Left-Sided Strokes Are More Often Recognized Than Right-Sided Strokes

The Rotterdam Study

Marileen L.P. Portegies, MD; Mariana Selwaness, MD, PhD; Albert Hofman, MD, PhD; Peter J. Koudstaal, MD, PhD; Meike W. Vernooij, MD, PhD; M. Arfan Ikram, MD, PhD

Background and Purpose—Left-sided strokes are reported to be more common than right-sided strokes, but it is unknown whether they occur more often or are simply recognized more easily by clinicians. In a large unselected community-dwelling population, we examined the frequency of clinical left- and right-sided strokes and transient ischemic attacks (TIAs) and compared it with the frequency of left- and right-sided infarcts on MRI.

Methods—This study was conducted within the population-based Rotterdam Study. Between 1990 and 2012, 13,894 participants were followed up for first-ever stroke and TIA. MRI scans were performed within a random subgroup of 5081 persons and were rated for the presence of supratentorial cortical and lacunar infarcts. We compared frequencies of left- and right-sided strokes, TIAs, or MRI infarcts using binomial and Fisher exact tests.

Results—After a mean follow-up of 9.6 ±6.0 years, 1252 patients had a stroke, of which 704 were ischemic, and 799 participants had a TIA. Within the subgroup with MRI, we identified 673 infarcts. Ischemic strokes were more frequently left-sided (57.7%; 95% confidence interval, 53.7–61.6) than right-sided, similar to TIAs (57.8% left-sided; 53.4–62.3). In contrast, we found no left-right difference in distribution of infarcts on MRI (51.9% left-sided; 48.1–55.6).

Conclusions—Clinical ischemic strokes and TIAs are more frequently left-sided than right-sided, whereas this difference is not present for infarcts on MRI. This suggests that left-sided strokes and TIAs are more easily recognized. Consequently, there should be more attention for symptoms of right-sided strokes and TIAs.

Key Words: epidemiology ■ magnetic resonance imaging ■ stroke

Several hospital-based studies have reported that left-sided strokes are more frequent than right-sided strokes.1–3 A predilection for the left side may be explained by characteristics of the atherosclerotic plaque in the left carotid artery or by anatomy.4 The finding that isolated aphasia is a typical presentation of cardioembolic stroke or transient ischemic attack (TIA) also suggests that cardiac thrombi may preferably affect the left hemisphere.4 Another hypothesis is that the strokes in hospitals are a selection of strokes with symptoms that are better recognized or perceived as more severe. Left-sided strokes might be referred more frequently because they lead to clear symptoms, such as aphasia, whereas right-sided strokes may lead to less explicit symptoms, such as heminegl ect or spatial disorientation.1,5

Previous MRI studies also suggested that right-sided strokes are more often unnoticed because they found more right-sided silent infarcts in patients with carotid stenosis and atrial fibrillation.6,7 An important advantage of MRI studies is that these not only detect clinical strokes but also clinically silent infarcts, thereby providing a better estimate of the true distribution of left- and right-sided infarcts. To our knowledge, no study has compared the distribution of clinical strokes with that of MRI-defined cerebral infarcts within an unselected community-dwelling population. This can distinguish between an actual higher frequency of left-sided infarcts versus a higher frequency of clinically recognized strokes.

In a population-based study, we investigated the frequency of left- and right-sided ischemic strokes and TIAs and compared this with the frequency of left- and right-sided cerebral infarcts on MRI.

Methods

Methods are available in the online-only Data Supplement.

Setting and Study Population

This study was embedded within the prospective population-based Rotterdam Study4 and Rotterdam Scan Study. From 1990 to 2012, we continuously followed up 13,894 participants (mean age, 65.5±10.3 years).
years; 59.3% women) for occurrence of stroke and TIA and between 2005 and 2011 examined 5081 random participants (mean age, 64.2±11.1 years; 55.0% women) for the presence of cerebral infarcts using MRI. The Rotterdam Study has been approved by the medical ethics committee according to the Population Study Act Rotterdam Study, and written informed consent was obtained.

### Assessment of Clinical Stroke and TIA

Strokes and TIs were identified from medical records and confirmed by a neurologist. Assessment of the hemispheric side was based on clinical symptoms and computed tomographic imaging/MRI described in these medical records. Ischemic strokes were identified based on neuroimaging reports.

### Assessment of Infarcts on MRI

Infarcts were rated on fluid-attenuated inversion recovery, proton density-weighted, and T1-weighted sequences. Lacunar infarcts were defined as focal lesions ≥3 mm and <15 mm in size with the same signal characteristics as cerebrospinal fluid on all sequences and with a hypointense rim on the fluid-attenuated inversion recovery sequence.

### Statistical Analysis

Frequencies of left- and right-sided supratentorial strokes, TIs and MRI infarcts were compared with the expected frequency of 50% using a binomial test. Fisher exact tests were used to compare the distribution of clinical strokes and TIs with the distribution of MRI infarcts. Analyses were performed using IBM SPSS Statistics version 21.0 (IBM Corp, Armonk, NY).

### Results

During 9.6±6.0 years of follow-up, 1252 participants had a clinical stroke and 799 a TIA (mean age, 78.7±9.2 years; 61.6% women). A total of 588 ischemic strokes and 465 TIs occurred supratentorially (Figure 1). A total of 673 supratentorial infarcts were identified on MRI. Ischemic strokes occurred more often left- than right-sided (57.7% left-sided; 95% confidence interval, 53.7–61.6), similar to TIs (57.8% left-sided; 53.4–62.3). We did not find a significant left–right difference for cerebral infarcts on MRI (51.9% left-sided; 48.1–55.6; Figure 2). Importantly, direct comparison revealed that clinical ischemic stroke and TIA were significantly more frequently left-sided than infarcts on MRI (P=0.02). Figure 2 and Figure I in the online-only Data Supplement also show the left–right distribution for various subtypes of clinical strokes and MRI infarcts (eg, lacunar versus cortical; symptomatic versus silent MRI infarct).

### Discussion

In this population-based study, we found that clinical ischemic strokes and TIs occur more often left-sided than right-sided, whereas we did not find such a difference for cerebral infarcts on MRI.

Previous studies found a similar higher incidence of clinical left-sided strokes and TIs, but did not compare their results with infarcts on MRI, which includes clinically silent infarcts. These studies, therefore, did not help to distinguish between a true higher incidence of left-sided stroke because of a predilection of infarcts for the left side versus a difference in recognition of left- and right-sided strokes. In our study, clinical ischemic strokes and TIs were more frequently left-sided than right-sided. This was different from the distribution of infarcts on MRI. This suggests that left-sided strokes are recognized better or perceived as more severe, whereas right-sided strokes are missed. This might be the consequence of complex right-sided symptoms, such as hemineglect and spatial disorientation. Furthermore, patients might not present themselves to the hospital because of anosognosia. However, this is speculative because we do not routinely examine our participants to detect symptoms that might have been missed.

To determine the effect of missing right-sided strokes, additional studies should examine differences in long-term disability between left- and right-sided strokes.

Strengths of this study are the thorough collection of strokes and the availability of MRI in a subgroup of the study population. A limitation is that we could not compare frequencies of clinical strokes and TIs with frequencies of MRI infarcts in exactly the same population because of small overlap. Also, participants with a severe stroke probably did not visit the study center for MRI scanning because of their physical limitations. This might have led to some selection bias in the MRI population. Furthermore, because of the lack of clinical neuroimaging after stroke, not all strokes could be classified into ischemic or hemorrhagic and remained unspecified. Many of those unspecified strokes were not referred to hospital, partly because of complex right-sided symptoms, such as hemineglect and spatial disorientation. Furthermore, patients might not present themselves to the hospital because of anosognosia. However, this is speculative because we do not routinely examine our participants to detect symptoms that might have been missed.

To determine the effect of missing right-sided strokes, additional studies should examine differences in long-term disability between left- and right-sided strokes.

Strengths of this study are the thorough collection of strokes and the availability of MRI in a subgroup of the study population. A limitation is that we could not compare frequencies of clinical strokes and TIs with frequencies of MRI infarcts in exactly the same population because of small overlap. Also, participants with a severe stroke probably did not visit the study center for MRI scanning because of their physical limitations. This might have led to some selection bias in the MRI population. Furthermore, because of the lack of clinical neuroimaging after stroke, not all strokes could be classified into ischemic or hemorrhagic and remained unspecified. Many of those unspecified strokes were not referred to hospital, partly because of complex right-sided symptoms, such as hemineglect and spatial disorientation. Furthermore, patients might not present themselves to the hospital because of anosognosia. However, this is speculative because we do not routinely examine our participants to detect symptoms that might have been missed.
because they were perceived as less severe. Left-sided strokes were not more frequent in this group, which supports our and other results that left-sided strokes are perceived as more severe and referred to a hospital more often. A final consideration is that the distribution of left-sided MRI infarcts was not exactly 50 to 50, especially for cortical MRI infarcts. It is therefore possible that there also is a small, but true predilection for left-sided strokes, which remained obscured in our study because of insufficient power.

In conclusion, our findings suggest that the higher frequency in clinical left-sided strokes and TIAs compared with right-sided events is in a large part because of a better recognition of those. Consequently, there should be more attention for symptoms of right-sided strokes and TIAs.

**Sources of Funding**
This study was supported by Netherlands Heart Foundation (Nederlandse Hartstichting) 2012T008 and Erasmus University Medical Center (Erasmus MC) Fellowship 2013.

**Disclosures**
None.

**References**
Left-Sided Strokes Are More Often Recognized Than Right-Sided Strokes: The Rotterdam Study
Marileen L.P. Portegies, Mariana Selwaness, Albert Hofman, Peter J. Koudstaal, Meike W. Vernooij and M. Arfan Ikram

Stroke. published online December 9, 2014;
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2014 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/early/2014/12/09/STROKEAHA.114.007385

Data Supplement (unedited) at:
http://stroke.ahajournals.org/content/suppl/2014/12/09/STROKEAHA.114.007385.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/
SUPPLEMENTAL MATERIAL

Left-sided strokes are more often recognized than right-sided strokes: the Rotterdam Study

Marileen L.P. Portegies MD\textsuperscript{1,2}, Mariana Selwaness MD\textsuperscript{1,3,4}, Albert Hofman MD PhD\textsuperscript{1}, Peter J. Koudstaal MD PhD\textsuperscript{2}, Meike W. Vernooij MD PhD\textsuperscript{1,4}, M. Arfan Ikram MD PhD\textsuperscript{1,2,4} Department of Epidemiology\textsuperscript{1}, Neurology\textsuperscript{2}, Biomedical Engineering\textsuperscript{3}, and Radiology\textsuperscript{4}, Erasmus MC University Medical Center, Rotterdam, the Netherlands

Corresponding author: M. Arfan Ikram, MD PhD
Department of Epidemiology, Erasmus MC University Medical Center, PO Box 2040, 3000CA Rotterdam, the Netherlands
Tel: +31107043489 / Fax: +31107044657 / E-mail: m.a.ikram@erasusmc.nl

Supplemental Appendix

Author contributions \hspace{1cm} Page 2
Supplemental Methods \hspace{1cm} Page 3
Supplemental Results \hspace{1cm} Page 4
Supplementary Figure I \hspace{1cm} Page 6
Author contributions

All authors have made substantial intellectual contributions to conception and design (Vernooij, Hofman, Ikram), or acquisition of data (Portegies), or analysis and interpretation of data (Portegies, Selwaness, Vernooij, Koudstaal, Ikram), drafting the article or revising it critically for important intellectual content (Portegies, Selwaness, Vernooij, Hofman, Koudstaal, Ikram), and gave final approval of the version to be published (Portegies, Selwaness, Vernooij, Hofman, Koudstaal, Ikram). Dr. Ikram has full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Supplemental Methods

Population

This study was embedded within the prospective population-based Rotterdam Study. Details regarding the objective and design of the Rotterdam Study have been described elsewhere. The study started in 1990 among 7983 subjects aged 55 years and older residing in Ommoord, a suburb of Rotterdam, the Netherlands. In 2000 the cohort was extended with 3011 participants who had become 55 years of age or moved into the study district. In 2006 another 3932 subjects living in Ommoord were included, aged 45-54 years. After excluding 256 participants that did not give informed consent for collection of follow-up information and excluding 776 persons with prevalent stroke or TIA, 13894 participants (mean age at baseline 65.5±10.3 years, 59.3% female) were followed-up for first ever stroke and TIA. MRI scans were performed in 5081 participants (mean age 64.2±11.1, 55.0% female) of the Rotterdam Scan Study, which is a substudy of the Rotterdam Study that started in 2005. The Rotterdam Study has been approved by the medical ethics committee according to the Population Study Act Rotterdam Study, executed by the Ministry of Health, Welfare and Sports of the Netherlands. A written informed consent was obtained from all participants.

Assessment of clinical stroke and TIA

History of stroke and transient ischemic attack (TIA) was assessed using home interviews and confirmed reviewing medical records. From baseline onwards persons were continuously followed-up for occurrence of stroke and TIA through automatic linkage of general practitioners’ files with the study database. Furthermore, nursing home physicians’ files and files from general practitioners of participants that moved out of the study area, were checked on a regular basis. Of all potential strokes and TIAs, hospital discharge letters and information from general practitioner was collected. Research physicians reviewed the information and an experienced vascular neurologist verified the strokes according to World Health Organization criteria. Strokes were further classified into ischemic or hemorrhagic on basis of neuroimaging reports. If no neuroimaging was performed, strokes were classified as unspecified. We defined TIAs as temporary attacks with presence of focal symptoms, which are attributable to dysfunction of one arterial territory of the brain. Assessment of the hemispheric side of strokes and TIAs was based on clinical symptoms and CT/MRI-images described in the medical records. Follow-up for both stroke and TIA was complete until January 1st, 2012 for 96.3% of potential person-years.

Cerebral infarcts on MRI

All scans were performed on a 1.5T MRI scanner (General Electric Healthcare, Milwaukee, USA). Infarcts were rated on FLAIR, PD-weighted, and T1-weighted sequences by experienced raters under supervision of a neuroradiologist. Lacunar infarcts were defined as focal lesions ≥ 3 mm and <15 mm in size with the same signal characteristics as CSF on all sequences, and with a hyperintense rim on the FLAIR sequence. To assess symptomatic and silent infarcts, we coupled our MRI-dataset with the clinical stroke and TIA dataset. We recorded an MRI-infarct as symptomatic if there was a previous clinical ischemic stroke or TIA (either a first-ever event or a recurrent event) matching with the
hemispheric side of the MRI-infarct. Similarly, to adjudicate an MRI-infarct as silent, there should be no previous clinical ischemic stroke or TIA matching with the hemispheric side of that MRI-infarct.

Statistical analysis

We restricted our analyses to the cerebral hemispheres. We calculated frequencies of first-ever left- and right-sided strokes, TIAs, and MRI-infarcts with 95% confidence intervals (CIs). These frequencies were compared with the expected frequency of 50 percent using a binomial test. Furthermore, the Fisher’s exact test was used to compare distribution of clinical stroke and TIA side with distribution of infarcts on MRI. For strokes and TIAs and the combination ischemic stroke and TIA we included only the first event. We included all MRI-infarcts, because we could not separate recent from chronic infarcts, also if a participant had infarcts on both sides. As sensitivity analysis we performed linear mixed models to account for multiple MRI-infarcts in one person. All analyses were done using IBM SPSS Statistics version 21.0 (IBM Corp., Armonk, NY).

Supplemental Results

Study population for MRI infarcts

We identified infarcts in 510 participants. Participants with only infratentorial infarcts were excluded (n=110). Of the remaining 400 participants, 166 had infarcts only on the left side, 149 only on the right side, and 85 on both sides. The location was not registered for 7 cortical and 5 lacunar infarcts. In total we identified 673 supratentorial infarcts, of which 224 were cortical and 449 lacunar.

Sensitivity analysis

Calculating the percentage of MRI-infarcts using linear mixed models did not change our results in any way (data not shown).

References

Supplementary Figure I.

Frequencies of symptomatic and silent infarcts on MRI. Data are presented as counts (percentages). p-values are presented for the left-right difference.

<table>
<thead>
<tr>
<th></th>
<th>left (n (%))</th>
<th>right (n (%))</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total infarcts</td>
<td>349 (51.9%)</td>
<td>324 (48.1%)</td>
<td>0.36</td>
</tr>
<tr>
<td>Symptomatic infarcts</td>
<td>54 (55.1%)</td>
<td>44 (44.9%)</td>
<td>0.36</td>
</tr>
<tr>
<td>Silent infarcts</td>
<td>295 (51.3%)</td>
<td>280 (48.7%)</td>
<td>0.56</td>
</tr>
</tbody>
</table>