Multimodal Magnetic Resonance Imaging Studies of Migraines Related to Increasing Risk Factors for Brain Lesions Would Be an Optimal Research Focus: A Pilot Literature Citation Analysis

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To the Editor: Migraine is the third most prevalent headache disorder and the seventh leading cause of disability worldwide. The first magnetic resonance imaging (MRI) migraine study was reported in 1995,[1] with many subsequent MRI migraine studies appearing after the development of structural brain and functional MRIs. Advanced MRI techniques such as voxel-based morphometry, advanced brain structure segment, and resting functional MRI (fMRI) have led to significant discoveries. MRI has played a key role in the diagnosis, evaluation, and understanding of migraine neuromechanisms.

Published MRI migraine studies have provided detailed information about migraines. The current study is a literature analysis investigating the citation links of MRI migraine research.

The search strategy assessed brain changes studied using MRI in patients with migraines. The keywords used were "migraine" and "magnetic resonance imaging" according to the MESH search strategy in PubMed (https://www.ncbi.nlm.nih.gov/pubmed). The Web of Science (WOS; Core Collection, http://isiknowledge.com) database was searched for the expressions "migraine" and "magnetic resonance imaging." The timespan included all years. The indexes included the Science Citation Index Expanded, the Conference Proceedings Citation Index-Science, the Current Chemical Reactions-Expanded, and the Index Chemicus.

All the selected documents were analyzed using HistCite (version 12.03.17, http://www.histcite.com/). The processing steps were as follows: (1) the search results were output as plain text files with full records (Recs) plus cited references (CRs); (2) the results were imported into the HistCite tool, and the analysis index included the number of Recs, local citation scores (LCSs), global citation scores (GCSs), local CRs (LCRs), CRs, total LCSs (TLCSs, the total citations in the authors' collection), and total GCSs (TGCSs, the total citations in WOS publications by the authors in the collection); and (3) a graph analysis including the backward and forward methods using the LCS index. The backward method corresponded to the citation links, and the forward method reflected the development progress.

In the current study, 840 Recs were obtained and listed as follows: 3571 authors, 302 journals, 16,822 CRs, 1920 keywords, 23 publication years (January 1, 1995, to September 14, 2017), 9 document types, 10 languages, 1109 institutions, 1872 institutions with subdivisions, and 50 countries.

According to the analysis of the LCS index, the top 10 documents are listed in Supplementary Table 1. The LCS was cited 29–61 times in the current collection. Kruit's study had the highest LCS (cited 61 times). The top 10 documents with the highest LCR are listed in Supplementary Table 2; Bhaska's study had the highest LCR (38 references).

The top 10 journals according to the Recs and the TLCS are listed in Supplementary Table 3. The journal with the highest Recs was *Cephalalgia* (87 documents), and the journal with the highest TLCS was *Headache* (cited 335 times).

The institutional subdivision with highest Recs was Harvard University Medical School (24 documents), and the institutional subdivision with the highest TLCS was Leiden University Medical Center (cited 195 times) [Supplementary Table 4]. The country with highest Recs and TLCS was the United States (260 documents and 667 citations, respectively) [Supplementary Table 5].

A graph analysis using the backward method demonstrated that MRI migraine studies were classified into two subdivisions: (1) migraine

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as a risk factor for subclinical brain lesions from a clinical viewpoint and (2) gray matter structural changes over the whole brain in migraine from an MRI perspective [Figure 1a]. Based on the forward method, MRI migraine studies were categorized into two branches: (1) migraines related to the increasing risk of brain lesions such as deep white matter lesions, subclinical posterior circulation infarcts, and brain iron accumulation and (2) alteration of fMRI in migraines [Figure 1b].

The current research demonstrated that from 1995 to 2017, MRI migraine studies evolved from conventional MRI visual observations to advanced neuroimaging. MRI and processing techniques improved the understanding of the migraine brain. The current study referred to 840 MRI studies, 50 countries, 1109 institutions, and 3571 authors, proving that MRI plays a key role in migraine research.

All of the documents searched in this study were evaluated using LCS and GCS. LCS reflected the citation scored in the current collection, and the literature with the highest LCS was considered the most important in this research field. For example, Kruit's study had the highest LCS, demonstrating that migraine as a risk factor for subclinical brain lesions has been widely accepted. However, GCS reflected the GCS in the WOS database, but did not indicate the importance of the literature in the research field. For example, for one Rec in the current analysis, it had the highest GCS (608), while its LCS was only 2, suggesting that it was cited only two times in the current data collection (the research field). Therefore, LCS was a very important citation index.

LCR represented the local CR, referring to the number of references of the Rec in the local data collection. The document with the highest LCR value was the most important research focus and indicated the research direction. In the current study, results indicated that MRIs could be used to reveal the role of cortical spreading depression to understand the pathophysiology of migraine in future research.

Based on Recs and the TLCS analysis, it was easy to locate the submitting journal and the most important journal in the research field and to find the institution producing the best research papers and the most important institution in the research field. The top 10 journals and institutions are listed in Supplementary Tables 3 and 4; these were the most helpful in locating the key journals and institutions in MRI migraine studies.

The graph analysis provided valuable information for research on MRI migraine studies. MRI studies from 1995 to 2017 were classified into two branches. One focused on clinical practice, which confirmed that the presence of migraines was a risk factor for subclinical brain lesions such as white matter lesions combined with conventional MRI. The other branch focused on gray matter's structural changes throughout the whole brain using advanced MRI techniques (voxel-based morphometry) in migraine patients with[2] or without[3] T2-visible white matter lesions. The forward method was used to assess the development progress in these two branches. The first branch developed from migraines as a risk factor to migraines related to the increasing risk of brain lesions,[4] and the second branch developed from gray matter structural analysis to fMRI studies.[5] Summarizing the aforementioned analysis, migraines related to increasing risk factors for brain lesions using multimodal MRI would be an appropriate focus of future research.

The graph analysis also introduced an interesting topic: the "cause or effect" relationship between migraines and subclinical brain lesions. Until recently, this was relatively difficult to assess due to the lack of diagnostic evidence. In clinical practice, migraine patients commonly undergo computed tomography (CT) examinations, and normal CT imaging findings could lead to the conclusion that migraines cause no definite brain lesions. However, MRI has a very high soft-tissue resolution and subclinical brain lesions can be clearly observed. Therefore, migraine patients should undergo MRI examinations, which might answer the aforementioned question as more MRI results are obtained and summarized.

The limits in the current study were as follows: (1) the database included only the WOS (Core Collection) because HistCite analyzed only data from the WOS, so other databases should be

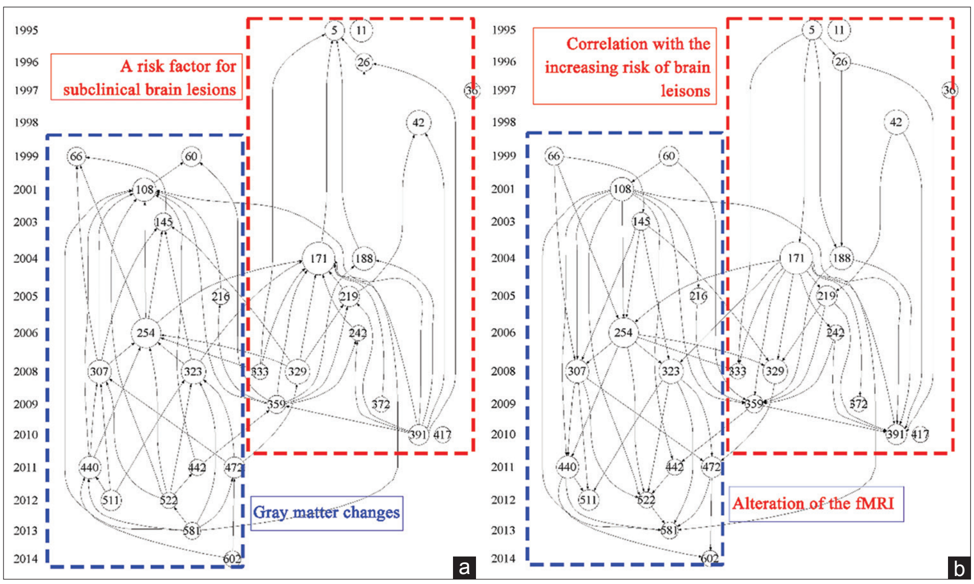

Figure 1: The graph of literature citation links using the backward (a) and forward (b) methods using HistCite software. The vertical axis represents time, and the nodes are placed on the horizontal axis. Each node represents a record, and the numbers represent LCS. The size of each node is proportional to the LCS. The red and blue boxes represent two research directions corresponding to the citation links. LCS: Local citation score; fMRI: Functional magnetic resonance imaging.

included for the future development of literature analysis tools; (2) only one literature analysis tool was used in this study, so other literature analysis tools should be used for comparison; and (3) other types of headaches should be included in future research.

In conclusion, the literature analysis herein assessed MRI migraine studies. Future research should focus on multimodal MRI migraine studies to elucidate if migraines increase the risk of brain lesions.

Supplementary information is linked to the online version of the paper on the Chinese Medical Journal website.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Top 10 documents with high LCS in the local data collection

Sequence	Top 10 documents	LCS
1	Kruit MC, *et al*. Migraine as a risk factor for subclinical brain lesions. JAMA 2004;291:427-34	61
2	Rocca MA, *et al*. Brain gray matter changes in migraine patients with T2-visible lesions – A 3-T MRI study. Stroke 2006;37:1765-70	51
3	Cutrer FM, *et al*. Perfusion-weighted imaging defects during spontaneous migrainous aura. Ann Neurol 1998;43:25-31	36
4	Kim J, *et al*. Regional grey matter changes in patients with migraine: A voxel-based morphometry study. Cephalalgia 2008;28:598-604	35
5	Schmitz N, *et al*. Attack frequency and disease duration as indicators for brain damage in migraine. Headache 2008;48:1044-55	35
6	Welch KM, *et al*. Periaqueductal gray matter dysfunction in migraine: Cause or the burden of illness? Headache 2001;41:629-37	33
7	Swartz RH, *et al*. Migraine is associated with magnetic resonance imaging white matter abnormalities – A meta-analysis. Arch Neurol 2004;61:1366-8	33
8	Valfre W, *et al*. Voxel-based morphometry reveals gray matter abnormalities in migraine. Headache 2008;48:109-17	33
9	Chabriat H, *et al*. Clinical spectrum of cadasil – A study of 7 families. Lancet 1995;346:934-9	30
10	Moulton EA, *et al*. Painful heat reveals hyperexcitability of the temporal pole in interictal and Ictal migraine states. Cereb Cortex 2011;21:435-48	29

LCS: Local citation score.

Supplementary Table 2: Top 10 documents with high LCR in the local data collection

Sequence	Top 10 documents	LCR
1	Bhaskar S, *et al*. Recent progress in migraine pathophysiology: Role of cortical spreading depression and magnetic resonance imaging. Eur J Neurosci 2013;38:3540-51	38
2	Lakhan SE, *et al*. Structural and functional neuroimaging in migraine: Insights from 3 decades of research. Headache 2013;53:46-66	35
3	Chong CD, *et al*. Migraine: What imaging reveals. Curr Neurol Neurosci Rep 2016;16:64	27
4	Lai TH, *et al*. Neural plasticity in common forms of chronic headaches. Neural Plast 2015;2015:205985	23
5	Evans RW. Diagnostic testing for migraine and other primary headaches. Neurol Clin 2009;27:393-415	18
6	Jia ZH, Yu SY. Grey matter alterations in migraine: A systematic review and meta-analysis. Neuroimage Clin 2017;14:130-40	17
7	Szabo N, *et al*. White matter microstructural alterations in migraine: A diffusion-weighted MRI study. Pain 2012;153:651-6	15
8	Bilgic B, *et al*. Volumetric differences suggest involvement of cerebellum and brainstem in chronic migraine. Cephalalgia 2016;36:301-8	14
9	Colombo B, *et al*. From neuroimaging to clinical setting: What have we learned from migraine pain? Neurol Sci 2012;33:S95-7	13
10	Gelfand AA, *et al*. Ophthalmoplegic "Migraine" or recurrent ophthalmoplegic cranial neuropathy: New cases and a systematic review. J Child Neurol 2012;27:759-66	13

LCR: Local cited reference.

Supplementary Table 3: Top 10 journals with highest Recs and TLCS

Sequence	Recs		TLCS	
	Journal	Value	Journal	Value
1	Cephalalgia	87	Headache	335
2	Headache	78	Cephalalgia	298
3	Journal of Headache and Pain	26	Annals of Neurology	101
4	Neurological Sciences	26	Jama-Journal of the American Medical Association	80
5	European Journal of Neurology	19	Stroke	80
6	Pediatric Neurology	19	Archives of Neurology	69
7	Archives of Neurology	14	European Journal of Neurology	50
8	Journal of Child Neurology	14	Brain	39
9	Current Pain and Headache Reports	11	Pediatric Neurology	34
10	Journal of Neurology	11	Journal of Neurology Neurosurgery and Psychiatry	33

Recs: The number of records; TLCS: Total local citation scores.

Supplementary Table 4: Top 10 institutional subdivision with highest Recs and TLCS

Sequence	Recs		TLCS	
	Institutional subdivision	Value	Institutional subdivision	Value
1	Harvard University, Medical School	24	Leiden University, Medical Center	195
2	Leiden University, Medical Center	19	Harvard University, Medical School	148
3	Chinese People's Liberation Army General Hospital, Department of Neurology	10	National Institute on Aging, Laboratory of Epidemiology, Demography, and Biometry	145
4	Mayo Clinic, Department of Neurology	9	National Institute for Public Healthe and the Enviroment, Department of Chronic Disease and Environmental Epidemiology	81
5	Chinese People's Liberation Army General Hospital, Department of Radiology	8	Osped San Raffaele Hospital, University of Milan	62
6	Franklin Medical Center, Department of Medicine	8	Academic Hospital Maastricht, Department of Radiology	61
7	University of Munich, Department of Neurology	8	Slingeland Hospital, Department of Radiology	61
8	Dartmouth Hitchcock Medical Center, Division of Neurology	7	Scientific Institute, Department of Neurology, Osped San Raffaele hospital, University of Milan	60
9	Harvard University, Massachusetts General Hospital	7	Scientific Institute, Department of Neuroradiology, Osped San Raffaele Hospital, University of Milan	58
10	Institute of Diagnosis and Care Hermitage-Capodimonte	7	Saint-Antoine Hospital, Service de Neurologie	53

Recs: The number of records; TLCS: Total local citation score.

Supplementary Table 5: Top 10 countries with highest Recs and TLCS

Sequence	Recs		TLCS	
	Country	Value	Country	Value
1	USA	260	USA	667
2	Italy	112	Italy	328
3	Germany	77	Netherlands	242
4	China	55	UK	146
5	UK	49	Germany	118
6	Turkey	45	France	93
7	Spain	42	Korea	54
8	Japan	40	China	49
9	Netherlands	33	Canada	46
10	France	32	Switzerland	45

Recs: The number of records; TLCS: Total local citation score.