Role Of AI In Predicting Acute Ischemic Stroke Outcomes: A Systematic Review

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Abstract:

Stroke is a leading cause of death and disability worldwide. Timely diagnosis and intervention are very important in managing stroke. With the emergence of artificial intelligence (AI), there is a growing focus on using machine learning and deep learning algorithms in stroke prediction, screening, management, prognosis etc. Through this systematic review, we try to synthesize the current evidence on the use of AI in predicting stroke outcomes, mainly sICH, LVO, final infarct and 90 day mRS. A comprehensive search of PubMed/Medline, Wiley Online Library, and ResearchGate yielded 33 studies meeting the inclusion criteria. AI models, such as artificial neural networks (ANNs), support vector machines (SVMs), convolutional neural networks (CNNs), XGBoost, and random forest, were utilized across these studies to analyze clinical data,imaging features, and demographic factors. Based on multimodal imaging data, AI models showed high accuracy in predicting sICH risk, detecting LVO, and calculating the final infarct size. These models also demonstrated promise for predicting 90-day post-stroke outcomes, which could help physicians with treatment planning and patient counseling. However, there are still issues with model validation, transparency, and workflow integration into clinical settings. In conclusion, AI holds significant promise in revolutionizing acute stroke management. While the studies highlight the potential benefits of AI in improving patient outcomes, further research is needed to address existing challenges and ensure the seamless integration of AI tools into clinical practice. ---

Date of Submission: 08-01-2025 Date of Acceptance: 18-01-2025

I. Introduction:

Often called a "brain attack," a stroke is caused by a sudden decrease or interruption of blood supply to a portion of the brain, which can have a cascading effect on neurological functions. This disruption may be caused by a blood vessel rupture (hemorrhagic stroke) or blockage (ischemic stroke), each of which poses unique difficulties for diagnosis, treatment, and long-term results. The term "stroke" describes a broad range of disorders brought on by blockage or bleeding into the blood arteries supplying the brain. Genetic factors, diabetes, atherosclerosis, high blood pressure, and homocysteine levels are risk factors. Blood flow deficiencies, low ATP and energy storage, ionic disturbance, metabolic failure, and cell death occur in the central region of the damaged brain and progress within minutes. Oxidative/nitrosative stress, apoptotic-like cell death, and excitotoxicity and ionic imbalance are the three primary processes that lead to cell death during stroke (Tadi, 2023).

The symptoms of a stroke can take many different forms, from sudden weakness or numbness on one side of the body to trouble speaking or interpreting words. Strokes are a major global cause of disability and death that affect people of all ages, genders, and socioeconomic backgrounds. For this reason, it is critical that people understand their risk factors, notice warning signals, and seek emergency medical assistance

Importance of early screening and detection:

Stroke is the second most common cause of mortality and third most common cause of disability worldwide (Chugh, 2019). Since stroke is an urgent medical emergency, it is critical to screen and detect patients as soon as possible. Certain treatments for stroke, such as thrombolytic therapy and endovascular interventions, are most effective when administered within a narrow time window after the onset of

symptoms. Prompt detection facilitates the timely implementation of these therapies, which may mitigate the degree of brain impairment and enhance overall results.

A stroke is characterized by an interruption of blood supply to the brain, which causes brain cells to die quickly. Early screening makes it easier to determine if a stroke is hemorrhagic or ischemic quickly, and it makes early measures to stop further damage or restore blood flow easier. Preserving important brain tissue is essential to avoid cognitive deficits and long-term disability. The overall prognosis of stroke patients is improved by early detection and treatments. Quick access to quality medical care can improve recovery prospects, lessen the degree of neurological abnormalities, and lower the risk of consequences, such as disability and death.

Overview of various AI techniques employed in stroke screening (ML,DL).

Some of the areas where AI has been used in stroke includes Decision automation, routine clinical decision support, hypo-density detection, automated ASPECT scoring, prediction of prognosis etc. Whether a CT scan shows hypodensities or early ischemic changes suggestive of a stroke are two examples of reasonably straight problems that can be addressed by computerisation of procedures with decision automation to streamline clinical decision making (Bivard et al., 2020). Another area where automation can be applied is perfusion imaging. With the use of post-processing software, perfusion parameters can be assessed via deconvolution of artery and tissue signals in perfusion imaging, with predetermined thresholds allowing for automated quantification and segmentation of the infarct core and tissue at risk. While there are a number of software programs available for post-processing CT and MR perfusion images, the international guidelines for stroke treatment currently mention the RApid processing of Perfusion and Diffusion [RAPID] program (iSchemaView), which has been used in several significant stroke trials (Corrias et al., 2021). Machine learning also has potential in automatic lesion identification or segmentation for accurate diagnosis. Machine learning based diagnosis attempts have been made in developing tools for ASPECT scoring, detection of hyperdense middle cerebral artery (MCA) dot sign on CT, automated quantification of cerebral edema in malignant hemispheric infarct patients etc. Recently, machine learning of CT images has been attempted for predicting the symptomatic ICH risk with a small cohort of acute ischemic stroke patients (Lee et al., 2017).

Rationale for conducting systematic review on this topic:

The complexity of acute stroke assessment has increased due to greater options for imaging and treatment, making it difficult for stroke physicians to stay current with developments. Parallel to this, advances in the breadth and depth of image analysis tools have raised the level of expertise needed to interpret imaging data, as evidenced by the rapid modifications made to stroke treatment and assessment recommendations in the last two years. Artificial intelligence (AI) in clinical decision making has the potential to decrease inter-rater variation in standard clinical practice and make it easier to extract crucial data that could enhance stroke patient identification, treatment response prediction, and patient outcomes.

An increasing amount of research is being done on the use of AI in the diagnosis and treatment of strokes. The effectiveness of AI algorithms in deciphering medical pictures, forecasting stroke risk, and assisting in clinical decision-making has been examined in a large number of research publications and reviews. With this growing body of evidence, there is a need for comprehensive evaluation and synthesis. As of now, there are no comprehensive systematic reviews trying to synthesize this large body of evidence. In order to determine the present state of knowledge, pinpoint methodological nuances, and determine the general effectiveness and dependability of AI in acute stroke scenarios,it is imperative that the literature be thoroughly reviewed.

Research Questions :

- Are AI methods for screening and diagnosis of stroke comparable to conventional clinical practice? - Does AI algorithms have real life potential to be integrated into clinical practice to assist clinicians in decision making?

II. Methodology:

An initial scoping search was conducted through Google scholar to gain information regarding the type of studies available in literature and to understand the kind of keywords usually seen in the titles. Afterwards, a thorough search was conducted using PubMed/Medline, Wiley Online library and Research gate. Original articles reporting AI tools used in diagnosis, screening or prognosis prediction will be included in the systematic review.

Studies were searched using the keywords 'Stroke' or 'Ischemic' or 'Hemorrhagic' or 'infarction' or 'Cerebrovascular accident' for terms related to stroke and 'AI' or 'artificial intelligence' or 'deep learning' or 'machine learning' for terms related to AI. Other inclusion criteria include full text articles published in English, human subjects, adult patients (age above 18 years) etc. Papers were further chosen based on the outcome measure that was studied. Only articles studying 90 day mRS, final infarct, large vessel occlusion (LVO), and intracerebral hemorrhage (sICH) were chosen.

Study Selection:

Studies to be included in the review were chosen by a two stage screening process. The articles were first screened using title and abstract. The studies deemed relevant based on this screening were further chosen for full text screening. Studies were considered eligible for inclusion if they met the following criteria: ● Full text primary research articles available in English, reviews, gray articles, letters etc were excluded

● Studies focusing on predicting clinical outcome; mainly focusing on the following 4 outcome measures - 90 day mRS, final infarct prediction, large vessel occlusion and intra cerebral hemorrhage occurrence.

Data Extraction:

A structured data extraction template was created to collect data related to the following: general study characteristics including author, year of publication, country, study objective, AI technique, outcome endpoint, sample size, analytical methods, input data and key findings. (See Excel Table.)

PRISMA diagram:

III. Results:

We identified 126 studies based on title and abstract screening and further full text screening based on inclusion criteria identified 33 articles to be considered in the final review. Out of the 33 selected studies, 16 studies are focused on 90 day mRS, 9 on final infarct, 4 on ICH and 4 on LVO. All the selected studies were published after 2011 and more than half of them were published after 2020. 16 of the selected studies were from Europe, 8 studies were from North America, and 9 studies were from Asia. Summary of the selected studies are given in the table …. (Excel Table)

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AI in predicting symptomatic intracerebral hemorrhage (sICH):

Four out of the 33 selected studies have used machine learning to predict occurrence of intracerebral hemorrhage in acute stroke patients. Two of the studies have used multilayer perceptron(MLP) (Wang et al., 2020, Chung et al., 2020), one study has used support vector machine (SVM) (Bentley et al., 2014) and another study has used SVM, MLP, Probabilistic neural network (PNN) and radial basis function (RBF) (Dharmasaroja & Dharmasaroja, 2012).

Chen-Chih Chung et. al., has used data from 331 acute ischemic stroke patients to predict the risk of intracerebral hemorrhage inpatients who received tPA treatment. In this study, they have trained Artificial neural network (ANN) to predict intra cerebral hemorrhage within 72 hrs as well as 3 month mortality. Their study reports a high validation performance, with AUC of 0.94 and 0.98 for ICH and 3 month mortality respectively. High AUC values are indicative of the ability of the model to distinguish between ICH vs non-ICH. (Chung et al., 2020). Similarly, a study by Feng Wang used a three layer neural network to predict ICH. They also report similar results showing high predictability. They have tested their model for clinical usability using independent test sets as well. All sICH patients were correctly predicted to be within the high-sICH risk rank,demonstrating the clinical applicability. (Wang et al., 2020).

Another study by Paul Bentley et.al, has used SVM to predict sICH. They have mainly used CT images and NIHSS score as input to predict sICH using SVM. They have compared SVM performance with established prognostication tools and they report that the predictive performance of SVM compared favorably with that of prognostic scores(Bentley et al., 2014). Another study has tested RBF, MLP, PNN and SVM in predicting ICH. They found no significant difference in predictive value between PNN, MLP and RBF, but PNN showed significantly better performance compared to SVM. They report that using multiple ANNs increases the reliability of the prediction result. Although RBF, MLP, and PNN showed similar performance for classifying SICH following tPA, the classification results were not totally alike, suggesting an advantage of using multiple classification models over a single model. (Dharmasaroja & Dharmasaroja, 2012)

AI in detecting large vessel occlusion (LVO):

In this review, 4 of the selected studies have developed methods to detect large vessel occlusion (LVO) in acute ischemic stroke patients. Studies by Stib et.al and Meijs et.al have used convolutional neural network (CNN) to detect LVO from CT angiography images. Stib et. al reports an AUC of 0.74 with sensitivity of 77% and specificity of 71% with single phase CT angiography . This increases to an AUC of 0.89,sensitivity of 100%, and specificity of 77%, ($p=0.01$), on using phase 1,2 and 3 together (arterial, phase 1; peak venous, phase 2; and late venous, phase 3). They conclude that their deep learning model was able to detect both anterior and posterior circulation occlusions, indicating it could function as a tool to prioritize the review of patients with potential LVO by radiologists and clinicians in the emergency

setting. (Stib et al., 2020). Meijs et. al has also used CNN to detect intracranial anterior circulation LVO using 4D- CT angiography images. They reported an accuracy, sensitivity, and specificity of 92%, 95%, and 92% with an overall computation time of less than 4 minutes per case. The area under the receiver operating characteristics curve was 0.98. (Meijset al., 2020)

A study by Wade S Smith has tried to utilize Cranial accelerometry which is normally used to detect cerebral vasospasm and concussion to identify signatures which could detect LVOs in stroke patients. Three minute recordings were done using the accelerometer immediately after CT or CTA and before/after thrombectomy and the resulting waveforms were subjected to machine learning. They were able to detect LVO with an AUC of 0.79, sensitivity of 73%, and specificity of 87%, \overline{P} < 0.0001. They conclude that Headpulse recordings performed on patients with suspected acute stroke significantly identify those with LVO (Smith et al., 2019)

Another study by You et. al has used demographic data, clinical data and non-contrast CT (NCCT) to automatically detect LVOs. They used multiple machine learning tools including logistic regression, random forest, support vector machine (SVM), and eXtreme Gradient Boosting (XGboost). Best performance was shown by XGBoost, which showed a Youden index, accuracy, sensitivity, specificity, F1 score, and area under the curve (AUC) of 0.638, 0.800, 0.953, 0.684, 0.804, and 0.847, respectively. Their system is reported to be capable of automatically providing preliminary evaluations at different prehospital stages for potential AIS patients (You et al., 2020).

AI in predicting final infarct/lesion volume:

Nine out of the 33 selected studies have looked at predicting the volume of final infarct as the outcome. Out of the nine, three have used CNN, 2 have used XGboost , and others have used random forest, logistic regression, SVM and multilayer perceptron for predicting final infarct.

Yu et.al, Lucas et.al and Nielsen et.al, has used CNN to predict final infarct. Yu and Nielsen have used magnetic resonance images as input to predict outcomes, whereas Lucas et.al has used CT images. Nielsen et.al., has used deep CNN and compared it with shallow CNN. CNN deep showed significantly better performance in predicting final outcome (AUC=0.88) than generalized linear model (Nielsen et al., 2018). In the study by Yu et.al, the model, an attention-gated U-Net, was trained on MRI data from 182 patients. It achieved good performance for predicting lesion location and size, with a Dice score of 0.53 on average. In subgroups of patients with minimal or major reperfusion, the model showed comparable or better prediction accuracy than existing clinical thresholding methods. The model also performed well inpatients with partial or unknown reperfusion status where current methods are not applicable (Yu etal., 2020)

The paper by Lucas et.al proposes a method to predict ischemic stroke lesion growth based on acute CT perfusion images. A U-Net is used to segment the core and penumbra, which are then encoded into a low-dimensional shape space using a convolutional auto encoder. Linear interpolation in the latent shape space according to time-to-treatment allows prediction of the follow-up lesion in a physiologically constrained manner. Evaluation on 29 patients showed the approach could predict lesions with a Dice score of 0.46 compared to manual segmentations, outperforming alternative methods. The work demonstrates the feasibility of predicting stroke progression from core and penumbra representations learned in a nonlinear shape space (Lucaset al., 2018).

Two studies have used Xgboost for final infarct prediction. Michelle Livine et.al., used MRI data from 195 patients with acute ischemic stroke to predict the final infarct size using XGBoost and compare it to a generalized linear model (GLM). XGBoost demonstrated significantly higher performance than GLM in predicting final infarct based on acute MRI data, according to AUC and accuracy measures. The improvement was significant for both cross-validation approaches. The imaging parameters that XGBoost identified as most important for predicting infarct were time-to-peak, mean transit time, time-tomaximum, and diffusion-weighted imaging. These accounted for 87% of the predictive gain (Livne etal., 2018). Study by Malte Grosser aimed to improve prediction of tissue outcome in acute ischemic stroke patients using machine learning models that incorporated spatial features from MR images. Logistic regression, random forest, and XGBoost models were trained on diffusion, perfusion and spatial features to predict voxel-wise lesion outcome. Including spatial features like MNI coordinates or lesion probability maps significantly improved prediction performance compared to models without spatial data. The best performing models were XGBoost and random forest, which achieved state-of-the-art results when including spatial features. Features like Tmax, ADC and MTT were generally most important for prediction, while spatial features had the highest contribution (Grosser et al., 2020).

Another study by the same team aimed to develop and evaluate a local tissue outcome prediction approach using logistic regression and random forest. The approach trained machine learning models for each brain voxel position using diffusion-weighted MRI, perfusion-weighted MRI, and follow-up lesion

segmentation data from 99 patients. Logistic regression and random forest models were trained using global, local, and hybrid approaches. The local approach led to higher accuracy results compared to the global approach according to evaluation metrics like ROC AUC and Dice coefficient. Highest performance was achieved with a hybrid approach combining global and local predictions (Grosser et al., 2020).

Another study by Giacalone et.al, has tried to predict the final lesion from MRI (only perfusion images) using a support vector machine (SVM). They have shown the importance of using raw perfusion data by encoding the local environment of each voxel as a spatio-temporal texture, with an observation scale larger than the voxel. Their study has shown 95% accuracy on average using only raw perfusion data. Usually diffusion images are known to be highly predictive images for final infarct. In this study, they were able to achieve high levels of accuracy from raw perfusion images possibly because in the small cohort considered here the lesions were quite compact with a good similarity between the early perfusion lesion and the diffusion lesion (Giacalone et al., 2018).

Another study by Hassen Bahger et.al has used acute phase MR images to train an ANN (artificial neural network) to predict the final size of the infarct as a 3- month outcome. Following training and optimization, the ANN generated maps of expected outcomes for each of the 12 patients that showed a strong correlation ($r = 0.80$, $p < 0.0001$) with the T2WI at 3 months. This study suggests that the trained artificial neural network (ANN) can reliably and accurately assess the 3-month ischemic lesion on T2WI (AUROC = 0.89) (Bagher-Ebadian et al., 2011). Wu Qiu et. al on the other hand has used multiphase CT angiograms (mCTA) and random forest to predict final infarct. They conclude that the mCTA machine learning models described in this study are able to predict tissue fate in patients with AIS similar to what current CTP (computed tomographic perfusion) techniques can do. The mCTA machine learning models could therefore help support physicians in making clinical decisions regarding acute stroke treatment, especially in hospitals without CTP capabilities (Qiuetal., 2021).

AI in predicting 90 days post-stroke outcome:

Out of the 33 selected studies, 16 studies are focused on predicting the 90 day outcome in acute ischemic stroke patients.

Study by Ezra Zhini compares the explainability of modern machine learning methods like artificial neural networks (ANNs) and tree boosting algorithms to traditional logistic regression models for clinical decision support. The researchers used clinical features to predict the 3-month outcome of stroke patients using different models. To assess explainability, they evaluated the importance of features to each model's predictions. While all models had similar predictive performance, the feature importance rankings varied. Age and initial stroke severity were consistently highly important across models. Differences were seen for less important predictors like diabetes and gender. This suggests modern methods can provide explainability comparable to traditional ones, but more validation of feature importance is needed. The study provides a first direct comparison of explainability in clinical prediction but more replication is required (Zihniet al., 2020).

Another study used machine learning techniques to predict clinical outcomes for patients undergoing endovascular treatment for acute ischemic stroke (AIS). Clinical, imaging, and angiographic data from 246 patients was analyzed. Baseline factors like age, pre-stroke status, and infarct size were important predictors of a favorable 3-month outcome. Adding data on treatment factors and follow-up imaging improved predictions. While CT perfusion captured core size well, it did not enhance predictions beyond other factors. The best model incorporated comprehensive pre, during, and post-treatment data, correctly predicting outcomes 86% of the time. The main conclusion from this study is that integrative assessment of clinical, multimodal imaging, and angiographic characteristics with machine-learning allowed the researchers to accurately predict the clinical outcome following endovascular treatment for acute ischemic stroke (Brugnara et al., 2020). Jiang et. al has reported that baseline NIHSS is the most significant predictor of outcomes among all the parameters studied (Jianget al., 2021).

Monteiro et. aland Hamann et. al has used random forest to predict functional outcome in patients after 3 months. Hamann concludes that outcome is correlated withinfarct volume, however both of them predict that ROI based imaging variables or pure machine language approach alone does not significantly improve the outcome prediction (Monteiro et al., 2018, Hamann et al., 2020).

Heo et.al has concluded that deep neural network can predict outcomes better than the ASTRAL score predictions and they found that the AUC while using deep neural network was significantly higher compared to ASTRAL scores, where as Ramos et.al is of the opinion that further studies are necessary before implementation in clinical practise since their models correctly identified 34% of the poor outcome patients at a cost of misclassifying 4% of non-poor outcome patients (Heo et al., 2019,Ramos et al., 2020).

Matsumoto et.al is also of the opinion that data driven models like linear regression and decision tree can be an alternative tool for predicting poststroke clinical outcomes in a real-world setting (Matsumoto et al., 2020).

Nishi et. al has used CNN and regularized LR for outcome prediction. They are of the opinion that, compared to standard neuroimaging biomarkers, their deep learning model was able to derive a greater amount of prognostic information. But CNN needs to be evaluated further before clinical practice and models like Random forest and logistic regression without regularization can predict clinical outcomes more accurately than previously developed pre-treatment scoring methods (Nishi et al., 2020, Nishi et al., 2019). Heo et.al has reported that deep learning based algorithms are better at predicting poor outcomes compared to machine learning based algorithms, and that the prediction of poor outcomes in documentlevel NLP DL was improved more by multi-CNN and CNN than by recurrent neural network-based algorithms (Heo et al., 2020). Kappelhoff et.al has compared fussy decision tree with CART algorithm and reports a better prediction capacity using fussy decision tree model compared to the benchmark decision tree algorithm CART (Kappelhofetal., 2021). Shakiru A Alaka has also compared different models including random forest, CART, decision tree, SVM etc. , but have concluded that machine language models and logistic regression had comparable predictive accuracy for predicting functional impairment in stroke patients (Alaka et al., 2020). Seiffge et. al on the other hand has compared an SVM with an existing score called DRAGON. They were of the conclusion that SVM is of comparable accuracy to DRAGON score for predicting outcomes after thrombolysis in stroke patients. They are of the opinion that SVM may be helpful in accelerating the pre-hospital triage of high risk patients after thrombolysis (Seiffge etal., 2013). Yuan Xie et. al has used extreme gradient boosting (XGB) and gradient boosting machine (GBM) models to predict mRS scores at 90 days using biomarkers available at admission and 24 hours. XGB and GBM showed an AUC of 0.746 and 0.748, respectively, which increased to 0.884 and 0.887 after including the NIHSS. They conclude that decision tree–based GBMs can predict the recovery outcome of stroke patients at admission with a high AUC (Xie et al., 2019).

IV. Discussion

In the near future, artificial intelligence (AI) approaches in stroke imaging may significantly alter the environment of stroke diagnosis and treatment. Medical professionals who are not trained in stroke imaging, such as general practitioners or paramedics, would benefit greatly from the machine-based diagnosis; as a result, the choice to provide thrombolysis might be made much more quickly. It might be feasible to provide an accurate risk assessment for stroke interventions or acute thrombolysis. Furthermore, predicting the level of post-stroke recovery and communicating the prognosis to patients and their families may improve the therapeutic alliance and the rehabilitation procedures.

AI model implementation in healthcare contexts may be difficult for a number of other reasons. When it comes to how the prediction was formed and how each individual predictor contributed to the final result, machine learning algorithms are usually not very apparent. For clinical decision makers, this could reduce the model's predictions' acceptance and validity. Furthermore, in the majority of published research, the model development and reporting are typically not explicit enough to allow for model replication in different datasets or external validation. This implies that the models may not be implementable at all in real-world circumstances, or they may provide only weak evidence of accuracy in various settings.

The data presented in this systematic review provides a comprehensive overview of the role of AI in different aspects of stroke management. One notable application of AI in stroke management is the prediction of sICH, a very serious complication associated with thrombolytic therapy. Studies employing machine learning models, such as artificial neural networks (ANNs) and support vector machines (SVMs), have demonstrated promising results in identifying patients at risk of sICH. These models utilize a combination of clinical data, imaging features, and demographic factors to improve predictive accuracy. Similarly, the review suggests that AI has potential in detecting LVO, especially using convolutional neural networks (CNN). Machine learning algorithms, including XGBoost and random forest, leverage multimodal imaging data to predict infarct size with high accuracy. By incorporating spatial features and deep learning techniques, these models offer valuable insights into tissue outcome prediction, aiding in treatment planning and patient counseling. AI also has a significant role to play in the 90-day poststroke outcome prediction, which enables clinicians to evaluate the long-term prognosis and adjust therapy plans accordingly.

While the papers underscore the potential of AI in stroke management, several challenges and limitations need to be considered. Thorough validation and transparency in model development are crucial given the ongoing concerns about the generalizability and interpretability of AI models. To guarantee seamless integration and user acceptability, the integration of AI tools into clinical workflows also

needs to be implemented cautiously. The field of AI in acute ischemic stroke therapy is still a developing area and presents great prospects for enhancing patient outcomes and care. To fully utilize AI technologies and successfully integrate them into clinical practice, further extensive research needs to be done.

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