



Frequency of Acute and Subacute Infarcts in a Population-Based Study

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Abstract

Objective: To determine the frequency of incidental acute or subacute cerebral infarction (CI) in a population-based study.

Patients and Methods: We identified 2095 participants aged 50 to 98 years in the population-based Mayo Clinic Study of Aging from October 23, 2009, to October 5, 2016, with a usable diffusion tensor imaging (DTI) sequence (total scans=3230). Acute and subacute infarcts were identified by neuroradiologists. For each participant, vascular risk factors, medications, clinical symptoms, and neurological examination near the time of the CI were abstracted from the medical record. The probable etiologic mechanism for the CI was determined.

Results: Nine CIs were identified with a frequency of 0.28% among individual magnetic resonance imaging (MRI) scans and 0.43% among unique individuals. Infarctions were detected in 0.097% of scans from participants younger than 70 years and in 0.36% of scans of those 70 years or older. Six CIs were acute, and 3 were subacute. Most participants with infarcts were men (78%), with a mean age of 76.9 ± 6.74 years. All were asymptomatic at the time of CI detection. The probable mechanisms of CI were small vessel (n=6), cardioembolic (n=2), and cryptogenic (n=1).

Conclusion: Acute and subacute cerebral infarcts occur as incidental findings in approximately 1 in 230 people aged 50 to 98 years, particularly in elderly men and those with vascular risk factors. As brain MRI becomes more widely used, incidentally detected acute or subacute infarcts will provide an opportunity to improve stroke prevention.

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With increased utilization of neuroimaging in clinical and research settings and improved imaging quality, incidental findings on brain magnetic resonance imaging (MRI) are becoming more common. The frequency of incidental findings has varied among studies because of differences in the study populations and specific type of findings included in each study (ie, tumors, aneurysms, infarcts, etc). The differences in the MRI field strength and pulse sequences also have added to this variability. However, a meta-analysis published in 2009 reviewing 16 studies reported the prevalence of incidental findings as 2.7% on brain MRI.¹ Cerebrovascular findings including infarcts were excluded from this particular

meta-analysis. Studies that included cerebrovascular disease typically focused on chronic infarcts or infarcts of unspecified chronicity, and therefore, the frequency of incidental acute or subacute infarcts is not clear.²⁻⁵

Data on incidentally found acute infarcts have mainly come from identifying areas of restricted diffusion on diffusion-weighted images on MRI in asymptomatic individuals. Through this investigative approach, the frequency of acute cerebral infarcts found incidentally has been described in both hospitalized and community-dwelling participants as 0.37% and 0%, respectively.^{6,7} A higher prevalence of acute or subacute infarction has been reported in clinical series of patients with progressive cognitive impairment

(1.2%),⁸ cerebral amyloid angiopathy (15%),⁹ and primary acute intracerebral hemorrhages (35%).¹⁰ The frequency in a population-based neuroimaging study has not been reported.

Our objective was to determine the frequency of incidentally found acute and subacute infarctions in a population-based sample.

PATIENTS AND METHODS

Subject Selection

Participants were enrolled in the Mayo Clinic Study of Aging (MCSA), a population-based longitudinal study including adult residents of Olmsted County, Minnesota. The MCSA design is described in detail elsewhere,¹¹ but briefly, the Rochester Epidemiology Project medical records linkage system¹² was used to identify Olmsted County residents aged 50 to 89 years. Participants were randomly selected and stratified by sex and age. As part of the study protocol, participants without contraindications were invited to undergo multimodality imaging studies, including brain MRI at 3T. The present analyses included both cognitively impaired and unimpaired individuals who had brain MRI (Signa; GE Healthcare) from October 23, 2009, to October 5, 2016, with a usable diffusion tensor imaging (DTI) sequence. During this time period, a fraction of participants was scanned with a DTI slice thickness of 2.5 mm that was later changed to 2.7 mm for a higher signal-to-noise ratio and to match the ADNI2 pulse sequence.¹³ Specifically, from January 2010 onward, 3174 scans had 2.7-mm slices; before that, 56 scans had 2.5-mm slices. The study protocols were approved by the Mayo Clinic and Olmsted Medical Center institutional review boards. All participants provided written informed consent.

Assessment of Incidental Acute/Subacute Infarcts

All MRI scans were reviewed by board-certified neuroradiologists at the time of the scan for abnormalities as part of routine clinical workflow. Pertinent findings including acute or subacute cerebral infarction were recorded in the radiology report. The radiology reports of each MRI scan performed during the study from

October 23, 2009, to October 5, 2016, were then searched for key terms including “restricted diffusion,” “acute ischemia,” “acute stroke,” “acute infarct,” “subacute ischemia,” “subacute stroke,” and “subacute infarct.” Scans fitting the inclusion criteria based on the key term search were reviewed by a cerebrovascular neurologist (J.G.R., A.A.R.). Acute and subacute infarctions were defined by traditional radiologic descriptions.¹⁴ Specifically, an acute infarct was considered present if the scan showed hyperintensity on DTI sequences, a correlating hypointensity on apparent diffusion coefficient (ADC), and isointense T1 and hyperintense T2/fluid-attenuated inversion recovery (FLAIR) signals. Subacute infarction (ie, infarct up to 14 days) was defined by variable hyperintensity of the DTI signal, variable isointense ADC correlate, and hypointense T1 and hyperintense T2/FLAIR signals. Scans with DTI hyperintensity thought secondary to T2 shine-through (ie, hyperintense on ADC correlate and hyperintense T2/FLAIR signal) were excluded.

Data including cerebrovascular risk factors (hypertension, hyperlipidemia, atrial fibrillation, diabetes mellitus, current or history of tobacco use) and medication regimen (antithrombotic, antihypertensive, cholesterol-lowering agent) were abstracted from the medical record from the clinic visit closest to the date of MRI. Per study protocol, participants or the primary care providers were notified of any abnormal findings on the MRI that were potentially clinically significant. The medical team in conjunction with the participant then determined the additional clinical evaluation. Additional evaluations for each participant with an acute or subacute infarct were reviewed, and the probable etiology of infarction was then determined. In addition, previously described criteria and definitions were applied to infarcts attributed to small vessel disease.¹⁵ To confirm that the infarct was clinically silent, neurologic examinations performed at the time of infarction recognition were also reviewed.

RESULTS

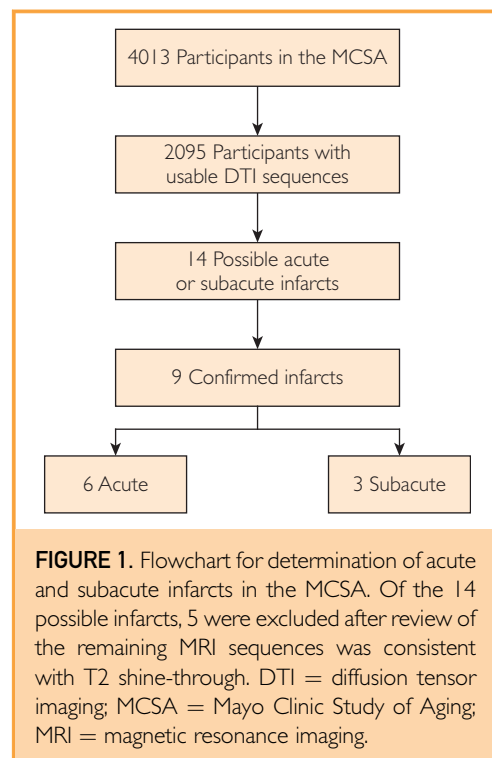
Of the 4013 MCSA participants who completed a clinic visit from October 23, 2009, to October 5, 2016, 2095 (52%) had at least 1 MRI brain scan. These 2095

TABLE 1. Total Number of Scans Per Subject

Serial scan no.	No. of subjects	Total scans
1	1239	1239
2	623	1246
3	192	576
4	36	144
5	5	25
	2095	3230

participants had a total of 3230 MRI scans with DTI sequences during the time period specified (Table 1). Fourteen scans revealed a possible infarct with hyperintensity on DTI, but 5 were excluded after the review of the remaining MRI sequences was consistent with T2 shine-through. Nine acute or subacute infarctions were identified in 9 unique subjects with a frequency of 0.28% among individual MRI scans (95% CI, 0.13%-0.53%) and 0.43% among unique individuals (95% CI, 0.20%-0.81%). Furthermore, 0.097% of scans in those younger than 70 years and 0.36% of scans in those 70 years or older showed an infarction. Of the 9 infarcts detected, 6 were acute and 3 were subacute (Figure 1). All the subjects were asymptomatic at the time of the MRI showing the infarction, and neurologic examinations performed around the time of the scan, per study protocol, were comparable to previous examinations with no abnormalities attributable to the infarct. In addition, multiple participants underwent serial MRI scans as part of the MCSA during the study period as shown in Table 1. Detected infarcts were found on the first scan in 5 unique individuals, on the second scan in 3 unique individuals, and on the third scan in 1 unique individual. No participants had infarcts detected on MRI at 2 different time points. As previously mentioned, DTI slice thickness changed during the study. Of the 9 infarcts, 8 were discovered on DTI with 2.7-mm slices.

Figure 2 includes examples of acute and subacute infarcts. The median size of the infarcts was 7.1 mm in greatest diameter with a range from 5.0 mm to 10.8 mm. Six (67%) of the infarcts were located in subcortical white matter, and 1 (11%) was located within the deep gray matter. One (11%) was cortically based, and another (11%) was located



within the cerebellum. Of the 9 cases of acute or subacute infarcts, 6 (67%) had evidence of previous chronic infarction on MRI and 8 (89%) had evidence of chronic ischemic small vessel disease represented as white matter hyperintensity on T2 or FLAIR images. Microbleeds were noted on MRI in only 1 (11%) of the cases. None of the 9 had a previous clinically apparent cerebral infarction or intracerebral hemorrhage.

Of the 9 participants with asymptomatic acute or subacute infarcts, 7 were men (78%) with a mean age of 76.9 ± 6.74 years. In addition, 8 of the 9 participants had at least 1 of the cerebrovascular risk factors collected in our study and 7 of 9 had 2 or more risk factors (Table 2). Only 1 participant was without a vascular risk factor. The most common risk factor present was hypertension, which was seen in 8 subjects. Hyperlipidemia was seen in 7 subjects. Two had atrial fibrillation, and 2 had type 2 diabetes mellitus. Most participants had been on an antiplatelet agent (56%), lipid-lowering therapy (78%), or an antihypertensive (78%) at the time of infarction. Please see Supplemental Table (available online at <http://www.mayoclinicproceedings.org>) for characteristics comparing participants of

MCSA who did not undergo brain imaging to those with imaging.

The probable etiology of each infarct was determined on the basis of participant's risk factors, imaging characteristics, and results of additional clinical evaluation and then classified according to the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) criteria; additional criteria described by Wardlaw et al¹⁵ were also applied to subcortical infarcts.¹⁶ Six infarcts were categorized as secondary to small vessel disease; 2 were categorized as cardioembolic; and the etiology of 1 was undetermined. Five participants were referred for a Neurology consultation for further evaluation after the infarct was found. Medication adjustments were recommended in 4 of these 5 cases for improved stroke prevention. Two of the 4 participants evaluated by primary care providers alone were recommended adjustments to their medication regimen for stroke prevention.

DISCUSSION

Our study shows that incidental acute and subacute infarcts were uncommon in a population-based study with a frequency of 0.28% among individual MRI scans and 0.43% among individual participants aged 50 to 98 years. Our rate of detection of silent acute/subacute brain infarctions was comparable to that of a previous study of hospitalized patients, which reported a frequency of 0.37%,⁶ but higher than that of a community-based study in which no acute/subacute infarctions were detected among 793 subjects who underwent brain MRI.^{6,7} This finding may be in part due to the older age of our cohort (mean age, 72.2 ± 10.2 years) and the hospital-based study (mean age, 70 ± 10 years) relative to the community-based study (mean age, 58.4 ± 8.0 years) as multiple studies have shown associations between increased age and incidental stroke.³⁻⁵

Our reported frequency of incidentally found acute or subacute ischemia was significantly lower than that described in studies involving elderly subjects with progressive cognitive impairment (1.2%),⁸ cerebral amyloid angiopathy (15%),⁹ and primary acute intracerebral hemorrhages (35%).¹⁰ Because patients with cerebral amyloid angiopathy also have a high prevalence of acute incidental

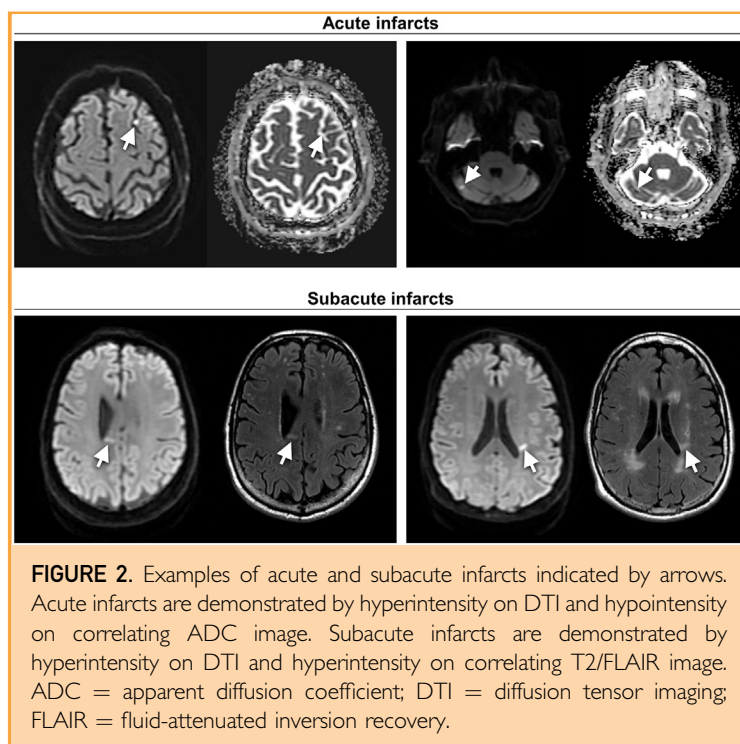


FIGURE 2. Examples of acute and subacute infarcts indicated by arrows. Acute infarcts are demonstrated by hyperintensity on DTI and hypointensity on correlating ADC image. Subacute infarcts are demonstrated by hyperintensity on DTI and hyperintensity on correlating T2/FLAIR image. ADC = apparent diffusion coefficient; DTI = diffusion tensor imaging; FLAIR = fluid-attenuated inversion recovery.

ischemia, it is not surprising that some studies have shown an association between incidental acute cerebral infarction and cerebral microbleeds.¹⁷ However, only 1 of our subjects with incidental ischemia had evidence of microbleeds on MRI. In addition, patients with dementia and cerebral amyloid angiopathy have a high burden of microinfarcts, which may be the pathologic substrate of some of these acute ischemic lesions.^{17,18} Interestingly, a study of serial MRI scans of 5 patients over a 16-week period with severe white matter disease revealed a higher incidence of acute, clinically silent infarcts that over time developed an appearance similar to leukoaraiosis, supporting the hypothesis that some of these infarcts contribute to leukoaraiosis, which is known to have deleterious effects on functional status.¹⁹ Similarly, cerebral microinfarcts impair functional status because of the disruption of innumerable neuronal connections. Whether some of these acute or subacute cerebral infarctions become cerebral microinfarcts is unclear but with more advanced imaging modalities and consistent rating criteria for microinfarcts, this will be an important future area of research.²⁰

TABLE 2. Characteristics of Participants With Acute or Subacute Infarcts on MRI

Age of infarct	Age (y)	Sex	Risk factors					Medication regimen at the time of infarction			
			HTN	HLD	AF	DM	Smoking	Antiplatelet	Anticoagulation	Lipid-lowering agent	Anti-HTN agent
Acute	74	M					N	ASA			
Acute	76	M	X	X	X		N	ASA	Warfarin	X	X
Acute	77	F	X	X			N			X	X
Acute	79	M	X				Y				X
Acute	83	M	X	X		X	N	ASA		X	X
Acute	89	F	X	X	X	X	Remote		Warfarin	X	X
Subacute	65	M	X	X			N			X	X
Subacute	72	M	X	X			N	ASA		X	X
Subacute	77	M	X	X			N	ASA-dipyridamole		X	

AF = atrial fibrillation; ASA = aspirin; DM = diabetes mellitus type 2; F = female; HLD = hyperlipidemia; HTN = hypertension; M = male; MRI = magnetic resonance imaging; N = no; X = present; Y = yes.

In the population-based Rotterdam study, approximately 20% of participants older than 60 years had a silent cerebral infarction on T2-weighted sequence. (The DWI sequence was not used in that study.)²¹ Compared with other cerebrovascular lesions, the described frequency of incidental acute or subacute clinical infarction is greater than other incidental findings such as cavernous malformations or arteriovenous malformations with previously reported prevalence of 0.16% and 0.05%, respectively.¹ A more recent study that also included participants of the MCSA found a frequency of cavernous malformations (0.44%) similar to the frequency of incidentally detected acute and subacute cerebral infarctions.²²

As expected, acute or subacute incidental infarcts were associated with traditional vascular risk factors. In fact, most of our subjects had 2 or more risk factors. This observation is congruent with previous studies that reported that the vascular risk factors for silent cerebral infarcts are similar to those for clinical stroke and chronic small vessel disease.^{3,6} Interestingly, many of the infarcts in our study occurred in participants who had already been prescribed stroke-preventive medications. Furthermore, most of our subjects with incidental acute or subacute infarcts had evidence of chronic infarcts and significant white matter disease on MRI, which coincides with a previous study that found an association between history of stroke/transient ischemic attack and incidentally detected acute infarcts.⁸ In addition, although participants 50 years and older were included in our study, the average

age of patients with incidental acute or subacute infarction was 76.9 years. Furthermore, infarctions were detected in only 0.097% of scans from participants younger than 70 years and in 0.36% of scans from participants 70 years or older. These findings further support that increasing age is a risk factor for incidental stroke.³⁻⁵ Since stroke-like symptoms are often underrecognized or underreported but are associated with cumulative silent cerebral infarction and future risk of transient ischemic attack and stroke, it may be beneficial to screen patients for such symptoms because they are at a higher risk of future cerebrovascular events.²³ Our results suggest that roughly 1 in 230 individuals undergoing brain MRI scanning will have an incidentally detected acute or subacute infarction. We suspect that this number will increase as imaging becomes more advanced and more frequently used for both clinical and research purposes. As more MRI brain scans are performed for various reasons, more acute or subacute infarctions will be incidentally detected and will provide practitioners and patients an opportunity to address and improve ongoing stroke prevention through risk factor modification and medication adjustments with the goal of preventing symptomatic stroke and accumulation of silent ischemic lesions, which are known to have deleterious consequences on a person's functional status.

Our study has multiple limitations. First, not all participants enrolled in the MCSA underwent MRI scan. Also, the MCSA sample population includes roughly the same number

of participants in each age and sex strata. In the general population, however, there are many more middle-aged adults (eg, 50-60 years old) than older adults (eg, 80-90 years old). Therefore, our reported frequency of incidentally detected cerebral infarctions may not accurately reflect that of the general population. In addition, by using clinical radiology reports, the reporting of acute or subacute infarction may be variable because of interrater variability among neuroradiologists. Furthermore, the MRI scans were performed between October 23, 2009, and October 5, 2016, and during that period, the diffusion sequences changed. Whether this affected the detection rate is not known; however, a 0.2-mm increase in slice thickness seems unlikely to affect visual ascertainment. Also, given that the participants were asymptomatic, the etiologic mechanism underlying the infarction may be less valid because clinical symptoms can be useful in defining the subtype, especially for those of small vessel mechanism.¹⁶

CONCLUSION

Acute and subacute cerebral infarcts occur as incidental findings in approximately 1 in 230 people aged 50 to 98 years, and are most commonly noted in elderly males and in those with traditional vascular risk factors. As brain MRI becomes more frequently and widely used in clinical practice and research, incidentally found acute or subacute cerebral infarction will provide an opportunity to improve stroke prevention.

SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at <http://www.mayoclinicproceedings.org>. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: ADC = apparent diffusion coefficient; DTI = diffusion tensor imaging; FLAIR = fluid-attenuated inversion recovery; MCSA = Mayo Clinic Study of Aging; MRI = magnetic resonance imaging

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