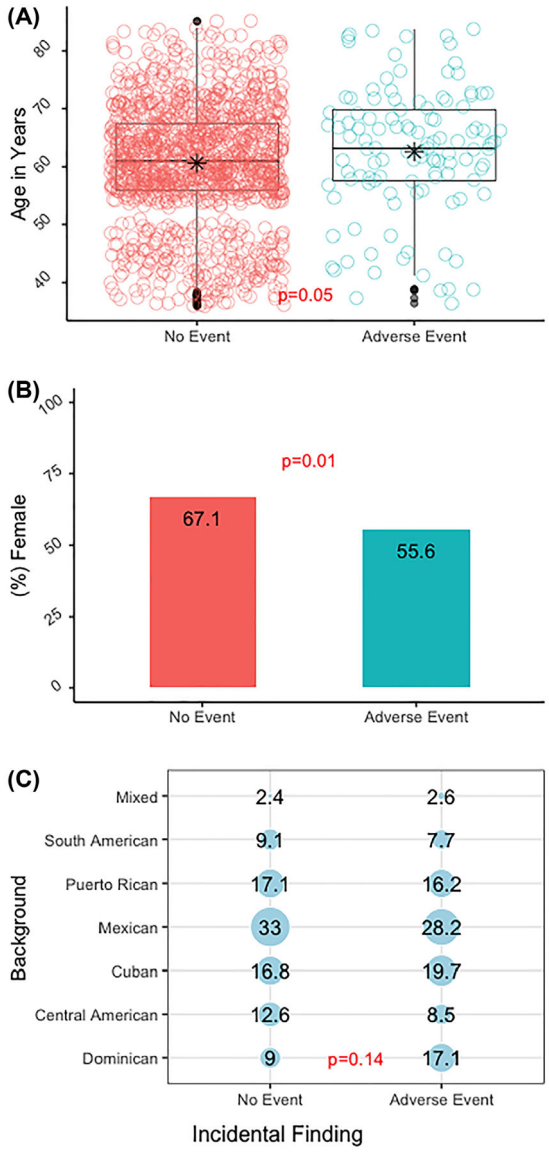

FIGURE 2.

Age, sex, and background with and without Level 2 or Level 3 incidental findings. Panel A is a boxplot representing the age distributions for individuals with (color green) and without (color red) Level 2 and Level 3 brain MRI findings. Panels B and C are bar and balloon plots representing the prevalence of females and Latino backgrounds, respectively, in participants with and without Level 2 or Level 3 incidental findings

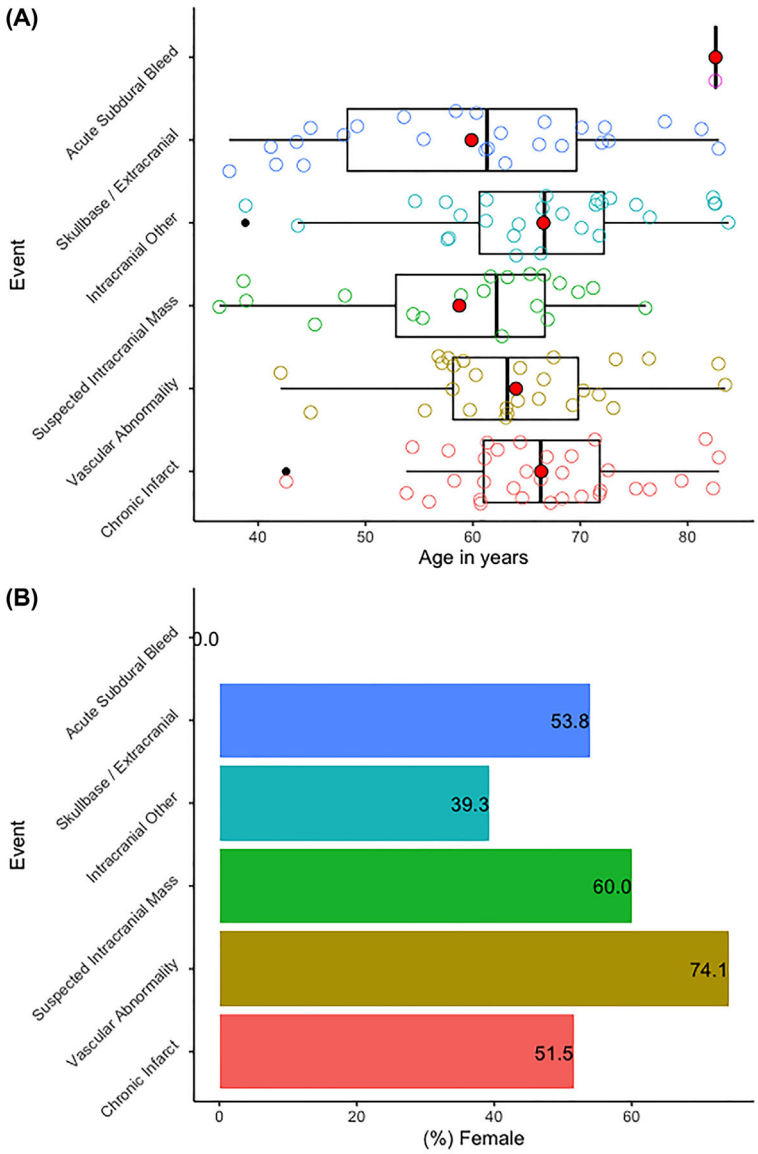

FIGURE 3.

Age, sex distributions within specific Level 2 and Level 3 brain MRI findings. Panel A is a boxplot representing the age distribution across the events considered in the analyses. The line inside the box represents the median age, whereas the red filled dot represents the mean age. The colors of the jittered scatters (panel A) and bars (panel B) represent the events included in the analyses

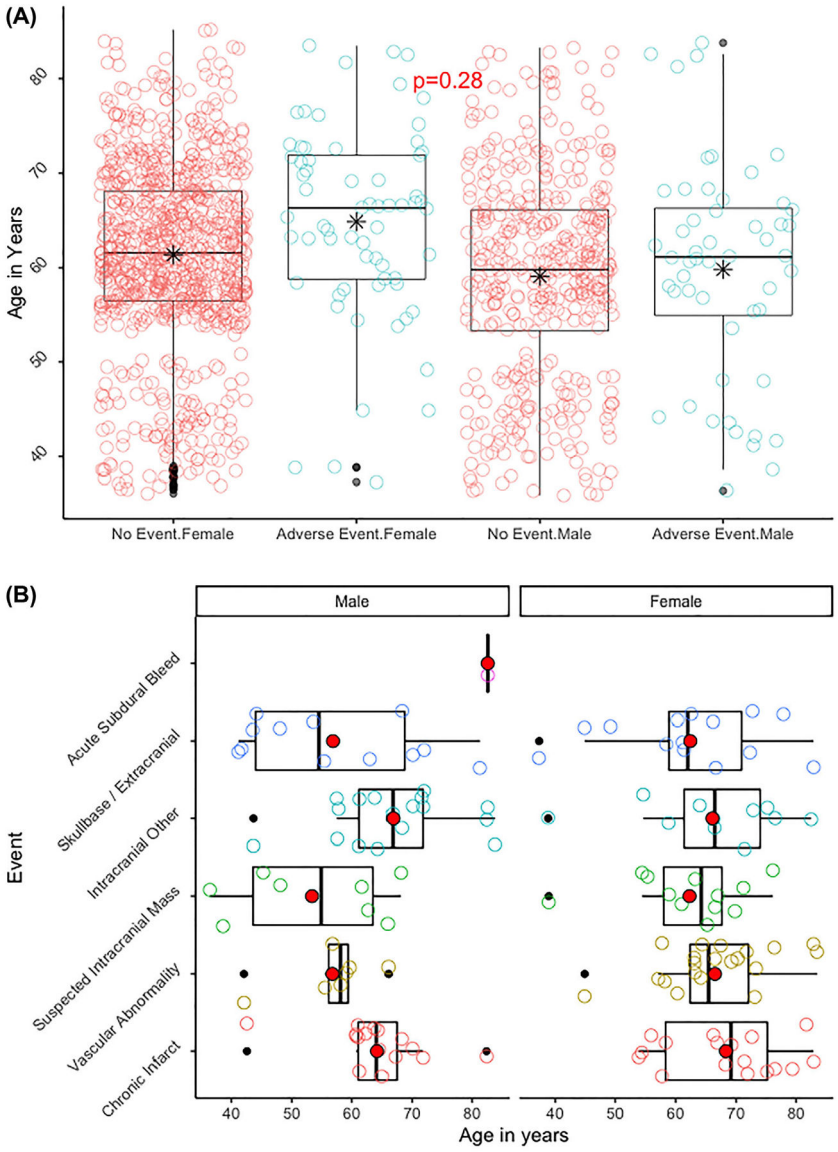

FIGURE 4.

Panel A includes age distributions within specific Level 2 and Level 3 brain MRI findings for males and females. Panel B includes age distributions by males and females within specific Level 2 and Level 3 findings. The *p*-value presented in panel A is a test for an interaction between sex and event as predictors of age. The difference (males vs. females) in mean age difference between participant with and without Level 2 and Level 3 findings was not statistically distinguishable. Panel A is a boxplot representing the age distribution for individuals with (color green) and without (color red) Level 2 and Level 3 findings for males and females. Panel B is a boxplot representing the age distribution across the events considered in the analyses for males and females. The lines inside the boxes represent the median age, whereas the red filled dots represent the mean age. The colors of the jittered scatters in panel B represent the events included in the analyses

TABLE 1

Participant characteristics by Hispanic/Latino background

	Age		Female		Male		Total	
Hispanic/Latino background	**Mean**	**SD**	**%**	***n***	**%**	***n***	**%**	***n***
Dominican	60.6	10.3	11	101	7	33	9.6	134
Central American	60.5	10.2	13.2	121	10.4	49	12.2	170
Cuban	61.2	9.4	15.9	146	19.3	91	17.1	237
Mexican	59.8	10.4	31.9	293	34	160	32.6	453
Puerto Rican	61.7	11.1	16.8	154	17.6	83	17.1	237
South American	62.7	10.1	9	83	8.9	42	9	125
Other/more than one	59.6	9.9	2.2	20	2.8	13	2.4	33

Abbreviations: *n*, number; SD, standard deviation.

TABLE 2

Summary of Level 2 or Level 3 incidental findings (some individuals had >1 abnormality)

Summary number (% total)	*n*	(%) Total
Chronic infarct	33	2.4
Vascular abnormality	27	1.9
Suspected intracranial mass	20	1.4
Intracranial	28	2.0
Skull base/extracranial	26	1.9
Acute subdural bleed	1	0.07

Abbreviation: *n*, number.

TABLE 3

Demographics

	Total group *N* = 1388	**Normal MRI*N* = 1271**	**Abnormal MRI*N* = 117**
Age (years)	60.8 ± 10.3	60.6 ± 10.2	62.6 ± 11.14[a]
Gender %female	66	67	56[b]

[a] $p = 0.0047$.

[b] $p = 0.012$.

Note: All the data represent mean±standard deviation.

Abbreviation: *N*, number of participants.