DOI:https://doi.org/10.53555/nnmhs.v9i5.1682 Publication URL: https://nnpub.org/index.php/MHS/article/view/1682

POST ISCHEMIC STROKE IMAGING AND ITS CLINICAL RELEVANCE: A SYSTEMATIC REVIEW

Assyifa Amalia Amin*

**Faculty of Medicine, Hasanuddin University, Indonesia*

Corresponding Author:
assyifamaliamin@gmail.com

Abstract

Stroke is a focal or global functional brain disorder that starts suddenly and lasts longer than 24 hours and is caused by changes in cerebral blood flow. It is not caused by transient cerebral circulatory abnormalities, brain tumors, or secondary strokes as a result of trauma or infection. Strokes can develop in any part of the brain. Ischemia or brain hemorrhage are also potential causes of a stroke that occurs suddenly and leads in neurologic impairments. Strokes are classified into two types: bleeding and non-bleeding. Both are potentially fatal. Several studies have found that imaging is required before treating an acute ischemic stroke. The importance of imaging after stroke treatment, on the other hand, is less obvious. Bleeding, particularly cerebral haemorrhage, is the most feared complication in people who have had acute ischemic stroke treatment. As a result, the AHA/ASA IV-tPA guidelines recommend that a non-contrast computed tomography (NCCT) brain scan be performed at least 24 hours after therapy. Non-contrast CT (NCCT) is still the cheapest, quickest, most generally available, and simplest method for diagnosing intracerebral bleeding after an ischemic stroke. However, MRI with the right sequences may be able to detect the same thing. The NCCT may frequently detect hyperdense regions following treatment for acute ischemic stroke. Magnetic resonance imaging (MRI) is one of the most commonly used imaging methods both before and after stroke treatment due to the wealth of information it gives. Finally, post-ischemic stroke imaging is becoming increasingly essential because it can provide both specific clinical guidance and a better knowledge of the processes that occur after such a severe impact on the brain. It may aid in the prediction of long-term outcomes and, in the future, may assist clinicians in tailoring and optimizing rehabilitation efforts for specific patients.

Katakunci: *Anatomy; Clinical; Imagig; Post ischemic stroke*

INTRODUCTION

Stroke is a focal or global functional disease of the brain that occurs abruptly, more than 24 hours, and originates from abnormalities in cerebral blood flow. It is not caused by temporary cerebral circulation disorders, brain tumors, or secondary strokes due to trauma or infection. Stroke can occur anywhere in the brain. Ischemia or bleeding in the brain are both potential causes of a stroke that comes on quickly and results in neurologic deficits. There are two categories of stroke: bleeding and non-bleeding. Both can be life-threatening.[1–3]

Endothelial cell damage and loss, which exposes the subendothelium and leads to the activation of platelets by the subendothelium, activation of the clotting cascade, suppression of fibrinolysis, and blood stasis, can be examples of thrombogenic causes. Turbulence in the flow of blood can be caused by arterial stenosis, which can then raise the risk of thrombus development, atherosclerosis, and platelet compliance, all of which can contribute to the creation of blood clots that can clog arteries.[1,4]

Based on statistical data in America, every year there are 750,000 new stroke cases in America. The data shows that every 45 minutes, one person in America has a stroke. As many as 57.9% of strokes have been diagnosed by health workers. The prevalence of coronary heart disease, heart failure, and stroke seems to increase with increasing age of the respondents.[2,5,6] The incidence of stroke continues to increase with age. The higher a person's age, the higher the chance of having a stroke. In general, it can be said that the incidence of stroke is 200/100,000 people in 1 year. When viewed from the age group aged 30-44 years with an incidence rate of 0.2/1000 people.[7]

Cerebral vessels have a major role in directing brain development, regulating homeostasis, and contributing to pathological processes. After an ischemic stroke, decreased blood flow causes changes and changes in the shape of the blood vessels. The temporal profile of vascular changes after stroke is not well understood. Growing evidence suggests that the early phase of increased cerebral blood volume (CBF) is likely due to increased collateral flow also known as arteriogenesis, whereas the late phase of increased CBV is associated with increased angiogenesis.[8]

Angiogenesis promotes pro-angiogenic factors and circulating endothelial progenitor cells (EPCs), while arteriogenesis causes endothelium activation and inflammation. Angiogenesis has not been found to improve functional recovery in acute stroke patients, but collateral status has various prognostic consequences. Studying collateral recruitment and CBF. Understanding arteriogenesis and angiogenesis improves ischemic stroke treatment.[8] Imaging modality is still debated and differs by institution.[9]

There are several elements to consider, including the differential diagnosis, imaging technique availability and reliability, and time and experience needed to execute and interpret the scanning. Other competing interests include the modality's cost, patient comfort, and monitoring during imaging.[9] We give some current and research-stage methods to clarify this topic.This article proved the post ischemic stroke imaging and its clinical relevance.

METHODS

The methodology of this systematic review was based on the criteria established by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 checklist. The purpose of this systematic review was to assess the clinical relevance of papers related to post ischemic stroke imaging. The subject matter being examined is the focus of the studies under evaluation. To effectively evaluate existing studies, it is important that these studies meet certain criteria, including: 1) It is important that articles are available online for easy accessibility; 2) It is preferred that articles are written in English; and 3) The systematic review will only consider articles published between 2015 and the present time.

The search for studies to be included in the systematic review was carried out from May 4th, 2023 using the PubMed and SagePub databases by inputting the words: “post ischemic stroke imaging” and “clinical relevance”. Where *"post"[All Fields] AND ("ischemic stroke"[MeSH Terms] OR ("ischemic"[All Fields] AND "stroke"[All Fields]) OR "ischemic stroke"[All Fields]) AND ("image"[All Fields] OR "image s"[All Fields] OR "imaged"[All Fields] OR "imager"[All Fields] OR "imager s"[All Fields] OR "imagers"[All Fields] OR "images"[All Fields] OR "imaging"[All Fields] OR "imaging s"[All Fields] OR "imagings"[All Fields]) AND ("clinical relevance"[MeSH Terms] OR ("clinical"[All Fields] AND "relevance"[All Fields]) OR "clinical relevance"[All Fields])* is used as search keywords.

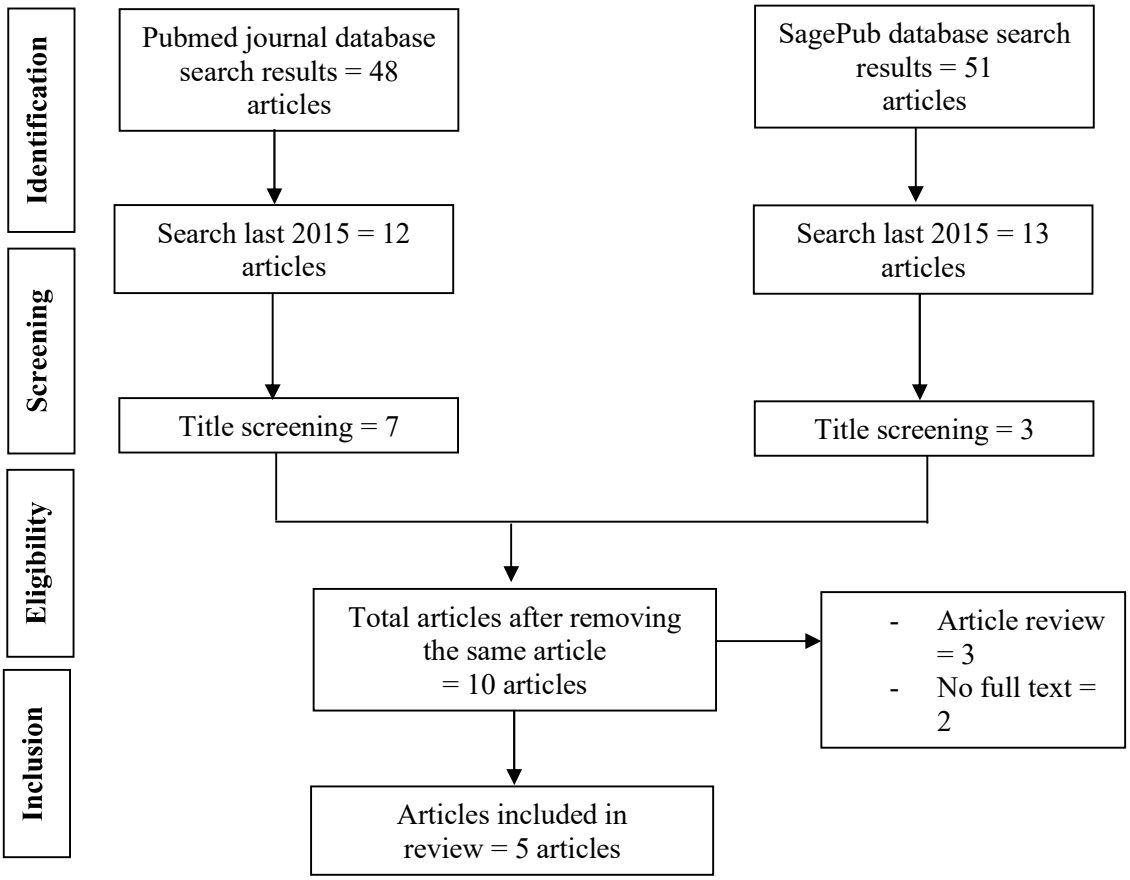

Figure 1. Article search flowchart

The study's inclusion and exclusion criteria were revised following a thorough review of the literature based on an inspection of the titles and abstracts of previously published research. Only research projects that met all of the requirements were included in the systematic review. The title, author, publication date, country of origin, research design, and variables being researched are just a few of the crucial factors to consider when comparing one research study to another.

The offered content has been presented in a specific format for your attention and critical evaluation. The writers conducted independent appraisals of a selection of research endeavors stated in the titles and abstracts of the publications to determine whether the investigations were eligible for inclusion. The full texts of the studies that meet the criteria for inclusion in the systematic review will then be assessed to determine which publications are eligible for categorical inclusion in the review.

RESULT

Veltkamp, et al (2020)[10] conducted a study with 309 patients (205 men [66%]; age = 68 ± 10 years) had ischemic stroke identified during the median follow-up of 11 (interquartile range [IQR] = 12) months (annualized rate, 4.6%). Diagnostic testing was insufficient for etiological classification in 39 patients (13%). Of 270 classifiable ischemic strokes, 156 (58%) were embolic stroke of undetermined source (ESUS) and 114 (42%) were non-ESUS (37 [32%] cardioembolic, 26 [23%] atherosclerotic, 35 [31%] lacunar, and 16 [14%] other determined cause).

Atrial fibrillation was found in 27 patients (9%) with recurrent ischemic stroke and was associated with higher morbidity (median change in modified Rankin scale score 2 [IQR, 3] vs 0 (IQR, 1]) and mortality (15% vs 1%) than other causes. Risk of recurrence did not differ significantly by subtype between treatment groups. For both the qualifying and recurrent strokes, location of infarct was more often in the left (46% and 54%, respectively) than right hemisphere (40% and 37%, respectively) or brainstem or cerebellum (14% and 9%, respectively).[10]

Portegies, et al (2015)[11]v conducted a study with 1,252 patients. 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 [CI] = 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).

Table 1. The litelature include in this study

Author	Origin	Method	Sample Size	Result
Veltkamp, 2020[10]	United Kingdom (UK), Canda, Brazil, Italy, Argentina	Randomized clinical trial	7,213 patients	In this secondary analysis of data from randomized clinical trials, the majority of recurrent strokes following ESUS were embolic and of unknown origin. Recurrences of atrial fibrillation were uncommon, but frequently fatal and incapacitating. Important for an effective antithrombotic strategy is a comprehensive investigation of the source of the embolism.
Portegies, 2015[11]	Netherland	Prospective study	1,252 patients	Ischemic strokes and transient ischemic attacks (TIAs) happen more often on the left side than on the right, but this is not true for infarcts on an MRI. This shows that strokes and TIAs on the left side are easier to spot. So, more attention should be paid to the signs of right-sided strokes and TIAs.
Rostanski, 2022[12]	USA	Randomized clinical trial	4,881 patients	The presence of an acute infarct on index imaging was found to be related with an elevated risk of recurrent stroke as well as a more apparent benefit from clopidogrel-aspirin in this particular trial. Validating these findings should be the primary focus of study to be done in the future before directing acute clopidogrel-aspirin treatment toward specific patient categories.
Coutts, 2019[13]	Canada	Cross sectional study	1,028 patients	This study suggested that patients with transient ischemic attack and traditionally low-risk symptoms bear a substantial risk of acute stroke, as defined by diffusion restriction (DWI-positive) on an MRI of the brain. An early MRI is required for a conclusive diagnosis.
Chaturvedi, 2017[14]	India	Prospective cohort study	7,889 patients	In a national health care system, approximately 40% of patients with TIA/minor stroke underwent MRI within two days. Several patient- and facility-level variables appeared to influence the performance of MRI, suggesting that there has been partial adoption of the previous guideline that recommended MRI for patients with TIA.

Rostanski showed 1,793 patients (36.8%) had an acute infarct on initial imaging. Infarct on index imaging was related to ischemic stroke during follow-up (hazard ratio [HR] = 3.68; 95% CI = 2.73-4.95; P = 0.001). Clopidogrel-aspirin versus aspirin alone was associated with a lower risk of ischemic stroke in patients with an infarct on index imaging (HR = 0.56; 95% CI = 0.41-0.77; P = 0.001) compared with those without an infarct on index imaging (HR = 1.11; 95% CI = 0.74-1.65; P = 0.62), with a significant interaction association (P for interaction = 0.008).[12]

Coutts, et al (2019)[13] showed 139 patients (13.5%) had an acute stroke as defined by diffusion restriction detected on MRI scans (DWI positive). The final diagnosis was revised in 308 patients (30.0%) after undergoing brain MRI. There were 7 (0.7%) recurrent strokes at 1 year. A DWI-positive brain MRI scan was associated with an increased risk of recurrent stroke (relative risk [RR] = 6.4; 95% CI = 2.4-16.8) at 1 year. Absence of a DWI-positive lesion on a brain MRI scan had a 99.8% negative predictive value for recurrent stroke.

Factors associated with MRI evidence of stroke in multivariable modeling were older age (OR = 1.02; 95% CI = 1.00-1.04), male sex (OR = 2.03; 95% CI = 1.39-2.96), motor or speech symptoms (OR = 2.12; 95% CI = 1.37-3.29), ongoing symptoms at assessment (OR = 1.97; 95% CI = 1.29-3.02), no prior identical symptomatic event (OR = 1.87; 95% CI = 1.12-3.11), and abnormal results of initial neurologic examination (OR = 1.71; 95% CI = 1.11-2.65).[13]

Other study with Age >80 years, prior stroke, history of atrial fibrillation, heart failure, coronary artery disease, anxiety, and low hospital complexity were associated with increased odds of CT performance, whereas blood pressure >140/90 mm Hg and high hospital complexity were associated with increased odds of MRI. MRI performance was associated with diplopia (87% had MRI, p = 0.03), neurologic consultation on the day of presentation (73% had MRI, p 0.0001), and symptom duration of >6 hours (74% had MRI, p = 0.0009).[14]

DISCUSSION

There are 3 main pathophysiological mechanisms underlying the occurrence of ischemic stroke including large blood vessel disease (atherosclerosis), small blood vessels (arteriosclerosis) and embolism (cardioembolic). Ischemic stroke causes disruption of the blood supply to the brain either due to thrombus formation or embolism.[3,15,16] Ischemia reduces cell ATP and hypoxia, thus the cell cannot maintain its ionic gradient and depolarization. Cytotoxic edema results from cell water and sodium and calcium ion inflow. Acute vascular blockage causes heterogeneous ischemia. Residual flow limits local blood flow.[1,2]

The process of ischemia and reperfusion can stimulate the production of reactive oxygen species (ROS), mitochondrial dysfunction and glutamate release which will be followed by repeated depolarizations and can cause changes in electrolyte content both intra and extracellular. Changes in nerve excitability and electrolytes that occur suddenly in the early phase of a stroke can cause changes in the structure of the nerves in the peri-infraction area so that they can affect the survival of the nerves in that area.[1,2,17]

Lack of oxygen causes acidosis and triggers impaired enzyme function. Acidosis is followed by cerebral edema, especially in the glial tissue, and affects the microcirculation. Therefore there is an increase in vascular resistance and then a decrease in perfusion pressure resulting in an expansion of the ischemic area. Cerebral ischemia impairs sodium-calcium exchange which also occurs in the plasma membrane of cells.[1,2]

The resulting calcium influx causes the release of a number of neurotransmitters, including large amounts of glutamate, which in turn activates N-methyl-D-aspartate (NMDA) and other expression receptors.[17] This causes calcium influx, glutamate release, and local amplification of ischemia. The calcium inflow activates various degradative enzymes that cause damage to cell membranes and neuronal structures. Free radicals, arachidonic acid, and nitric oxide are generated, causing further neuronal damage.[1,3]

Several reviews have confirmed that imaging is necessary before treating an acute ischemic stroke. However, the importance of imaging after stroke treatment is less clear. Bleeding, especially cerebral haemorrhage, is the most dreaded consequence in individuals who have undergone therapy for acute ischemic stroke. Therefore, the AHA/ASA IV-tPA guidelines propose getting a non-contrast computed tomography (NCCT) brain scan at least 24 hours after therapy.[18,19]

Study found that qualifying ESUS and recurrent ischemic stroke were more often in the left hemisphere than in the right. This is possibly because symptoms in the left hemisphere are easier to notice.[10,11] There may be a preference for emboli to travel from the heart to the brain via the left carotid territory rather than the right carotid territory, although this is a hypothesis rather than a proven fact.[20] Instead, it is possible that qualifying and recurrent strokes were caused by the same vascular culprit lesion in a carotid or vertebrobasilar artery. This would mean that the lesion was initially nonstenotic.[21]

Non-contrast CT (NCCT) is still the approach that is cheapest, quickest, most widely available, and easiest for detecting intracerebral hemorrhage following an ischemic stroke. However, MRI with the necessary sequences may come close to being able to detect the same. After therapy for acute ischemic stroke, the NCCT may frequently reveal hyperdense regions. These can occur as a result of a rupture in the blood-brain barrier, extravasation (enhancement) of contrast medium, or hemorrhage.[22]

Based on study findings, it may be preferable to use MRI in the acute evaluation of patients with TIAMS to identify those with the highest risk of recurrent stroke. Currently, the use of MRI for TIAMS evaluation is highly variable, and clinicians have limited ability to predict which patients will have infarct based on imaging.[12–14] Further research is required to determine whether MRI should be used to target TIAMS patients who are most likely to benefit from clopidogrel-aspirin. The use of this MRI to detect infarcts may be especially important in patients with a higher risk of hemorrhagic complications.[23]

Because of the abundance of information it provides, magnetic resonance imaging (MRI) is one of the imaging procedures that is most often conducted both before and after stroke treatment. There is a wide variety of possible sequences, each of which has the potential to extract meaningful information dependent on the requirements of the therapeutic setting. The primary obstacles are the expenses, the amount of time it takes, and the lack of readily available scanners and medical professionals who are trained to read and report the results.[24]

CONCLUSION

Finally, post-ischemic stroke imaging is becoming increasingly essential because it can provide both specific clinical guidance and a better knowledge of the processes that occur after such a severe impact on the brain. It may aid in the prediction of long-term outcomes and, in the future, may assist clinicians in tailoring and optimizing rehabilitation efforts for specific patients.

REFERENCES

[1]. Donnan GA; Fisher M; Macleod M; et al. Stroke. Lancet. 2008;371(9624):1612–23.
[2]. Ginsberg L. Lecture Notes Neurology. Jakarta: Erlangga; 2009.
[3]. Awad IA; Chireau MV. Stroke Overview. Stroke. 2014;12(3):34–50.
[4]. Goldstein LB; Bushnell CD; Adams RJ; et al. Guidelines for the primary prevention of stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2011;42(2):517–84.
[5]. Catalan Society of Neurology. Official Guidelines for diagnosis and treatment. In: Cerebrovascular Diseases. 2nd ed. Societat Catalana de Neurologia. Barcelona: Societat Catalana de Neurologia; 2011. 159–240 p.
[6]. Zheng H; Cao N; Yin Y; et al. Stroke recovery and rehabilitation in 2016: a year in review of basic science and clinical science. Stroke Vasc Neurol. 2017;2(4):222–229.

[7]. Dourman K. Waspadai Stroke Usia Muda. Cermin Dunia Kedokt. 2013;
[8]. Liu J; Wang Y; Akamatsu Y; et al. Vascular remodeling after ischemic stroke: mechanisms and therapeutic potentials. Prog Neurobiol. 2014;115:138–56.
[9]. Yeo LLL, Tan BYQ, Andersson T. Review of Post Ischemic Stroke Imaging and Its Clinical Relevance. Eur J Radiol. 2017 Nov;96:145–52.
[10]. Veltkamp R, Pearce LA, Korompoki E, Sharma M, Kasner SE, Toni D, et al. Characteristics of Recurrent Ischemic Stroke After Embolic Stroke of Undetermined Source: Secondary Analysis of a Randomized Clinical Trial. JAMA Neurol. 2020 Oct;77(10):1233–40.
[11]. Portegies MLP, Selwaness M, Hofman A, Koudstaal PJ, Vernooij MW, Ikram MA. Left-sided strokes are more often recognized than right-sided strokes: the Rotterdam study. Stroke. 2015 Jan;46(1):252–4.
[12]. Rostanski SK, Kvernland A, Liberman AL, de Havenon A, Henninger N, Mac Grory B, et al. Infarct on Brain Imaging, Subsequent Ischemic Stroke, and Clopidogrel-Aspirin Efficacy: A Post Hoc Analysis of a Randomized Clinical Trial. JAMA Neurol. 2022 Mar;79(3):244–50.
[13]. Coutts SB, Moreau F, Asdaghi N, Boulanger J-M, Camden M-C, Campbell BC V, et al. Rate and Prognosis of Brain Ischemia in Patients With Lower-Risk Transient or Persistent Minor Neurologic Events. JAMA Neurol. 2019 Dec;76(12):1439–45.
[14]. Chaturvedi S, Ofner S, Baye F, Myers LJ, Phipps M, Sico JJ, et al. Have clinicians adopted the use of brain MRI for patients with TIA and minor stroke? Neurology. 2017 Jan;88(3):237–44.
[15]. Lumbantobing SM. Neurologi Klinik Pemeriksaan Fisik dan Mental. Jakarta: Balai Penerbit FKUI; 2018.
[16]. Price SA LM. Patofisiologi Konsep Klinis Proses-Proses Penyakit. Jakarta: EGC; 2016.
[17]. Dichgans M. Cognition in CADASIL. Stroke. 2009;40(3):45–7.
[18]. Adams Jr HP, Del Zoppo G, Alberts MJ, Bhatt DL, Brass L, Furlan A, et al. Guidelines for the early management of adults with ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: the American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists. Stroke. 2007;38(5):1655–711.
[19]. De Lucas EM, Sánchez E, Gutiérrez A, Mandly AG, Ruiz E, Flórez AF, et al. CT protocol for acute stroke: tips and tricks for general radiologists. Radiographics. 2008;28(6):1673–87.
[20]. Rodríguez Hernández SA, Kroon AA, van Boxtel MPJ, Mess WH, Lodder J, Jolles J, et al. Is there a side predilection for cerebrovascular disease? Hypertens (Dallas, Tex 1979). 2003 Jul;42(1):56–60.
[21]. Ntaios G, Swaminathan B, Berkowitz SD, Gagliardi RJ, Lang W, Siegler JE, et al. Efficacy and Safety of Rivaroxaban Versus Aspirin in Embolic Stroke of Undetermined Source and Carotid Atherosclerosis. Stroke. 2019 Sep;50(9):2477–85.
[22]. Manvel A, Vladimir K, Alexander T, Dmitry U. Radiologist-level stroke classification on non-contrast CT scans with deep U-Net. In: Medical Image Computing and Computer Assisted Intervention–MICCAI 2019: 22nd International Conference, Shenzhen, China, October 13–17, 2019, Proceedings, Part III 22. Springer; 2019. p. 820–8.
[23]. Wang D, Gui L, Dong Y, Li H, Li S, Zheng H, et al. Dual antiplatelet therapy may increase the risk of non-intracranial haemorrhage in patients with minor strokes: a subgroup analysis of the CHANCE trial. Stroke Vasc Neurol. 2016 Jun;1(2):29–36.
[24]. Heo TS, Kim YS, Choi JM, Jeong YS, Seo SY, Lee JH, et al. Prediction of stroke outcome using natural language processing-based machine learning of radiology report of brain MRI. J Pers Med. 2020;10(4):286.