Silent Brain Infarcts
A Review of MRI Diagnostic Criteria

Yi-Cheng Zhu, MD, PhD; Carole Dufouil, PhD; Christophe Tzourio, MD, PhD; Hugues Chabriat, MD, PhD

Background and Purpose—Silent brain infarcts (SBIs) have been recognized as common lesions in elderly subjects and their diagnosis relies on brain imaging. In this study, we aimed to evaluate the different MRI parameters and criteria used for their evaluation in the literature to better understand the variation across studies and related limitations.

Method—Original MRI studies of SBI performed in human populations and reported in the English literature were reviewed. Analyses were restricted to population-based studies or studies in which at least 50 subjects with SBI were detected. The MRI parameters as well as the MRI criteria of SBI (size, signal characteristics, and criteria for differentiation of dilated Virchow-Robin spaces) were described and analyzed.

Result—Magnetic field strength, slice thickness, and gap between slices greatly varied among the 45 articles included in this review. The MRI definition of SBI was inconsistent across studies. In half of them, SBI was defined as hypointense on T1 and hyperintense on T2-weighted images. Exclusion criteria for dilated Virchow-Robin spaces were used only in 7 studies.

Conclusions—The variation in MRI characteristics and diagnostic criteria for SBI represent a major limitation for interpretation and comparison of data between studies. Efforts are needed to reach unified imaging criteria for SBI. (Stroke. 2011;42:1140-1145.)

Key Words: magnetic resonance imaging ■ MRI criteria ■ silent brain infarct

The term “silent brain infarcts (SBIs)” is widely used to describe cerebral infarcts seen on brain CT or MRI without any corresponding stroke episode. Although SBIs have been found to be highly prevalent and associated with adverse health outcomes, MRI reports of SBI appear limited and contradictory. A recent review described that the prevalence of SBI ranged from 8% to 28% in population-based studies.1 We hypothesize that this large variation may be partly related to the lack of uniform MRI criterion for SBI. In this review, we analyze the MRI techniques and MRI diagnostic criteria used to detect SBI in the literature to better understand their variation across studies.

Methods
Search Strategy and Selection Criteria
Original articles from 1966 to December 2009 were first identified through searches with PubMed using the following terms: “silent brain infarction,” “silent cerebral infarction,” “subclinical brain infarction,” “subclinical cerebral infarction,” and “silent lacune.” The searches were limited to original studies relating to human populations and written in English. The PubMed searches identified 490 articles. We focused on MRI studies in population-based studies and 23 (51%) were clinical series of healthy volunteers or patients with stroke or patients with vascular risk factors.

Data Analysis
Forty-five articles were selected according to the previously mentioned criteria. The MRI parameters (magnet strength, sequences, slice thickness, section gap, and in-plane resolution) as well as the MRI criteria of SBI (size, signal characteristics, and differential criteria of dilated Virchow-Robin spaces) were systematically reviewed and analyzed descriptively.

Results
Among the 45 articles selected, 22 (49%) were from 9 population-based studies and 23 (51%) were clinical series of healthy volunteers or patients with stroke or patients with vascular risk factors.

MRI Parameters
The information concerning the MRI technique, sequences, and imaging criteria used for diagnosis of SBI are detailed in the Table. The magnet strength ranged from 0.02 to 1.5 T.2–10 The section thickness varied from 4 to 6 mm in 11
### Table. MRI Parameter and MRI Criteria in the Identification of Silent Brain Infarction

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size (Total/SI)</th>
<th>Matrix</th>
<th>Section Thickness/Section Gap, mm</th>
<th>Sequence</th>
<th>Criteria in Silent Brain Infarction Identification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Framingham Offspring Study²</td>
<td>2040/220</td>
<td>256×256</td>
<td>4/0</td>
<td>PD-T2, T2, proton density</td>
<td>&gt;3 mm CSF intensity</td>
</tr>
<tr>
<td>The Rotterdam Scan Study⁴</td>
<td>1077/233</td>
<td>192×256</td>
<td>5–6/1</td>
<td>T1, T2, proton density</td>
<td>≥3 mm In GM: hyperintense on T2, hypointense on T1 Using proton density</td>
</tr>
<tr>
<td>Atherosclerosis Risk in Communities (ARIC) study⁴</td>
<td>1737/238</td>
<td>192×256</td>
<td>5/0</td>
<td>T1, T2, proton density</td>
<td>≥3 mm In GM: hyperintense on T2, hypointense on T1</td>
</tr>
<tr>
<td>Cardiovascular Health Study (CHS) study¹¹</td>
<td>3647/961</td>
<td>...</td>
<td>5/0</td>
<td>T1, T2, proton density</td>
<td>≥3 mm In GM: hyperintense on T2, hypointense on T1</td>
</tr>
<tr>
<td>National Institute for Longevity Sciences, Longitudinal Study of Aging (NILS-LSA)¹⁹</td>
<td>1758/178</td>
<td>192×256</td>
<td>8/1.5</td>
<td>T1, T2</td>
<td>≥3 mm Hyperintense on T2</td>
</tr>
<tr>
<td>The Northern Manhattan Study¹²</td>
<td>892/158</td>
<td>256×256</td>
<td>3/0</td>
<td>T1, T2, proton density</td>
<td>≥3 mm CSF intensity</td>
</tr>
<tr>
<td>Memory and Morbidity in Augsburg Elderly (MEMO) Study¹³</td>
<td>267/34</td>
<td>...</td>
<td>5–6/1.2</td>
<td>T1, T2, proton density</td>
<td>≥2 mm Hyperintense on T1 Hyperintense on T2 and hypointense on T2</td>
</tr>
<tr>
<td>Helsinki Aging Brain Study (HABS)⁵</td>
<td>128/22</td>
<td>128×256</td>
<td>10/0</td>
<td>T2</td>
<td>...</td>
</tr>
<tr>
<td>The Ohasama Study²⁰</td>
<td>958/...</td>
<td>...</td>
<td>10/...</td>
<td>T1, T2</td>
<td>3–15 mm Hyperintense on T1 Hyperintense on T2</td>
</tr>
<tr>
<td>Study on healthy subjects or patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Nomura et al, 2009¹⁰</td>
<td>217/131</td>
<td>...</td>
<td>...</td>
<td>T1, T2, FLAIR</td>
<td>≥3 mm Hypointense on T1 Hyperintense on T2 Hyperintense rim on FLAIR</td>
</tr>
<tr>
<td>Kwon, 2009¹⁴</td>
<td>1254/197</td>
<td>...</td>
<td>5/0</td>
<td>T1, T2, FLAIR</td>
<td>≥3 mm Hypointense on T1 Hyperintense on T2 Hyperintense rim on FLAIR</td>
</tr>
<tr>
<td>Putala et al, 2009¹¹</td>
<td>669/86</td>
<td>...</td>
<td>...</td>
<td>T1, T2</td>
<td>≥3 mm Hypointense on T1 Hyperintense on T2 Hyperintense rim on FLAIR</td>
</tr>
<tr>
<td>Henskens et al, 2009¹⁵</td>
<td>192/56</td>
<td>256×256</td>
<td>5/0.5</td>
<td>T2, FLAIR</td>
<td>≥3 mm Hypointense on T1 Hyperintense on T2 Hyperintense rim on FLAIR</td>
</tr>
<tr>
<td>Koga et al, 2009¹⁶</td>
<td>350/56</td>
<td>...</td>
<td>6/1</td>
<td>T1, T2, FLAIR</td>
<td>≥5 mm Hyperintense on T1 Hyperintense on T2 Hyperintense rim on FLAIR</td>
</tr>
<tr>
<td>Hoshino et al, 2009¹⁷</td>
<td>100/55</td>
<td>...</td>
<td>5/1</td>
<td>T1, T2, FLAIR</td>
<td>≥3 mm CSF intensity Hyperintense on T1 Hyperintense on T2 Hyperintense rim on FLAIR</td>
</tr>
<tr>
<td>Kanai et al, 2009¹²</td>
<td>179/51</td>
<td>...</td>
<td>...</td>
<td>T1, T2, FLAIR, proton density</td>
<td>&gt;3 mm Hypointense on T1 Hyperintense on T2 Hyperintense rim on FLAIR</td>
</tr>
<tr>
<td>Park et al, 2008¹⁶</td>
<td>2076/118</td>
<td>...</td>
<td>...</td>
<td>T1, T2, FLAIR</td>
<td>≥3 mm CSF intensity Hyperintense on T2 Hyperintense rim on FLAIR</td>
</tr>
<tr>
<td>Bokura et al, 2008²¹</td>
<td>1151/153</td>
<td>...</td>
<td>7/...</td>
<td>T1, T2, FLAIR</td>
<td>≥3 mm Hypointense on T1 Hyperintense on T2 Hyperintense rim on FLAIR</td>
</tr>
<tr>
<td>Serizawa et al, 2008⁷</td>
<td>792/295</td>
<td>...</td>
<td>...</td>
<td>T1, T2</td>
<td>≥3 mm Hypointense on T1 Hyperintense on T2 Hyperintense rim on FLAIR</td>
</tr>
<tr>
<td>Matsumoto et al, 2007²²</td>
<td>476/99</td>
<td>320×224</td>
<td>8/2</td>
<td>T2, FLAIR</td>
<td>&lt;15 mm Hyperintense on T2 Hyperintense on FLAIR</td>
</tr>
</tbody>
</table>

(Continued)
studies, was thicker than 6 mm in 14 studies and was not stated in 7 studies. The in-plane resolution was described with the corresponding matrix only in 6 population-based studies and 3 clinical series.

### MRI Criteria of SBI

#### Size

In most studies (7 of 9 of population-based studies and 20 of 23 of other studies) only lesions ≥3 mm in diameter were considered as potential SBI. However, in the Cardiovascular Health Study (CHS) as well as in the Atherosclerosis Risk in Communities (ARIC) study, all “infarction-like lesions” were recorded as SBI regardless of their diameter. In these 2 studies, >80% of SBIs were of diameter ≥3 mm. In the CHS, the frequency of SBI ≥3 mm overall was 28% and small infarct-like lesions (<3 mm) were detected in 196 (5.4%) participants. Of note, in the ARIC study, both the inter- and intraobserver agreement were found to be lower for detection of lesions <3 mm (64% and 75%; κ, 0.25 and 0.54) than for lesions ≥3 mm (79% and 82%; κ, 0.52 and 0.78).

Lesions of diameter >15 mm were excluded from analysis of SBI only in some studies. Conversely, in the CHS, one sixth of participants had SBIs ≥15 mm in diameter. Similar results were reported in the ARIC study showing that 18.9% of patients had SBIs ≥15 mm and 9.6% SBIs ≥25 mm.

#### MR Signal Characteristics

The MRI sequences applied in the different studies are listed in the Table. The MR signal considered for identification of SBI lesions largely varied across studies. Three types of major criteria were applied: (1) SBIs were defined as “hypointense lesions on T1-weighted images (WI) and hyperintense on T2-WI” with no more details in one third (3 of 9) of population-based studies and in 52.2% (12 of 23) of other studies; (2) SBIs were defined as hyperintense on T1 and hypointense on T2; (3) SBIs were defined as hyperintense on T1 and T2, FLAIR/proton density ≥3 mm and CSF density ≤3 mm.

### Table. Continued

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size (Total/SI)</th>
<th>Matrix</th>
<th>Section Thickness/Gap, mm</th>
<th>Sequence</th>
<th>Criteria in Silent Brain Infarction Identification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ishikawa et al, 2007</td>
<td>514/257</td>
<td>. . .</td>
<td>7.8–8/. . .</td>
<td>T1, T2</td>
<td>Hypointense on T1; Hyperintense on T2</td>
</tr>
<tr>
<td>Kwon et al, 2007</td>
<td>550/96</td>
<td>. . .</td>
<td>8/0</td>
<td>T1, T2, FLAIR</td>
<td>≥3 mm; CSF density; Hyperintense rim on FLAIR</td>
</tr>
<tr>
<td>Bokura et al, 2006</td>
<td>2684/380</td>
<td>. . .</td>
<td>10/. . .</td>
<td>T1, T2, FLAIR/proton density</td>
<td>≥3 mm; Hyperintense on T1; Hyperintense on T2; Hyperintense rim on FLAIR</td>
</tr>
<tr>
<td>Kwon et al, 2006</td>
<td>1588/88</td>
<td>. . .</td>
<td>8/0</td>
<td>T1, T2, FLAIR</td>
<td>≥3 mm; CSF intensity; Hyperintense rim on FLAIR</td>
</tr>
<tr>
<td>Kario et al, 2004</td>
<td>515/257</td>
<td>. . .</td>
<td>7–8/. . .</td>
<td>T1, T2</td>
<td>3–15 mm; Hyperintense on T1; Hyperintense on T2</td>
</tr>
<tr>
<td>Giele et al, 2004</td>
<td>308/51</td>
<td>. . .</td>
<td>4/0</td>
<td>T2, FLAIR</td>
<td>≥3 mm; CSF intensity; Hyperintense rim on FLAIR</td>
</tr>
<tr>
<td>Eguchi et al, 2003</td>
<td>360/246</td>
<td>256×256</td>
<td>7/. . .</td>
<td>T1, T2</td>
<td>3–15 mm; Hyperintense on T1; Hyperintense on T2</td>
</tr>
<tr>
<td>Kario et al, 2001</td>
<td>585/282</td>
<td>. . .</td>
<td>6.8–8/. . .</td>
<td>T1, T2</td>
<td>3–15 mm; Hyperintense on T1; Hyperintense on T2</td>
</tr>
<tr>
<td>Lee et al, 2000</td>
<td>994/58</td>
<td>. . .</td>
<td>. . .</td>
<td>T1, T2</td>
<td>. . .</td>
</tr>
<tr>
<td>Notsu et al, 1999</td>
<td>361/147</td>
<td>. . .</td>
<td>. . .</td>
<td>T1, T2</td>
<td>. . .</td>
</tr>
<tr>
<td>Kobayashi et al, 1997</td>
<td>933/99</td>
<td>. . .</td>
<td>7/. . .</td>
<td>T1, T2, FLAIR/proton density</td>
<td>≥3 mm; Hyperintense on T1; Hypointense on T2</td>
</tr>
<tr>
<td>Yamashita et al, 1996</td>
<td>365/86</td>
<td>. . .</td>
<td>10/. . .</td>
<td>T1, T2</td>
<td>≥3 mm; Hyperintense on T2; Hyperintensity ≥5 mm in diameter: T2</td>
</tr>
</tbody>
</table>

SI indicates silent infarction; dVRS, dilated Virchow-Robin spaces; PD, proton density; FLAIR, fluid-attenuated inversion recovery; CSF, cerebrospinal fluid; GM, gray matter; WM, white matter.
T2-WI and iso- or hypointense on T1-WI in the gray matter and as strongly hypointense on T1-WI with cerebrospinal fluid-like signal aspect in the white matter (distinct from leukoaraiosis) in 3 population-based studies\(^3,4,11\); and (3) only lesions with cerebrospinal fluid (CSF)-like signal intensity were considered as SBI in the Framingham Offspring Study and Northern Manhattan Study.\(^2,12\)

**Differential Criteria of Dilated Virchow-Robin Spaces**

For lesions >3 mm, the differential diagnosis criteria of dilated Virchow-Robin spaces (dVRS) were clearly stated only in 12 studies.\(^3,6,8,12,14–18,24,25,30\) A location criterion (presence of dVRS along perforating or medullary arteries or in the lower third of the basal ganglia) was stated in 5 studies. The aspect of MR signal on fluid-attenuated inversion recovery images was considered in several studies as a distinctive criterion for separating dVRS from infarcts based on the absence or presence of a hyperintense rim around each suspected lesion.\(^6,8,14–17,24,25,30\) Proton density scans were rarely used.\(^34\)

**Discussion**

The results of this review illustrate the large heterogeneity of MRI studies of SBI in the literature and emphasize 3 major sources of heterogeneity: (1) the different MRI parameters used to collect imaging data; (2) the variable diagnostic criteria used for identifying SBI on MRI; and (3) the different strategies applied in separating infarctions from dVRS.

The variations in MRI sequences and parameters of the different studies can obviously influence the detection of SBI. Although millimeter-level in-plane resolution was largely used, slice thickness appears widely variable among studies. Half of data were obtained using slices thicker than 6 mm, and 4 studies were performed with a gap of 0.5 to 2 mm between slices. A large slice thickness associated with a large interslice gap will automatically result in a lower detection of lesions, especially of small diameter, and therefore a lower prevalence of SBI. The impact of these technical differences is however difficult to assess. As an example, in 2 population-based elderly samples, the prevalence of SBI was 15.6% in the Helsinki Aging Brain Study using a 0.02-T MRI and 10-mm section thickness and 10.7% in the Framingham Offspring Study using 1-T MRI and 4-mm section thickness.\(^2,5\) Therefore, large differences in image resolution do not necessarily result in large variation between previous reports, probably because there are other additional sources of variation that have to be considered.

Differences in imaging diagnostic criteria may be an important source of variation. For example, some studies defined SBI by the following rule: “hypointense lesions on T1-WI and hyperintense on T2-WI,” whereas others referred to cavitated infarcts by taking only CSF-like signals into account. Lesions identified as SBI in the former studies would be regarded as leukoaraiosis in the latter (Figure). Such differences may partially account for the discrepancies in various studies. In pathological studies, white matter hyper-
intense foci on T2-weighted MRI were found to correspond to complete infarcts, incomplete infarcts, gliosis, areas of demyelination, dVRS, brain cysts, or even normal brain tissue. 

Therefore, studies with SBI simply defined as lesions that are “hyperintense on T2 and hypointense on T1” may overestimate the prevalence of infarcts. Conversely, counting only CSF-containing cavities may underestimate the prevalence of SBI because only complete cerebral infarcts replaced by fluid-filled cavities are regarded as SBI. Although neither of the 2 approaches is perfect, counting only CSF-containing cavities seems to be the most pragmatic option. Indeed, only chronic and cavitated ischemic lesions can be easily differentiated from the other types of MRI lesions because they are isointense relative to CSF on all pulse sequences.

The distinction of cavitated infarction from dilated perivascular spaces presents the most important diagnostic difficulty. In most previous reports, lesions <3 mm were not considered in the assessment of SBI because of the high risk of misdiagnosis with dVRS and also due to poor reader reproducibility. However, although helpful, the threshold of 3 mm is arbitrary and dVRS >3 mm are not rare. Postmortem examination of 8 elderly subjects showed that 9 of 16 (56%) cavities responsible for T2 hyperintensities >7 mm (corresponding to a diameter >3 mm) were actually large dVRS.

More recently, a prevalence of 33.2% of large dVRS (≥3 mm) was reported in a population-based 3-dimensional MRI study of 1818 elderly subjects aged between 65 and 80 years. These data show that the lack of discrimination between SBI and dVRS may result in a gross overestimation of the frequency of SBI. In this context, it is noteworthy that only half of previous studies mentioned a strategy for discriminating dVRS from SBI. Moreover, various and questionable methods were applied for this purpose. For example, the presence or absence of a hyperintense rim around CSF-like lesions on fluid-attenuated inversion recovery images is not always helpful to discriminate small infarcts from dVRS, because astrocytic gliosis has been observed postmortem around large dVRS. The use of proton density sequences for separating infarcts from dVRS based on the CSF signal could also be inefficient because both cavitated infarcts and dVRS are filled with fluid.

The imaging analysis of the shape of cavities was recently shown to be crucial in the discrimination of dVRS. However, shape analysis requires high-resolution MRI and 3-dimensional image analyses, which were not used in the previous studies on SBI.

This review includes all large studies of SBI, particularly all population-based studies of SBI thus far reported. We decided to exclude studies with samples <50 SBI subjects, which represents an arbitrary cutoff. However, after an initial review of all published studies, we determined that inclusion of these small-sample studies would not alter the overall conclusions of the present study. Finally, we also excluded studies performed in specific disease conditions. Therefore, the criticisms raised in the present review may not apply to studies performed in these disorders.

In conclusion, variations of MRI characteristics and diagnostic criteria may lead to great discrepancies in the definition of SBI and thus present major limitations for interpretation and comparison of studies on SBI. Efforts are needed to reach unified imaging criteria of SBI in the future.

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Disclosures

None.

References


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무중상 뇌경색
MRI 진단 기준에 대한 리뷰

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(Stroke. 2011;42:1140-1145.)

Key Words: magnetic resonance imaging ■ MRI criteria ■ silent brain infarct

배경과 목적: 무중상 뇌경색(silent brain infarct, SBI)은 노인에게 흔한 병변으로 알려져 있고, 그 진단은 뇌 영상에 의존하고 있다. 본 연구는 각 SBI 연구 간 차이 및 관련 재현성에 대한 보다 나은 이해를 위해 문헌들에서 평가되었던 다른 MRI 변수 및 진단 기준에 대하여 연구한 것이다.

방법: 사람을 대상으로 하고 영문으로 보고된 SBI에 대한 MRI 연구들을 검토하였다. 연구들은 인구 기반 연구이며, 최소 50명의 SBI가 확인된 연구들을만 제외하였다. MRI 변수 및 SBI의 MRI 진단 기준(크기, 신호 강도 특성, 확장된 Virchow–Robin 공간(dilated Virchow–Robin spaces, dVRS)과의 구분에 대한 기준)들을 기술하고 분석하였다.

결과: 자기장 강도, 슬라이스 두께 및 슬라이스 간 갇겨이 검토에 포함된 45개의 연구마다 상이하였다. SBI에 대한 MRI 정의는 연구마다 불일치하였다. 검토 중인 연구에서 SBI는 T1 강조영상(weighted image, WD)에서 저신호 강도, T2–WI에서 고신호 강도로 정의되었다, dVRS에 대한 재현을 가지는 연구는 7개에 불과하였다.

결론: SBI에 대한 MRI 특성 및 진단 기준의 변화가 연구들 간 데이터의 비교 및 해석에 있어 주요 재현으로 확인되었다. SBI의 단일화된 영상 기준을 마련하기 위한 노력이 요구된다.

‘무중상 뇌경색(silent brain infarct, SBI)’이라는 용어는 뇌졸중 사례에 해당하는 병력 없이 CTA나 MRA에서 보이지는 뇌경색으로 자주 기술되고 있다. SBI의 유병률이 높고 불명확한 건강 결과와 연관되어 있을에도 불구하고, SBI에 대한 MRI 보고는 제한적이고 모순적이다. 최근의 논문에 의하면 SBI의 유병률은 인구 기반 연구에서 8~28%로 보고되었다. 저자들은 이러한 큰 유병률의 차이가 SBI의 단일화된 MRI 진단 기준의 검토에서 부분적으로 비롯된 것으로 가설을 설정하였다. 이 리뷰에서 저자들은 SBI 진단을 위한 각 연구의 차이점에 대한 보다 나은 이해를 위해 MRI 기법 및 진단 기준에 대하여 분석하였다.

방법

검색 전략 및 선택 기준

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### Table. MRI Parameter and MRI Criteria in the Identification of Silent Brain Infarction

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size (Total/SI)</th>
<th>Matrix</th>
<th>Section Thickness/Section Gap, mm</th>
<th>Sequence</th>
<th>Criteria in Silent Brain Infarction Identification</th>
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<tbody>
<tr>
<td><strong>Population-based studies</strong></td>
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<tr>
<td>Framingham Offspring Study&lt;sup&gt;8&lt;/sup&gt;</td>
<td>2040/220</td>
<td>256×256</td>
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<td>PD-T2, T2, proton density</td>
<td>≥3 mm CSF intensity</td>
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<tr>
<td>The Rotterdam Scan Study&lt;sup&gt;9&lt;/sup&gt;</td>
<td>1077/233</td>
<td>192×256</td>
<td>5–6/1</td>
<td>T1, T2, proton density</td>
<td>≥3 mm In GM: hyperintense on T2</td>
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<tr>
<td>Atherosclerosis Risk in Communities (ARIC) study&lt;sup&gt;4&lt;/sup&gt;</td>
<td>1737/234</td>
<td>192×256</td>
<td>5/0</td>
<td>T1, T2, proton density</td>
<td>... In WM: hyperintense on T2, prominent hypointense on T1</td>
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<td>267/34</td>
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<td>5–6/1–1.2</td>
<td>T1, T2, proton density</td>
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<td><strong>Study on healthy subjects or patients</strong></td>
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<td>T1, T2, FLAIR</td>
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<td>≥3 mm Hypointense on T1 Hyperintense on T2 Hyperintense rim on FLAIR</td>
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<td>≥3 mm Hyperintense on T1 Hyperintense on T2 Hyperintense rim on FLAIR</td>
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<td>Seraizawa et al, 2008&lt;sup&gt;7&lt;/sup&gt;</td>
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(Continued)
Table. Continued

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<td>Ishikawa et al, 200773</td>
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<td>Hypointense on T1</td>
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<td>Hypointense on T1</td>
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<td>7–8/...</td>
<td>T1, T2</td>
<td>3–15 mm</td>
<td>Hypointense on T1</td>
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<tr>
<td>Giele et al, 200477</td>
<td>308/51</td>
<td>...</td>
<td>4/0</td>
<td>T2, FLAIR</td>
<td>≥3 mm</td>
<td>CSF intensity</td>
<td>Hyperintense rim on FLAIR</td>
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<td>Eguchi et al, 200378</td>
<td>360/246</td>
<td>256×256</td>
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<td>T1, T2</td>
<td>3–15 mm</td>
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<td>Kario et al, 200178</td>
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<td>3–15 mm</td>
<td>Hypointense on T1</td>
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<tr>
<td>Lee et al, 200079</td>
<td>994/58</td>
<td>...</td>
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<td>T1, T2</td>
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<td>Notsu et al, 19999</td>
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<td>≥3 mm</td>
<td>Hypointense on T1</td>
<td>...</td>
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<td>Kobayashi et al, 199773</td>
<td>933/99</td>
<td>...</td>
<td>7/...</td>
<td>T1, T2, proton density</td>
<td>&gt;3 mm</td>
<td>Hypointense on T1</td>
<td>Hyperintense on T2</td>
</tr>
<tr>
<td>Yamashita et al, 199610</td>
<td>365/86</td>
<td>...</td>
<td>10/...</td>
<td>T1, T2</td>
<td>≥3 mm</td>
<td>&gt;5 mm in diameter:T2 Hyperintensity</td>
<td>3–5 mm: hypointense on T2 and hypointense on T1</td>
</tr>
</tbody>
</table>

1. Indicates silent infarction; dVRS, dilated Virchow-Robin spaces; PD, proton density; FLAIR, fluid-attenuated inversion recovery; CSF, cerebrospinal fluid; GM, gray matter; WM, white matter.

가의견 및 논평은 대상에 제외하였다. 저작들은 또한 만성 신장병, 심부전, 낮적혈구(sickle cell) 질환, 신형성 C 단백 결

법, 카다실(cerebral autosomal-dominant arteriopathy with subcortical infarcts and leukoencephalopathy, CADASIL), 점도값 수술 및 스텐트와 같은 특정 질환에 대한 연구는 제외하였다.

데이터 분석

45개의 연구가 앞서 제시된 기준에 따라 선택되었다. MRI

변수(자가 강도, 시퀀스, 슬라이스 두께 및 구획 간격 및 평면

해상도) 및 SBI에 대한 MRI 진단 기준(크기, 신호 강도 특

성 및 확장된 Virchow-Robin 공간(dilated Virchow-Robin spaces, dVRS)의 구분에 대한 기준)이 제공적으로 분

석되었다.

결과

선택된 45개의 연구에서 22개(49%)는 지역 인구 기반 연구

였고, 23개(51%)는 건강한 자원, 뇌졸중 환자 혹은 뇌졸중

위험인자를 가진 환자들에 대한 임상 연구였다.

MRI 변수

MRI 기법, 시퀀스 및 SBI 진단에 사용된 영상 기준이

Table에 요약되어 있다. 자기 강도는 0.02에서 1.5T로 분포되

었다.10-14 구획 간격은 11개의 연구에서 4-6 mm,2-4.10-14 14개의

연구에서는 6 mm 초과였으며,4.10-13-13 7개의 연구에서는 이에

대한 언급이 없었다.4.10-13 평면 해상도로 해상 메트릭스에 따

라 기술한 연구는 지역 기반 연구에서 6개, 임상 연구에서 3개

로 조사되었다.
SBI에 대한 MRI 진단 기준

1. 크기

 대부분의 연구(인구 기반 연구 9개 중 7개, 12,13,20)에서 적정 3 mm 이상의 병변이 SBI로 간주되었다. 그러나 Cardiovascular Health Study (CHS)와 Atherosclerosis Risk in Communities (ARIC) 연구에서는 모든 '뇌경색 유사 병변(infarction-like lesion)' 크기에 관계 없이 SBI로 기록되었다. 이 두 연구에서 SBI의 80% 이상에서 크기는 3 mm 이상이었다. CHS 연구에서 적정 3 mm 이상의 SBI의 비도는 28%였으며, 3 mm 미만의 작은 뇌경색 유사 병변은 196명(5.4%)에서 관찰되었다. 흔히도 큰 것은 ARIC 연구에서 관찰자 간 및 관찰자 내 동의음은 3 mm 초과 병변(79%와 82%; κ, 0.52와 0.78)보다보다 3 mm 미만
에서 낮았다(64%와 75%; κ, 0.25와 0.54). 14

15 mm보다 큰 직경을 가진 병변은 어떤 연구에서는 제외되

았고, CHS 연구에서는 50 6mm의 환자가 적정 15
mm보다 큰 SBI가 있었다. 14 비슷한 결과가 ARIC 연구에서도 보고되었는데, 적정 15 mm보다 큰 병변을 가지는 환자는 18.9%였고, 적정 25 mm보다 큰 SBI를 가지는 환자는 9.6%로 보고되었다. 14

2. MR 신호 특성

 각각의 연구에 대한 다양한 MRI 시편들이 Table에 기술
되며 있다. SBI 병변 확인을 위한 MR 신호가 각 연구마다 다
양하였다. 세 가지 유형의 주요 기준이 적용되었다. (1) SBI는
T1 강조영상(weighted image, WI)에서는 저신호 강도, T2-
WI에서는 고신호 강도로 정의하였고, 인구 기반 연구의 1/3 (9
개 연구 중 3개), 12,13,20 다른 연구에서의 52.2% (23개 연구 중
12개)에서는 더 자세한 언급은 없었다. (2) 3개의 인구 기반 연
구에서는 SBI를 T2-WI에서 저신호 강도, 회색질(gray mat-
ter)-에서는 T1-WI에서 동등 혹은 저신호 강도, 백색질(white matter)-에서는(백절변성(leukoaraiosis)의 구분을 위해)
T1-WI에서 저 erot수액(cerebrospinal fluid, CSF) 유사 신호
강도와 유사한 저신호 강도로 정의하였다. 1,13 (3) Framingham
Offspring Study와 Northern Manhattan Study에서는
CSF 유사 신호 강도를 가지는 병변만을 SBI로 정의하였다. 1,12

3. dVRS에 대한 구분 기준

 적정 3 mm보다 큰 병변에 대하여 dVRS를 구분할 수 있는
기준이 자세히 언급된 내용은 12개였다. 1,4,6,8,12,20,23,26,30, 5개의
연구에서 위치 기준(기저막 아래 1/3에 위치하거나, 판동맥
(perforating artery) 혹은 양수동맥(medullary artery)을
따라 분포하는 경우)이 기술되어 있었다. 여러 연구에서
FLAIR영상(fluid–attenuated inversion recovery imaging)
에서 의심되는 병변 주변의 고신호 강도 대두리의 존재 유
무에 따라 뇌경색과 dVRS를 확실하게 구분하였던 연구가 몇
고찰

본 고찰 결과, SBI를 연구하였던 MRI 연구들 간의 상이성이 확인되었다. 이러한 상이성의 세 가지 주요인은 다음과 같다. (1) 영상 데이터를 얻기 위해 다양한 MRI 변수가 사용되었고, (2) MRI에서 SBI를 확인하기 위해 다양한 진단 기준이 사용되었다. (3) dVRS로부터 뇌경색을 구분하기 위해 다양한 전략이 적용되었다.

다양한 연구에서 MRI 시리즈와 변수의 차이가 SBI 진단에 명확하게 영향을 미친 것으로 해석된다. 대개 mm 수준의 정밀 해상도가 사용되었으나, 슈라고 두개는 연구마다 상이하다. 6 mm보다 두 개를 사용한 연구의 변수 정도는 해당하였고, 0.5~2 mm의 슈라고 두개는 연구는 4개였다. 슈라고 간격이 큰 것은 슈라고 두개가 큰 것과 연관되어 이러한 결과로 작은 경계에 의한 결과들이 이어져 결과적으로 SBI의 유병률이 낮게 나타났다. 그러나 이러한 기술적 차이가 어느 정도 영향을 미쳤는지는 평가하기 어렵다. 한 예로, 0.02-T MRI, 10 mm 두개를 이용한 Helsinki Aging Brain Study에서 SBI의 유병률은 15.6%였고, 1-T MRI, 4 mm 두개를 이용한 Framingham Offspring Study에서는 10.7%었다. 따라서 영상 해상도의 큰 차이가 어떤 영향으로 보고 간의 큰 차이를 초래하지 않을 수도 있으며, 이러한 변이에 영향을 미칠 수 있는 다른 변이가 고려되어야 한다.

영상 진단 기준에 대한 차이가 변이의 중요한 원인일 수 있다. 예를 들면 연구에서는 SBI를 T1-WI에서 저신호 강도 및 T2-WI에서 고신호 강도로 정의하였고, 다른 연구에서는 CSF 유사 신호 강도가 있는 공통 뇌조직(cavitated infarct)으로 정의하였다. 전자의 연구에서 SBI로 확인된 뇌병은 후자의 연구에서는 백질변성으로 간주될 수도 있다. 이러한 차이가 연구들 간의 끊임없는 변동성을 부분적으로 설명할 수 있을 것이다. 뇌병학적 연구에서는 T2 강도 MRI에서 백질변성 고신호 뇌병은 완벽한 뇌조직, 불완전한 뇌조직, 신경아교중 (gliosis), 탈수조(demelination) 영역, dVRS, 뇌 납중 (brain cyst) 혹은 정상 뇌 조직으로 확인되었다. 따라서 단순히 SBI를 T1-WI에서 저신호 강도, T2-WI에서 고신호 강도로 정의한 연구에서는 뇌조직의 유병률이 과장될 수 있다. 반대로 CSF로 채워진 공간(cavity)만을 인정하는 것은 식수액으로 채워진 공간들로 대체된 완전한 뇌조직만을 SBI로 인정하게 되며, SBI의 유병률이 낮아질 수 있다. 두 가지 방법 모두 완벽한 것은 아니며, CSF로 채워진 공간만을 SBI로 인정하는 것이 더욱 실용적일 수 있다. 반면적으로 공통을 형성하고 있는 허혈성 뇌병변이 MRI의 모든 방법 시리즈에서36,39 CSF보다 동일 신호 강도로 나타나기 때문에, MRI를 통해 이러한 뇌병변은 다른 양상의 MRI 뇌병변과 쉽게 구분할 수 있다. 공통 뇌조직과 확장된 혈관 주위 공간의 구분이 진단적 여러 용에 있어 가장 중요한 요인으로 꼽을 수 있다. 이전의 대부분의 보고에서 직경 3 mm 미만의 뇌병 변은 dVRS로 정밀한 위치를 높고 관측자들마다의 재현성이 높게 임으로 인하여, SBI의 평가에 있어 고려 대상이 되지 않았다. 그러나 3 mm의 기준은 인위적인 것이며, 3 mm보다 큰 dVRS로도 다름. 8명의 노인을 대상으로 한 부경 연구에서 T2-WI에서 고신호 강도를 보이는 7 mm3(직경 3 mm 이상에 해당)보다 큰 16개 중 9개(56%)의 뇌병 변이 큰 dVRS로 확인되었다. 최근 65~80세의 1,818명의 지역 노인 인구 기반의 삼차원 MRI 영상 연구에서 직경 3 mm 이상의 큰 dVRS의 유병률이 33.2%로 보고되었다. 이 결과는 SBI와 dVRS의 구분이 함들기 때문에 SBI의 유병률이 과장될 수 있다는 것을 보여준다. 이와 관련하여 이전의 연구의 변수 정도에도 많은 dVRS로부터 SBI를 구분하기 위한 방법을 연구하고 있었던 것은 고려해두자. 또한 다양한 통합방법들이 이와 비슷하게 적용되고 있다. 한 예로 FLAIR 영상에서 CSF 유사 변형 주위의 고신호 강도 세부의 존재 유무가 상당한 dVRS와 작은 뇌조직을 구분해내는 데 유용한 것은 아니다. 왜냐하면 부경 결과에서도 백질 여포형(atrocytic) 신경아교증이 큰 dVRS의 주로에서 관찰되지 때문이다.36,42 CSF 신호 강도에서 기반하여 뇌조직과 dVRS를 구분하기 위한 양상자율로 MRI 시리즈의 사용은 공동 뇌조직과 dVRS 모두 적수액으로 채워져 있으며 이들은 구분하는 데에는 비효율적일 수 있다.43,44 한편 뇌조직과 dVRS의 구분에 있어 공동확산 공간의 모양에 대한 영상 분석이 유용할 수 있다.45,46 그러나 이러한 모양에 관한 영상 연구에서는 이전 연구에서 사용된 적이 없는 고해상도 MRI 혹은 삼차원 영상 분석이 필요하다.44

본 논문은 지금까지 보고된 SBI에 관련된 인구 기반 연구들 모두 포함하고 있다. 저자들은 50개 미만의 SBI를 보고한 연구들의 경우 인위적인 재현성을 설정하여 SBI를 정의하고 있어, 이들을 분석으로 제외하였다. 그러나 이 연구들은 포함한 초기 검토 결과, 저자들은 이러한 작은 환자를 대상으로 한 연구 결과들을 포함하는 것이 현재 연구의 전반적인 결과에 미치는 영향은 적은 것으로 보고하였다. 또한 저자들은 특정 질환에서 수행된 연구들을 제외하였다. 그러므로 현재 검토에서 제외하고 있는 비평은 특정 질환에서 수행된 연구에 적용할 수 없다.

결론적으로 MRI 독성 및 진단 기준의 차이가 SBI를 정의하는 데 있어 다양한 복합적일 수 있음 주요 원인이며, SBI에 대한 연구 결과들의 비교와 해석에 있어 중요한 재현성이 요구된다. SBI의 영상 진단 기준을 마련하기 위한 노력이 필요하다.
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References