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Incidental Detection of Previously Unknown Chronic Infarcts on Outpatient Neuroimaging: A Target for Opportunistic Screening

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Abstract

Purpose

Chronic infarcts on neuroimaging may represent previously unrecognized stroke and are an opportunity to initiate or escalate secondary prevention. The purpose of the study is to determine the prevalence of previously unknown chronic infarcts on outpatient neuroimaging and identify associated factors.

Methods

This retrospective, cross-sectional study evaluated adult outpatient imaging encounters including portions of the brain between October 1 and December 31, 2025. A database search for terms related to encephalomalacia was used to identify encounters. Medical record review determined if chronic infarcts were previously unknown or known, and infarcts were measured and localized. Univariate and multivariate regression analyses were performed to identify characteristics associated with unknown infarcts.

Result

Of 13,668 relevant neuroimaging encounters, 446 encounters from 419 unique patients demonstrated chronic infarcts, 45.6% (n = 191) of which were previously unknown. Univariate analysis associated previously unknown infarcts with MRI modality (OR: 2.26, 95% CI: 1.49–3.44, $p < 0.001$), and brainstem (OR: 5.59, 95% CI: 1.19–26.18, $p = 0.03$), gangliocapsular (OR: 2.33, 95% CI: 1.43–3.78, $p < 0.001$), or cerebellar location (OR: 2.29, 95% CI: 1.40–3.74, $p < 0.001$). Multivariate analysis identified small infarct size (OR: 2.44, 95% CI: 1.85–3.33, $p < 0.001$) as an independent predictor of previously unknown infarcts.

Conclusion

45.6% of chronic infarcts identified on outpatient neuroimaging were previously unknown. Smaller infarct size was independently associated with previously unknown stroke. Incidentally detection represents an opportunity to evaluate patients for stroke etiology and initiate secondary stroke prevention.

INTRODUCTION

Stroke is a leading cause of death and disability worldwide, with up to 500,000 new strokes each year in the US [1]. Patients who have experienced a stroke are at risk of developing a recurrent stroke at a rate of approximately 26% within 5 years [2]. Stroke patients often have unknown modifiable risk factors, such as atrial fibrillation, obstructive sleep apnea, or atherosclerosis, that are addressed upon stroke diagnosis and workup [3, 4]. Prior estimates indicate that the risk for recurrent stroke can be decreased by 80–90% with existing preventative treatments [5]. Though recurrence risk is greatest in the first year

after initial stroke, annual recurrence risk past the one year timeframe remains around 2% per year, which is four times higher than the population baseline annual stroke risk [4, 6], even with risk factor management efforts [7, 8]. Without secondary prevention, it is predicted that the recurrence risk may be up to 40% in the 10 years following a primary stroke [9]. Current guidelines indicate that it is reasonable for all patients with incidentally detected brain infarcts to be assessed for common risk factors for secondary stroke prevention [10].

Many cerebral infarcts go unrecognized at initial presentation, spanning a spectrum from clinically silent lesions to overt strokes that are initially misdiagnosed. Silent brain infarcts occur without a recognized acute neurological episode, whereas covert infarcts may present with subtle, nonspecific, or atypical symptoms that do not prompt recognition of a cerebrovascular event. At the other end of this spectrum, strokes with recognizable symptoms may be missed or misdiagnosed; an estimated 12.7% of stroke presentations are initially misdiagnosed [11–13]. Neuroimaging can reveal previously unrecognized infarcts across this spectrum, including lesions associated with an increased risk of future symptomatic stroke. Identifying these infarcts creates an opportunity to initiate appropriate preventive interventions, optimize vascular risk-factor management, and reduce the risk of subsequent cerebrovascular events. Accordingly, missed or unrecognized strokes may leave patients vulnerable to preventable death and disability [14].

Previous research found that the incidence of an unknown stroke in head CT imaging in the emergency department setting was 1.7% [15]. Of approximately 16 million ED head CT scans in the US per year, this represents a potential 100,000 to 200,000 unknown infarcts detected annually. Emergent head CT scans represent a significant portion of neuroimaging exams, but not the entirety, and thus, the prevalence of unknown chronic infarcts on outpatient neuroimaging is unknown. Based on the proportion of imaging in outpatient settings and the subset of head CT and brain MRI [16–18], there are an estimated 20 million outpatient imaging exams of the whole brain brain annually in the US. If outpatient neuroimaging shows a similar proportion of unknown infarcts, this represents great, untapped potential for stroke prevention and care.

We conducted an analysis of outpatient imaging encounters to assess the prevalence of previously unknown infarcts. We hypothesized that differing population characteristics, and a smaller (though non-zero) proportion of outpatient neuroimaging will contain unknown remote infarcts compared to ED neuroimaging.

METHODS

This retrospective study was approved by the local institutional review board (No. 2000041061), with patient consent waived.

Study Design

We conducted a retrospective, cross-sectional review of outpatient imaging encounters in a large healthcare system, with approximately 3.6 million outpatient encounters annually across a multi-state catchment area. The study period was between the dates of October 1, 2025 to December 31, 2025. Eligibility criteria include adult (≥ 18 years old) patients who received neuroimaging that includes portions of the brain (such as head CT, CTA, cervical spine CT, brain MRI, orbital MRI, PET/CT, etc.).

Imaging examinations were identified from the radiology database using a key word search of the radiological report for terms such as “encephalomalacia,” “stroke,” “infarct”, or “ischemia” via the search program mPower MONTAGE. Patient age, sex, and imaging modality were also extracted from the database. After the initial search, encounters were excluded if they did not include true encephalomalacia or chronic infarct. Findings of encephalomalacia or remote infarct were determined based on radiological report. In circumstances where the cause of encephalomalacia was unclear, classification was determined by manual review of the imaging, chart, and prior imaging. Imaging for indications related to known or suspected stroke, TIA, or hemorrhagic stroke were excluded from the primary analysis, as chronic infarcts found on stroke-related imaging would not be considered incidental. In a secondary analysis, all imaging indications were included to assess the detection of all previously unknown chronic infarcts, regardless of imaging indication. This approach can retain chronic infarcts detected on studies performed for evaluation of suspected cerebrovascular events, including cases in which imaging prompted by a recent or suspected stroke revealed a previously unknown remote infarct.

Radiological reports were used to determine the presence of one or multiple chronic infarcts. The size of the largest infarct was measured using the largest measurement on any of the three standard planes (axial, sagittal, or coronal). Location of largest infarct was reported using laterality and anatomical area. Chronic infarcts spanning multiple anatomical locations are reported to include all areas.

Chronic infarcts were classified as previously known or previously unknown by the care team by a search through the patient’s electronic medical record for the mention of "stroke" prior to the imaging encounter date. The top ten imaging indications (after exclusion of stroke-related indications) were included for analysis, alongside a pooled "other" indication. If multiple indications were listed, examinations were coded to include all indications in the report.

Patient MRNs were collected for each imaging encounter. For patients with multiple encounters, the data was filtered to include one encounter only, prioritizing encounters showing chronic infarct if possible, or the most recent encounter otherwise. Patient ages over 90 were pooled into one category for analysis. Data analysis was performed on a per-patient level after removing duplicate patients.

Statistical Analysis

Statistical analysis was performed using Python 3.11 in Visual Studio Code. Differences in patient and imaging characteristics were assessed using t-tests and $\chi 2$ tests for continuous and categorical data, respectively. Univariate logistic regression models were completed for all variables, with a p-value of < 0.05 considered to be potentially significant. No adjustment was made for multiple comparisons, as this

analysis was considered exploratory. For additional analysis, chronic infarcts were grouped by supratentorial and infratentorial location, or anterior and posterior circulation, for further analysis using univariate logistic regression. Multivariate logistic regression models were completed for all variables where $p < 0.10$ from univariate analysis. Reciprocals of select odds ratios were calculated depending on the direction of association with unknown stroke. Confidence intervals and p-values were computed using the Wald statistic. A p-value of < 0.05 was considered to be significant.

Additionally, to evaluate robustness of the findings to an indication-based cohort selection, sensitivity analysis was conducted. An inclusive sensitivity analysis retained examinations across all indication categories, including stroke, thrombus, or transient ischemic attack. Results were compared to those of the primary analysis to assess robustness of findings. For each cohort, we compared the number of patients with remote infarct, proportion of infarcts that were previously unknown, demographic characteristics, and factors associated with previously unknown infarct to assess consistency of the findings.

Additional details on statistical methods, packages, and the analysis code can be found in supplemental materials.

RESULTS

231,649 outpatient imaging exams were completed during the three-month study period. This included 13,668 neuroimaging encounters of relevant modality (CT, MRI, or PET/CT) and anatomy; 9,829 encounters included advanced imaging of the entire brain (e.g. head CT or brain MRI); 3,839 encounters of advanced neuroimaging incidentally included parts of the brain (e.g. orbit CT or sinus MRI). The most common imaging examinations were MRI brain with and without contrast (n = 3,621), CT head without contrast (n = 1,931), MRI brain without contrast (n = 1,725).

After excluding indications related to stroke, 979 encounters demonstrated encephalomalacia, 446 (45.6%) of which were determined to represent chronic infarcts, of which 200 (44.8%) were previously unknown. Therefore, previously unknown chronic infarct was found on 0.09% (200/231,649) of all outpatient imaging encounters, and 1.46% (200/13,668) of all potentially relevant neuroimaging. Of potentially relevant neuroimaging, previously unknown chronic infarcts were found on 1.83% (180/9,829) of imaging including the whole brain. Imaging including the whole brain accounting for 90.0% (n = 180) of detected unknown remote infarcts; partial imaging of the brain counted for remaining 10.0% (n = 20). Further details of unknown infarct detection are described in Supplemental Materials.

The 446 cases of remote infarct were found in 419 unique patients. All subsequent data analysis was performed on a per-patient level. Of these patients with remote infarct, 45.6% (n = 191) were previously unknown to the medical team (Figure 1).

Figure 1: Flowchart of selection of outpatient neuroimaging. A database search using terms in the radiological report related to encephalomalacia or stroke was used to return cases of encephalomalacia.

Review of the radiological report and images was used to confirm presence of encephalomalacia and chronic infarct. Extraneous results (e.g. cases returned from the search process that were determined to not contain true encephalomalacia, or encephalomalacia from causes other than remote stroke, such as postsurgical changes, infectious or inflammatory processes, or hemorrhage) were excluded. Imaging indications related to ischemic stroke or TIA were excluded. Cases were determined to be previously unknown or known to the medical team based on chart review. For patients with multiple studies, encounters demonstrating chronic infarct (or, if equivalent, the most recent encounter) were included for final, per-patient analysis.

There was no missing data for imaging examination findings or patient-level variables. All 419 patients with chronic infarcts were included in the analysis. The average age of patients in the study was 71.5 (±12.4 SD) years. 52.7% (n = 221) of the patients were male, 47.2% (n = 198) were female. The most common imaging indications were malignancy, post-surgical, and post-stroke. Patient and imaging factors that differed between previously known and unknown stroke include patient age, imaging indication, imaging modality, size of largest chronic infarct, and infarct location (Table 1).

Table 1: Baseline patient demographics, including patient sex, age, imaging indication, imaging modality, size and laterality of largest stroke, and presence of multiple chronic infarcts.

Significant differences ($p<0.05$) were found between previously known and previously unknown cases for MRI or CT imaging modality, imaging of the neck region, size of largest chronic infarct, and location of the largest infarct in the gangliocapsular region, frontal lobe, parietal lobe, temporal lobe, occipital lobe, cerebellum, and brainstem.

Variable	Total	Previously Known	Previously Unknown	P-Value
n	419	228	191	
Patient Sex (Male), n (%)	221 (52.7)	119 (52.2)	102 (53.4)	0.882
Patient Age, mean (SD)	71.5 (12.4)	70.8 (12.7)	72.3 (12.1)	0.205
Indication:				
Malignancy/malignancy monitoring/tumor, n (%)	107 (25.5)	53 (23.2)	54 (28.3)	0.288
Post-surgical, n (%)	41 (9.8)	17 (7.5)	24 (12.6)	0.112
Cognitive deficit/dementia, n (%)	34 (8.1)	16 (7.0)	18 (9.4)	0.472
Bleed/hemorrhage/ICH/SDH, n (%)	30 (7.2)	20 (8.8)	10 (5.2)	0.227
Memory loss, n (%)	27 (6.4)	12 (5.3)	15 (7.9)	0.381
MS, n (%)	22 (5.3)	15 (6.6)	7 (3.7)	0.266
Headache, n (%)	27 (6.4)	14 (6.1)	13 (6.8)	0.939
Fall/found down, n (%)	28 (6.7)	13 (5.7)	15 (7.9)	0.495
Dizziness, n (%)	19 (4.5)	9 (3.9)	10 (5.2)	0.692
AMS/Mental status change/delirium, n (%)	18 (4.3)	14 (6.1)	4 (2.1)	0.073
Other, n (%)	194 (46.3)	110 (48.2)	84 (44.0)	0.439
Modality:				
MRI, n (%)	270 (64.4)	128 (56.1)	142 (74.3)	**<0.001**
CT, n (%)	139 (33.2)	92 (40.4)	47 (24.6)	**<0.001**
PET/CT, n (%)	10 (2.4)	8 (3.5)	2 (1.0)	0.119
Brain/Head, n (%)	382 (91.2)	210 (92.1)	172 (90.1)	0.572
Neck, n (%)	21 (5.0)	17 (7.5)	4 (2.1)	**0.023**
Orbits, n (%)	1 (0.2)	0 (0.0)	1 (0.5)	0.456
Auditory, n (%)	8 (1.9)	2 (0.9)	6 (3.1)	0.149
Sinus, n (%)	1 (0.2)	0 (0.0)	1 (0.5)	0.456

Pituitary, n (%)	4 (1.0)	1 (0.4)	3 (1.6)	0.335
Face, n (%)	3 (0.7)	3 (1.3)	0 (0.0)	0.254
Cervical Spine, n (%)	9 (2.1)	6 (2.6)	3 (1.6)	0.519
Spine, n (%)	3 (0.7)	1 (0.4)	2 (1.0)	0.594
Location of largest infarct:				
Gangliocapsular, n (%)	87 (20.8)	33 (14.5)	54 (28.3)	**<0.001**
Thalamus, n (%)	18 (4.3)	5 (2.2)	13 (6.8)	0.038
Frontal, n (%)	96 (22.9)	67 (29.4)	29 (15.2)	**<0.001**
Parietal, n (%)	73 (17.4)	59 (25.9)	14 (7.3)	**<0.001**
Temporal, n (%)	40 (9.5)	32 (14.0)	8 (4.2)	**0.001**
Occipital, n (%)	60 (14.3)	46 (20.2)	14 (7.3)	**<0.001**
Cerebellum, n (%)	84 (20.0)	32 (14.0)	52 (27.2)	**0.001**
Brainstem, n (%)	11 (2.6)	2 (0.9)	9 (4.7)	0.032
White matter, n (%)	17 (4.1)	7 (3.1)	10 (5.2)	0.384
Size (cm) (Largest Chronic Infarct), mean (SD)	1.8 (1.8)	2.5 (2.0)	1.0 (0.9)	**<0.001**
Laterality (Largest Chronic Infarct), n (%)	211 (50.4)	114 (50.0)	97 (50.8)	0.951
Multiple Chronic Infarcts, n (%)	217 (51.8)	122 (53.5)	95 (49.7)	0.502

Univariate Analysis

Among statistically significant variables on univariate analysis, the strongest positive associations with previously unknown strokes were MRI imaging modality (OR: 2.26, 95% CI: 1.49-3.44, $p < 0.001$), brainstem location (OR: 5.59, 95% CI: 1.19-26.18, $p = 0.03$), gangliocapsular location (OR: 2.33, 95% CI: 1.43-3.78, $p < 0.001$), and cerebellar location (OR: 2.29, 95% CI: 1.40-3.74, $p < 0.001$).

Among statistically significant variables, the smallest odds ratio for unknown stroke (e.g. most associated with previously known stroke) were parietal (OR: 0.23, 95% CI: 0.12-0.42, $p < 0.001$) or temporal lobe (OR: 0.27, 95% CI: 0.12-0.60, $p = 0.001$) location, and larger infarct size (OR: 0.38, 95% CI: 0.30-0.49, $p < 0.001$) (Table 2, Figure 2).

Grouping of strokes anatomically by supratentorial (OR: 0.36, 95% CI: 0.23-0.59, $p < 0.001$) and infratentorial (OR: 2.68, 95% CI: 1.67-4.30, $p < 0.001$) location had statistically significant associations with previously known and unknown strokes, respectively. Similarly, after grouping by blood supply, anterior circulation infarcts were associated with previously known stroke (OR: 0.51, 95% CI: 0.34-0.76, $p < 0.001$).

Table 2: Results of univariate analysis of patient and imaging factors and their association with previously unknown strokes.

Factors significantly associated with previously unknown prior infarct ($p < 0.05$) include MRI modality, and remote infarct location in the gangliocapsular region, thalamus, cerebellum, or brainstem. Factors significantly associated with previously known chronic infarct include CT modality, remote stroke location in the frontal, parietal, temporal, and occipital lobes, and larger infarct size. OR, Odds Ratio; CI, Confidence Interval.

	Coefficients	p-values	Odds Ratios	OR 95% CI Lower	OR 95% CI Upper
Patient Sex (Male)	0.049	0.80	1.05	0.71	1.54
Patient Age	0.010	0.21	1.01	0.99	1.03
Indication:					
Malignancy/malignancy monitoring/tumor	0.263	0.24	1.30	0.84	2.02
Post-surgical	0.579	0.08	1.78	0.93	3.43
Cognitive deficit/dementia	0.321	0.37	1.38	0.68	2.78
Bleed/hemorrhage/ICH/SDH	-0.554	0.17	0.57	0.26	1.26
Memory loss	0.428	0.29	1.53	0.70	3.36
MS	-0.616	0.19	0.54	0.22	1.35
Headache	0.110	0.78	1.12	0.51	2.44
Fall/found down	0.343	0.38	1.41	0.65	3.04
Dizziness	0.296	0.53	1.34	0.53	3.38
AMS/Mental status change/delirium	-1.118	0.05	0.33	0.11	1.01
Other	-0.172	0.38	0.84	0.57	1.24
Modality:					
MRI	0.817	**<0.001**	2.26	1.49	3.44
CT	-0.729	**<0.001**	0.48	0.32	0.74
PET/CT	-1.234	0.12	0.29	0.06	1.39
Region imaged:					
Brain/Head	-0.254	0.46	0.78	0.39	1.52
Neck	-1.326	**0.02**	0.27	0.09	0.80
Auditory	1.299	0.11	3.66	0.73	18.37
Cervical Spine	-0.527	0.46	0.59	0.15	2.39
Location of Largest Infarct:					
Gangliocapsular	0.845	**<0.001**	2.33	1.43	3.78
Thalamus	1.181	**0.03**	3.26	1.14	9.31

Frontal	-0.844	**<0.001**	0.43	0.26	0.70
Parietal	-1.485	**<0.001**	0.23	0.12	0.42
Temporal	-1.318	**0.001**	0.27	0.12	0.60
Occipital	-1.162	**<0.001**	0.31	0.17	0.59
Cerebellum	0.829	**<0.001**	2.29	1.40	3.74
Brainstem	1.721	**0.03**	5.59	1.19	26.18
White matter	0.556	0.27	1.74	0.65	4.67
Size (cm) (Largest Infarct)	-0.963	**<0.001**	0.38	0.30	0.49
Laterality (Right) (Largest Infarct)	0.031	0.87	1.03	0.70	1.52
Multiple Chronic Infarcts	-0.151	0.44	0.86	0.59	1.26

Figure 2: Univariate regression. Forest plot illustrates the odds ratios and 95% confidence intervals for the indications included in univariate regression. Patient and imaging factors, such as sex, age, stroke size, laterality, presence of multiple infarcts, and the top 10 indications for imaging were included. Dashed vertical line represents the null hypothesis (Odds Ratio = 1.0). Points to the right of the dashed vertical line indicate positive association with unknown chronic infarct, while points to the left indicate negative association with unknown chronic infarct (association with previously known infarct). Factors significantly associated with previously unknown infarct ($p < 0.05$) include remote stroke location in the gangliocapsular region, thalamus, cerebellum, or brainstem. Factors significantly associated with previously known chronic infarct include remote stroke location in the frontal, parietal, temporal, and occipital lobes, and larger infarct size. MS, multiple sclerosis; ICH, intracerebral hemorrhage; SDH, subdural hemorrhage.

Multivariate Analysis

Variables with $p < 0.10$ in the univariate analysis were included in the multivariate model (Table 3). After adjustment, larger infarct size (OR: 0.41, 95% CI: 0.30-0.54, $p < 0.001$) and imaging of the neck region (OR: 0.20, 95% CI: 0.06-0.73, $p = 0.01$) remained independently associated with previously known stroke. Post-surgical imaging indication (OR: 2.31, 95% CI: 1.01–5.29, $p = 0.047$) remained independently associated with previously unknown stroke. The reciprocal of the odds ratio for infarct size was calculated, quantifying the independent association of smaller strokes (OR: 2.44, 95% CI: 1.85-3.33, $p < 0.001$) with previously unknown stroke.

Variables with $p < 0.10$ in the univariate analysis were included in the multivariate model (Table 3). After adjustment, larger infarct size (OR: 0.43, 95% CI: 0.32-0.57, $p < 0.001$) remained independently associated with previously known stroke. Imaging of the neck region was also independently associated

with previously known stroke (OR: 0.24, 95% CI: 0.06-0.88, p = 0.03). Post-surgical imaging indication was associated with previously unknown stroke (OR: 2.31, 95% CI: 1.01-5.29, p = 0.047). The reciprocal of the odds ratios for infarct size and imaging of the neck region were calculated, quantifying the independent association of smaller strokes (OR: 2.33, 95% CI: 1.75-3.13, p < 0.001) and imaging of the neck (OR: 5.0, 95% CI: 1.37-16.67, p = 0.01) with previously unknown stroke (Table 3, Figure 3).

Table 3: Results of multivariate analysis of patient and imaging factors and their association with previously unknown strokes.

Factors independently associated with previously unknown infarct (p < 0.05) include post-surgical imaging indication. Factors independently associated with previously known infarct (p < 0.05) include larger infarct size, and imaging location in the neck. OR, Odds Ratio; CI, Confidence Interval

Variable	Coefficient	Odds Ratio	OR 95% CI Lower	OR 95% CI Upper	Standard Error	p-value
Indication:						
Post-surgical	0.839	2.31	1.01	5.29	0.42	**0.047**
AMS/Mental status change/delirium	-0.599	0.55	0.14	2.22	0.71	0.40
Imaging Modality:						
MRI	-0.713	0.49	0.08	2.92	0.91	0.43
CT	-0.639	0.53	0.09	3.17	0.91	0.48
Location imaged:						
Neck	-1.593	0.20	0.06	0.73	0.65	**0.01**
Location of largest old stroke:						
Gangliocapsular	0.594	1.81	0.67	4.91	0.51	0.24
Thalamus	1.285	3.61	0.76	17.18	0.80	0.11
Frontal	0.125	1.13	0.41	3.10	0.51	0.81
Parietal	-0.307	0.74	0.30	1.81	0.46	0.50
Temporal	0.478	1.61	0.50	5.24	0.60	0.43
Occipital	0.061	1.06	0.39	2.93	0.52	0.91
Cerebellum	0.910	2.48	0.90	6.88	0.52	0.08
Brainstem	1.232	3.43	0.57	20.57	0.91	0.18
Size (cm) (Largest Chronic Infarct)	-0.901	0.41	0.30	0.54	0.15	<**0.001**

Figure 3: Multivariate regression. Forest plot illustrates odds ratios and 95% confidence intervals for the independent association between variables and unknown chronic infarct. Variables with P values < .10 in the univariable analysis were included in multivariate analysis. This included MRI and CT modality, imaging of the neck, selected stroke locations (gangliocapsular region, cerebellum, brainstem, and frontal, parietal, temporal, and occipital lobes), and infarct size. Factors independently associated with previously unknown infarct ($p < 0.05$) include post-surgical imaging indication. Factors independently associated with previously known infarct ($p < 0.05$) include larger infarct size and imaged region in the neck.

Sensitivity Analysis

In analysis including all indications, 551 patients had findings of remote infarct, including 221 (40.1%) with previously unknown stroke. The proportion of previously unknown strokes was 5.5% higher in the primary cohort than the inclusive cohort. Compared to the primary analysis, analysis including all imaging indications had several differences. In addition to the associations found in primary analysis, previously unknown remote infarcts were also associated with malignancy-related indication and age; previously unknown remote infarcts were associated with presence of multiple chronic infarcts (Supplementary Table 3). Demographic and imaging characteristics did not differ significantly between the two cohorts. Other results were consistent with the primary analysis, suggesting that inclusion of stroke and hemorrhage-related examinations did not materially change the estimated prevalence and associations of previously unknown stroke.

DISCUSSION

In our study, 45.6% of remote infarcts incidentally identified on outpatient neuroimaging were previously unknown to the medical team. This corresponds to 1.46% of potentially relevant outpatient neuroimaging, and 0.08% of all outpatient imaging within our healthcare system during the study period. Larger infarct size was independently associated with previously known stroke on multivariate analysis. On univariate analysis, previously unknown chronic infarcts were associated with infratentorial and posterior circulation location (brainstem and cerebellum), and MRI modality. Frontal, temporal, occipital, and parietal lobar location, and CT imaging modality were associated with previously known stroke.

A previous study demonstrated that 1.7% of emergency department Head CT examinations identify previously unknown stroke [15] and that 43% of chronic infarcts found on emergent head CT scans were previously unknown. Despite differences in emergency and outpatient patient populations, this study found that a similar proportion of remote infarcts were previously unknown. Additionally, characteristics associated with previously unknown stroke were qualitatively similar across both settings, suggesting that factors contributing to missed or unrecognized stroke may be similar across clinical contexts.

Previous literature describes larger infarcts as being more likely to produce neurological deficits prompting medical evaluation, while smaller infarcts are more likely to present with milder symptoms and therefore be misdiagnosed or unrecognized [11, 12]. Similarly, posterior circulation strokes often present with nonspecific symptoms (such as dizziness, ataxia, and visual disturbances) rather than classic cortical stroke signs [11, 12, 19], potentially contributing to delayed or missed diagnoses. Our study is consistent with these observations: larger infarcts were more likely to be previously known, and posterior circulation strokes were more likely to be unknown. Posterior circulation infarcts presenting to the ED are misdiagnosed at much higher rates than anterior circulation infarcts (37% vs. 16%) [12, 20], which is potentially related to the prevalence of previously unknown posterior circulation strokes observed in this study.

Post-surgical imaging indication was independently associated with previously unknown infarct. This may reflect several factors related to patient disease processes, comorbidity, and presentation. Patients receiving surgery often have underlying conditions and can be medically complex. Covert brain infarcts are common in medically complex populations, associated with advanced age, hypertension, chronic kidney disease, and other underlying health conditions [21]. In these cases, underlying comorbid conditions could contribute to stroke risk. Additionally, recognition of stroke in these populations could be limited by complex neurologic presentation or other disease processes, increasing likelihood of covert infarct. Collectively, these factors could potentially explain the association between unknown chronic infarcts and post-surgical imaging indication; however, further investigation accounting for patient comorbidities, underlying disease processes, and surgical history is needed to better characterize this relationship

The presence of multiple infarcts was independently associated with previously known stroke on multivariate analysis inclusive of all imaging indications. However, upon exclusion of stroke and TIA-related indications, the association between multiple infarcts and previously known stroke was not significant. While it’s possible that this could represent the study being underpowered once cases were excluded, this is potentially due to multiple infarcts not being a strong predictor of previously unknown status.

MRI modality was also associated with previously unknown stroke on univariate analysis. This likely reflects MRI's increased sensitivity for small infarcts and infarcts in the posterior fossa compared to CT [10]. However, associations of MRI modality and unknown stroke did not persist after multivariate adjustment. This suggests that rather than being an independent predictor, patients receiving MRI imaging may share underlying characteristics with other predictors of unknown stroke.

Prior work has shown that patients with unknown remote infarct on ED head CT have significant gaps in secondary prevention compared to those with known infarct [22]. The focus of this study was primarily to characterize imaging features of infarcts that may help radiologists assess whether infarcts are potentially unrecognized, rather than establishing patient-level predictors of stroke based on individual risk factors. However, most patients with unknown strokes would have been eligible for escalation of secondary prevention (such as further optimization of antihypertensives, more intensive lifestyle counseling, antiplatelet therapy, etc.), representing a large gap in care. Incidental unknown stroke detection is thus a valuable marker for neurovascular and cardiovascular risk and an opportunity for intervention.

The detection of a similar proportion of unknown strokes on outpatient neuroimaging as emergent neuroimaging has broad implications for the total volume of patients with elevated recurrent stroke risk. Previously unknown chronic infarcts were identified in 1.83% of outpatient imaging encounters involving the whole brain. Applying this prevalence to an estimated 20 million annual outpatient whole-brain imaging exams in the United States yields approximately 366,000 previously unknown chronic infarcts detected annually. Additionally, extrapolating the proportion of partial- to whole-brain imaging observed

in our study and the corresponding prevalence of unknown infarcts on partial-brain imaging yields an estimated 41,000 additional cases annually. Together, these estimates suggest that approximately 407,000 previously unknown chronic infarcts may be detected on outpatient imaging annually. Though ED and outpatient neuroimaging populations may overlap, this still represents many opportunities for intervention.

Our study has several potential limitations. Due to reporting differences between individual radiologists, search may not return all imaging findings of encephalomalacia. Additionally, not all prior unknown strokes will be visualized by imaging, as they may be obscured by other lesions or imaging artifacts. There are likely differences in sensitivity between exam types, due to variations in modality and degree of brain anatomy coverage. Partial brain imaging may introduce bias toward infarcts within the imaged regions, and modalities such as PET/CT have lower sensitivity for detecting chronic infarcts. However, incidentally identified infarcts on these examinations may represent clinically actionable findings warranting assessment for secondary stroke prevention. Categorization of strokes as known or unknown is dependent on medical chart documentation, which may be incomplete. Although non-incidental findings were excluded by excluding indications referencing stroke or infarction, this approach may exclude some cases of primary intracranial hemorrhage described as “hemorrhagic stroke.” Additionally, “hemorrhagic stroke” may refer to primary hemorrhage or hemorrhagic transformation of ischemic infarct, which may not be distinguished by indication alone. Though this study was completed in a healthcare system with a socioeconomically diverse patient population across a large multistate catchment area, it may not be representative of other patient populations.

Further developments in this work could explore factors associated with unknown chronic infarcts within nationally representative samples. Future work could explore whether automated systems can identify potentially unrecognized chronic infarcts and support structured workflows to determine whether findings are actionable and warrant further evaluation. Additionally, prospective studies are also needed to determine the cost-effectiveness and clinical impact of standardized follow-up pathways after incidental detection of chronic infarct.

In conclusion, a substantial proportion of outpatient neuroimaging incidentally detects remote stroke that is unknown to patients and their medical team. This incidental finding represents a large, untapped opportunity to initiate or escalate management of vascular risk factors, which is expected to reduce the risk of recurrent stroke and impact long-term outcomes.

Declarations

Competing Interests

L.T. reports receiving royalties for 4 textbooks, Search Pattern: A Systematic Approach to Diagnostic Imaging (2020), A Brief Guide to the Neuroradiology Fellowship (2021), and How to be a More Efficient Radiologist: A Guide to Practice, Reporting, and Workflow Optimization (2023), and STAT DDX: A

Systematic Approach to Differential Diagnosis and Avoiding Diagnostic Error (2025). L.T. also reports speaking fees from Medality (MRI Online). A.D. reports consulting fees from Novo Nordisk and equity in Certus and TitinKM.

Author Contribution

A.P. collected and reviewed data, ran statistical analysis, wrote the main manuscript text and supplemental files, and prepared figures and tables. K.S., C.K., N.S., O.Z., and S.R. collected and reviewed data. C.W. and A.D. reviewed statistical analysis and results and edited the main manuscript text. L.T. reviewed data and statistical analysis, wrote and edited the main manuscript text, figures, and tables. All authors reviewed the manuscript.

Data Availability

The data supporting the findings of this study were obtained from electronic medical records and imaging studies. Restrictions apply to the availability of these data due to patient confidentiality and privacy regulations. The data are not publicly available but may be available upon reasonable request and with appropriate institutional approval.

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Figures

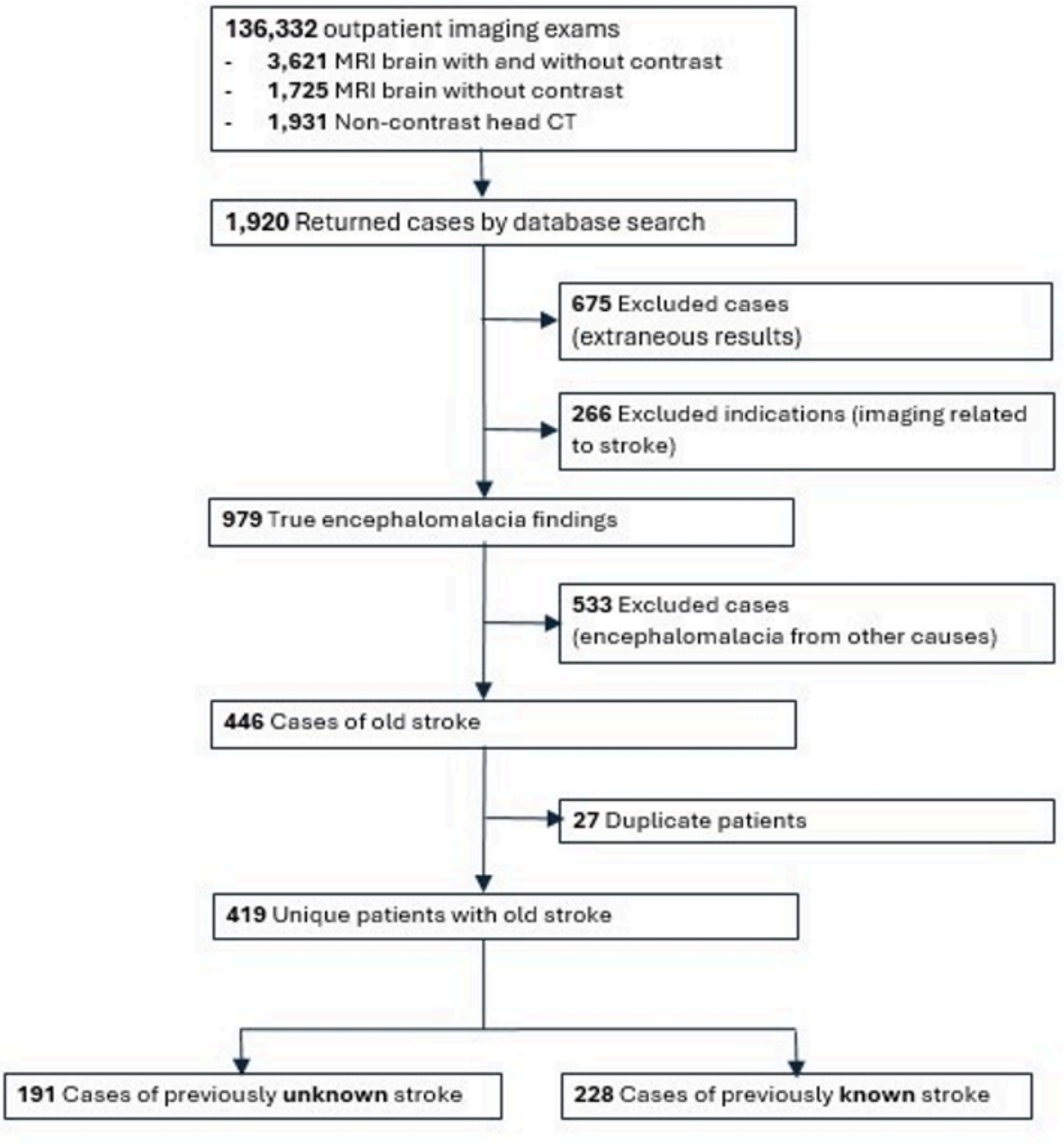


Figure 1

Flowchart of selection of outpatient neuroimaging. A database search using terms in the radiological report related to encephalomalacia or stroke was used to return cases of encephalomalacia. Review of the radiological report and images was used to confirm presence of encephalomalacia and chronic infarct. Extraneous results (e.g. cases returned from the search process that were determined to not contain true encephalomalacia, or encephalomalacia from causes other than remote stroke, such as postsurgical changes, infectious or inflammatory processes, or hemorrhage) were excluded. Imaging indications related to ischemic stroke or TIA were excluded. Cases were determined to be previously unknown or known to the medical team based on chart review. For patients with multiple studies,

encounters demonstrating chronic infarct (or, if equivalent, the most recent encounter) were included for final, per-patient analysis.

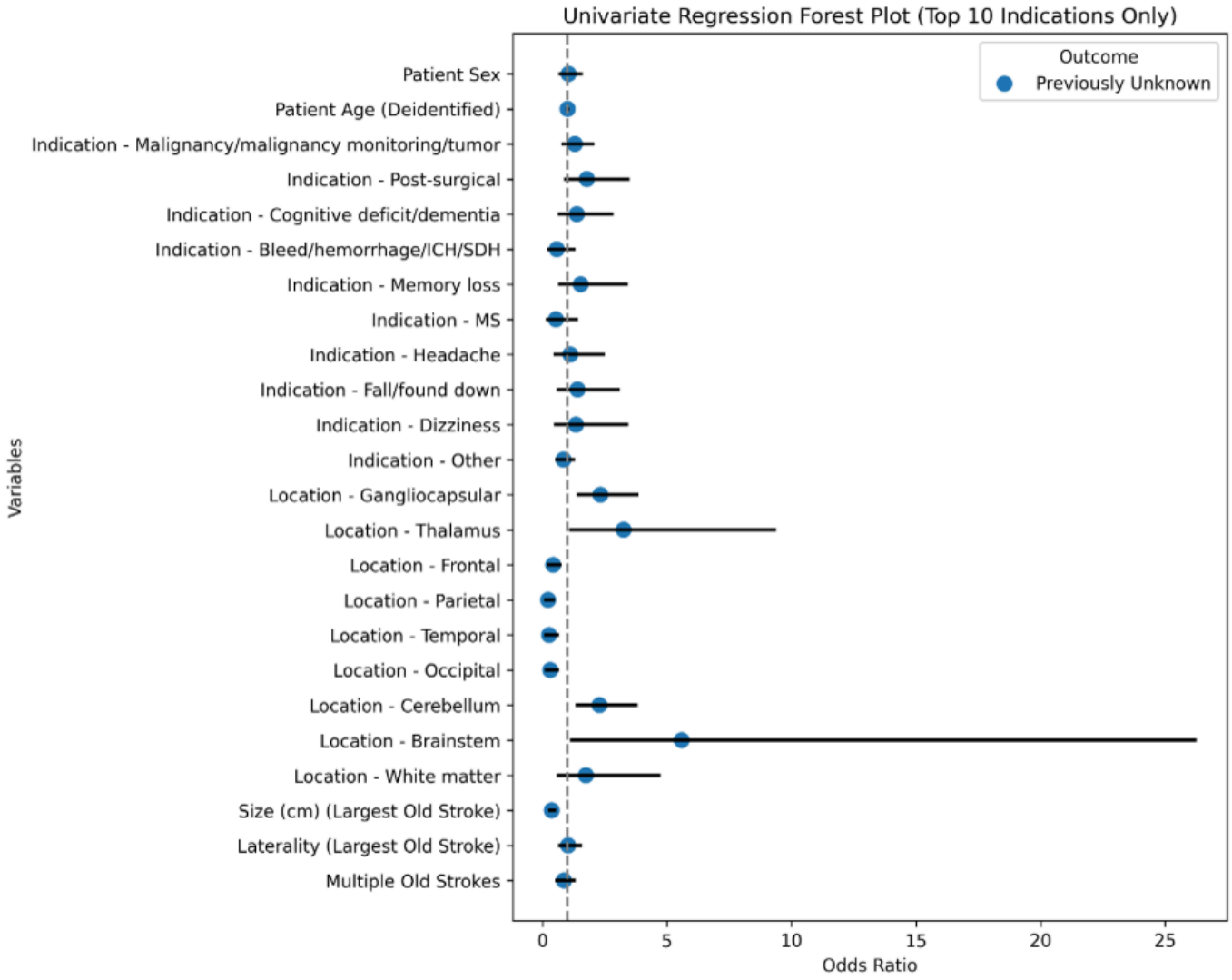


Figure 2

Univariate regression. Forest plot illustrates the odds ratios and 95% confidence intervals for the indications included in univariate regression. Patient and imaging factors, such as sex, age, stroke size, laterality, presence of multiple infarcts, and the top 10 indications for imaging were included. Dashed vertical line represents the null hypothesis (Odds Ratio = 1.0). Points to the right of the dashed vertical line indicate positive association with unknown chronic infarct, while points to the left indicate negative association with unknown chronic infarct (association with previously known infarct). Factors significantly associated with previously unknown infarct ($p < 0.05$) include remote stroke location in the gangliocapsular region, thalamus, cerebellum, or brainstem. Factors significantly associated with previously known chronic infarct include remote stroke location in the frontal, parietal, temporal, and occipital lobes, and larger infarct size. MS, multiple sclerosis; ICH, intracerebral hemorrhage; SDH, subdural hemorrhage.

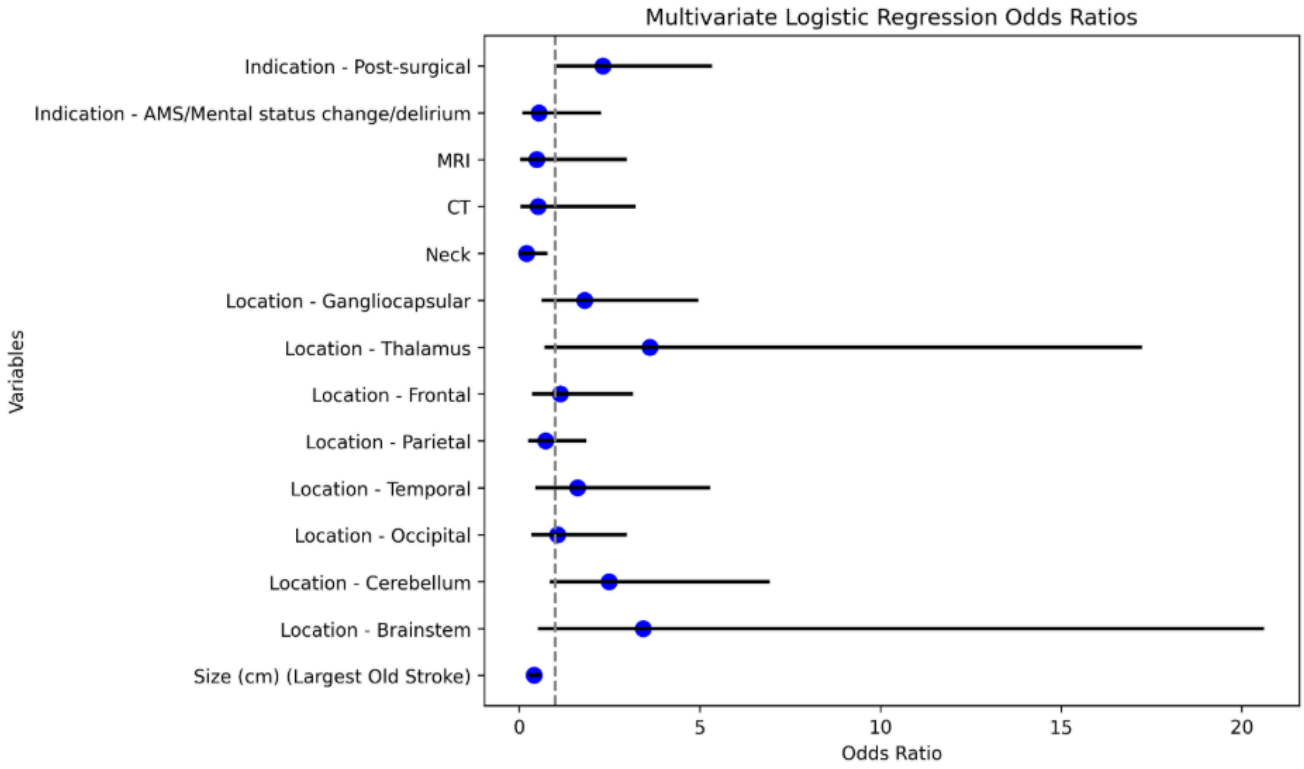


Figure 3

Multivariate regression. Forest plot illustrates odds ratios and 95% confidence intervals for the independent association between variables and unknown chronic infarct. Variables with P values < .10 in the univariable analysis were included in multivariate analysis. This included MRI and CT modality, imaging of the neck, selected stroke locations (gangliocapsular region, cerebellum, brainstem, and frontal, parietal, temporal, and occipital lobes), and infarct size. Factors independently associated with previously unknown infarct ($p < 0.05$) include post-surgical imaging indication. Factors independently associated with previously known infarct ($p < 0.05$) include larger infarct size and imaged region in the neck.

Supplementary Files

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