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Review Article

Comparative Diagnostic Test Accuracy of Multiparametric MRI versus CT Scan in Emergency Assessment of Patients with Suspected Acute Stroke

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ABSTRACT

Background: The non-contrast computed tomography (CT) is a routine brain imaging modality for stroke diagnosis. However, the multiparametric magnetic resonance imaging (MRI) is increasingly being used for acute stroke diagnosis owing to its better sensitivity in detecting ischaemic brain infarcts.

Objectives: To evaluate the best available evidence on the comparative diagnostic test accuracies between CT and multimodal MRI for the diagnosis of acute haemorrhagic and ischaemic strokes in patients presenting to the emergency department within 6 hours after the onset of stroke-like symptoms.

Methods: MEDLINE-Ovid, AMED, CINAHL and ENBASE electronic bibliographic databases were searched in English from January 2004 to August 2014 and supplemented with manual bibliographic hand search. Prospective and retrospective cohort studies, which directly compared the diagnostic test accuracies between CT (as reference standard) and DW-MRI or GRE-MRI in detecting ischaemic or haemorrhagic stroke in the same patient population within 6 hours after the onset of stroke-like symptoms, were considered in the review. Only studies with diagnostic outcomes in terms of sensitivity and specificity of MRI versus CT in detecting acute stroke were considered. The quality of the selected studies in terms of risk of bias and clinical applicability were appraised using the QUality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool.

Results: A total of 780 patients were evaluated in the four selected cohort studies. Three and two studies contributed data on the diagnosis of acute ICH and ischaemic stroke, respectively. Three studies were of good quality while one was of poor quality. GRE-MRI exhibited high sensitivity of 83-100% (95% CI) in detecting acute ICH compared to 100% for CT used as the reference standard. CT exhibited poor sensitivity (12-81%) but better specificity (88-100%) in detecting acute ischaemic stroke as compared to DW-MRI, which had a sensitivity of 73% (95% CI) and specificity of 92% (95% CI).

Conclusions: It appears that GRE-MRI has comparable sensitivity as CT in detecting acute ICH. Similarly, DWI is excellently sensitive and specific in detecting acute ischaemic lesions. These strongly suggest that MRI is sufficiently accurate for routine evaluation of patients with suspected acute stroke in the emergency setting. However, the studies generally lack applicability aspects to the general population and current clinical practice therefore, warranting further research. In the meantime, CT and/or MRI tests can be used for routine assessment of patients with suspected stroke in the emergency setting.

Keywords: Diagnostic Test, Acute Stroke, Multiparametric MRI, CT Scan.

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INTRODUCTION

STROKE AETIOLOGY AND EPIDEMIOLOGY

Cerebrovascular accident (stroke) is a neurological deficit that occurs when part(s) of the brain is damaged due to rapid focal interruption of cerebral blood flow. Depending on the mechanism of brain injury, stroke events are classified into ischaemic and haemorrhagic.[1,2] Ischaemic stroke is the most frequent type of stroke (80-85%) that occurs due to occlusion of the arterial blood supply to the brain. This blockage may occur due to the formation of a blood clot (thrombus) in one of the main arteries in the head or neck.[3] Conversely, ischaemic stroke can occur due to cerebral embolism caused by a detached thrombus formed elsewhere in the circulatory systems (usually the heart), which travels and blocks a key blood vessel of the brain. In addition, ischaemic stroke can occur due to in situ occlusion of one of the arteries that supply blood to the core structures located deep in the brain (lacunar stroke).[3,4] Temporary disruption of blood supply to some parts of the brain but completely resolves without interventions within 24 hours is called transient ischaemic attack (TIA) or a mini-stroke (non-disabling stroke). TIA is often an early sign of an impending acute stroke to occur within few hours, days, weeks or even months.[5]

Haemorrhagic stroke, which accounts for about 15-20% of all stroke cases, is the most severe type of stroke.[6] It occurs due to severe cerebrovascular oedema (subacute haemorrhage), which cause blood leakage into the space surrounding the brain mass (subarachnoid haemorrhage) or within the brain tissue itself (intracerebral/intracranial haemorrhage). Intracranial haemorrhage accounts for the majority of haemorrhagic stroke cases (75%) and results in most disabling stroke outcome.[1,3,6]

Strokes often result in neurological deficits that are variable depending on the magnitude of brain injury and parts of the brain involved. Cognitive deficits, motor impairments, language deficits (dysphasia), sensory deficits and visual impairments are neurological domains frequently affected by stroke events.[3]

ACUTE STROKE DIAGNOSIS

Accurate and prompt diagnosis of acute ischaemic stroke allow timely interventions within 3–6 hours of onset, because thrombolytic therapies for acute ischaemic stroke have relatively narrow therapeutic window of effectiveness when compared to that of myocardial infarctio.[7-9] The central goal of early treatment of acute ischaemic stroke is to remove the blockage and enhance reperfusion of brain lesions to preserve healthy brain tissue surrounding the lesions.[3,7,10] The criteria for qualifying patients suspected with stroke to receive thrombolytic therapy are outlined in the guidelines established by National Institute of Neurological Disorders and Stroke (NINDS).[10] Intracranial haemorrhage detectable on CT is the basic NINDS criterion for excluding patients from thrombolytic therapies to avoid the risk of fatal intracranial haemorrhage augmented by thrombolysis. By this account thrombolysis is only beneficial to patients with acute ischaemic stroke.[9,10]

Haemorrhagic and ischaemic strokes can be reliably distinguished using neuroimaging techniques, particularly the noncontrast computed tomography (CT) scan and the multimodal magnetic resonance imaging (MRI).[3,8] In the emergency setting, an ideal neuroimaging modality for assessment of patients presenting with stroke-like symptoms should be adequately sensitive and specific in differentiating between cerebral ischaemia and intracranial haemorrhage and able to rule out potential nonvascular brain disorders that mimic acute stroke.[11]

COMPARATIVE DIAGNOSTIC TEST ACCURACY (CT VERSUS MRI)

The non-contrast head CT scan has for the long time used as the standard neuroimaging modality for routine evaluation of patients with suspected stroke because it is sufficiently sensitive in detecting acute intracranial haemorrhages in the brain .[12-14] This imaging modality is therefore, preferably used for differential diagnosis of ischaemic and haemorrhagic stroke and for ruling out various other nonvascular brain disorders.[11] However, CT scans have reduced sensitivity in detecting ischaemic strokes, which are relatively small, with acute onset, and those located in the posterior fossa of the brain.[11,12] In this case, patients who truly have acute ischaemic stroke may have normal CT scan appearance, suggesting that a normal CT scan should not be used to rule out the diagnosis of acute ischaemic stroke in the emergency setting.[12,15] On the other hand, multimodal MRI with diffusion-weighted (DWI) and gradient-echo (GRE) sequences are extensively reported to have better accuracy than the conventional CT in detecting acute ischaemic stroke.[15,16] Some emerging evidence indicates that stroke GRE-MRI can detect intracerebral haemorrhagic stroke with comparable accuracy to that of noncontrast CT.[15,17] A GRE-MRI has been shown to be as accurate as CT in detecting acute intracranial haemorrhage in patients presented 6 hours after the onset of stroke-like symptoms.[13] On the other hand, DW-MRI can detect very small changes following acute ischaemic injury as compared to the conventional CT scan. Furthermore, interpretation of stroke DWI images has better reliability within and between interpreters when compared to CT.[11]

By this account, the use of MRI as an alternative neuroimaging modality to the noncontrast CT has gained relevance in the emergency acute stroke diagnoses.[11,18] However, there are mixed evidences on the superiority of MRI over the conventional CT in the evaluation of patients with suspected acute stroke in the emergency setting.

The present review study aimed at evaluating comparative diagnostic accuracy between the multimodal MRI and noncontrast CT in detecting acute stroke in adult patients presenting with stroke-like neurological symptoms in the emergency department within six hours after the onset of symptoms.

METHODS

Systematic reviews and meta-analyses are adopted. They are methodologies entail systematic selection of the best primary clinical evidences to answer a given clinical question based on stringent inclusion/exclusion criteria.[19]

The present review targeted clinical studies that quantitatively evaluated the diagnostic test accuracy of MRI and CT scan in detecting acute ischemic or haemorrhagic stroke in patients with suspected stroke in the emergency setting. This study aimed to include only comparative studies that directly compared the two brain imaging modalities for acute stroke detection in the same patient population with the final diagnosis of acute stroke based on clinical assessment and imaging results as the reference or 'gold' standard. The present review study included primary diagnostic test accuracy studies with prospective design with blind comparison and retrospective design.

In a prospective design with blind comparison, clinicians involved in the diagnostic accuracy study are asked to carry out specific diagnostic tests to patients who have undergone or scheduled to undergo a reference or 'gold standard' diagnostic test. The clinicians carrying out diagnostic tests or reference/gold standard diagnostic test are both blinded to results of the other diagnostic test. Similarly, the independent assessors evaluating diagnostic test results of a given diagnostic test against a corresponding reference/gold standard diagnostic test are blinded to diagnostic procedures and patient data.[20] Therefore, a prospective, blind comparison design has low risk of bias from investigators. A retrospective design provides readily available retrospective data for present researchers who have no hand in any procedural-related biases. Therefore, a retrospective design provides a data with low risk of investigator biases.

To ensure strong clinical evidence that reflects the current evidence-based clinical practice in neuroimaging and stroke diagnosis, the present review aimed to search for primary diagnostic test accuracy studies published from January 2004 to August 2014.

Participants and Target Conditions

The present review study targeted comparative diagnostic accuracy studies based on adult patients (aged ≥18 years) presented to the emergency department with stroke-like symptoms that are typically indicative of acute ischaemic or haemorrhagic stroke as the target condition. Patients presented to the emergency department in <6 hrs after the onset of stroke-like symptoms are the ideal patient population to answerer the present review question. This is because noncontrast CT scan typically loses its sensitivity in detecting subarachnoid haemorrhage with time as demonstrated by Renowden (2014).[21] Therefore, delays beyond 6 hours would disadvantage the accuracy of noncontrast CT scan over MRI.

Outcome Measures

Only studies that presented quantitative evaluation of diagnostic accuracy between MRI and CT scan were considered for review. In this case, quantitative studies, which presented the actual test results along with the reference standard results determined in the same patient population, were ideal to answer the question in the present review. [22] The diagnostic test accuracy results targeted for the review where sensitivity and specificity of MRI and CT scan in detecting acute ischaemic or haemorrhagic stroke, presented as absolute counts of true/false-positives and true/false-negatives stroke diagnoses. This could be useful in allowing a meta-analysis.[23] Studies with high false positive and/or false negative counts would imply low diagnostic accuracy and vice versa.

Search Criteria for Identification of Studies

To locate evidence-based-medicine (EBM) resources eligible for evaluation in the present study, four EBM electronic publication databases were searched from January 2004 to August, 2014: Library of Medicine and National Institutes of Health (MEDLINE)-Ovid, Allied and Complementary Medicine (AMED), Cumulative Index to Nursing and Allied Health Literature (CINAHL) and Excerpta Medica database (EMBASE).

The electronic searches for MEDLINE, AMED, CINAHL and EMBASE were all performed based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Liberati et al, 2009). The electronic searches were performed through the Glasgow Caledonian University (GCU) library using appropriate Medical Subject Headings (MeSH) or CINAHL headings, and text words indexed by individual databases based on the PICO search strategy for the target patient population (patients with suspected acute stroke presented to the emergency department within 6 hours of onset of symptoms), diagnostic interventions (the multimodal MRI), comparator diagnostic test (conventional CT scan as reference or gold standard) and outcome (diagnostic accuracy). This was guided by the following PICO question:

In adult patients presented with stroke-like neurological symptoms in the emergency department, is the multimodal MRI more sensitive and specific in detecting both acute ischaemic and haemorrhagic strokes compared to the conventional CT scan within the first 6 hours after the onset of acute stroke-like symptoms?

Key words and MeSH terms defining the target population, clinical condition and clinical setting include: adult, middle aged, aged, acute disease, acute stroke, acute haemorrhagic stroke, acute ischaemic stroke, acute intracerebral haemorrhage, intracranial haemorrhage, brain infarction, brain ischaemia, humans, and clinical emergency service. Key words and MeSH terms related to stroke diagnosis include: Magnetic resonance imaging, X-Ray computed tomography, emergency service, emergency assessment, emergency diagnosis, early diagnosis, emergency department, time factors, sensitivity and specificity. The different combinations of the keywords, MeSH terms and text words were performed using Boolean operators (AND, OR, NOT) to enhance the relevance of returned search hits.

The electronic search hits were restricted to comparative studies published from January, 2004 to August, 2014. Due to complexities and costs associated with acquisition of translation service for scientific research papers, the electronic searches were restricted to English language. The electronic searches were validated by supplementation with manual bibliographic hand searches to locate additional potentially relevant articles not traceable through electronic searches.

Inclusion and Exclusion Criteria

To ensure relevance, only primary diagnostic accuracy studies that evaluated the comparative diagnostic accuracy between MRI and CT scan in detecting acute ischaemic or haemorrhagic stroke in adult human patients (aged ≥18 years) were included. In this case, studies, which only presented convenience or specific technical aspects of MRI and CT scan in the diagnoses of acute stroke, evaluated younger patients (aged <18 years) or animal models were excluded.

The present review included comparative diagnostic test accuracy studies with prospective design with blind comparison and retrospective design, because these were the only practical and ethical study designs for the present clinical question and setting.11 The nature of neuroimaging tests (CT and MRI) and the emergency setting could not allow true randomized controlled trial (RCT) studies due to possible unethical implications of this study design. By this account, it would be outrightly unethical if a patient presenting with stroke-like symptoms in the emergency department is assessed with either MRI or CT when acute stroke diagnosis can be enhanced using both tests. However, comparative diagnostic test accuracy studies, where patients in the same population were randomised to either MRI or CT scanning were considered in the present review.

Therefore, for acute ischaemic stroke detection, studies were included if the same participants were evaluated using both DW-MRI and noncontrast CT (as reference standard) within 6 hours of onset of acute stroke-like symptoms. On the other hand, studies evaluating the detection of haemorrhagic stroke were included if the same participants were evaluated using MRI sequences (GRE or DWI) against noncontrast CT findings (reference standard) within 6 hours of symptoms onset. Only studies that reported sensitivity and specificity of the diagnostic tests relative to the reference standard were included for the review. Consequently, studies were excluded based on the following exclusion criteria

1. Studies that merely presented technical aspects of CT versus MRI in acute stroke diagnosis were excluded.
2. Non-quantitative studies such as review articles, editorials, case reports, letters, and commentaries on this research

question were excluded from the review. This is because such studies generally lack quantitative data on the comparative accuracy between MRI and CT and may be opinion based rather than evidence based.

3. Studies that assessed acute stroke beyond 6 hours after the onset of stroke-like symptoms were excluded because this is a non-emergency setting.
4. Studies, which did not provide quantitative outcome measures (sensitivity and specificity) of the diagnostic test accuracy between MRI and CT scans in the detection of acute stroke, were excluded.
5. Articles that were published in non-English languages were excluded due to complexities associated with acquisition of translating service and questionable quality of translated research papers.
6. To summarise the best current evidence, articles that were published before the year 2004 and those that were not peer-reviewed were excluded.

Methodological Quality Appraisal of the Included Studies

The methodological quality of the included studies was appraised separately using the updated QUADAS-2 tool. It is extensively recommended by The Cochrane Collaboration, Agency for Healthcare Research and Quality (AHRQ) and the UK's National Institute for Health and Clinical Excellence (NICE) for use in diagnostic test accuracy reviews.[24] It comprises four main domains of quality appraisal: criteria for patient selection; actual diagnostic test(s) (the index test), the diagnostic reference standard and the overall diagnostic flow and timing.[24,25]

Based on QUADAS-2 tool, adult patients presented with stroke-like symptoms who received brain imaging within 6 hours of the onset of their symptoms were considered the appropriate patient population. The diagnostic reference standards used in the included studies were deemed appropriate provided that they involved clinical reviews coupled with brain imaging findings to facilitate accurate diagnoses of the acute stroke. Lastly, for the diagnostic flow timing, any time delay between the acquisition of CT and MRI scan was acceptable provided the tests were performed within 6 hours from the onset stroke-like symptoms.

Data Extraction and Presentation

A template of evidence table for studies of diagnostic test accuracy was adapted from the UK's NICE with slight modifications, specifically to collect and present data from the selected studies.[26] Data on authors, study design (particularly randomised controlled trial, prospective study, retrospective study, cross-sectional survey), target patient population, sample size, patient characteristics (age, sex, ethnicity and previous history of stroke), clinical presentation of stroke and setting, classification of stroke based on the National Institutes of Health Stroke Scale (NIHSS), diagnostic brain imaging tests performed (both index and reference standard tests), specific technical aspects of MRI and CT modalities, time delay between imaging modalities, study quality with respect to risk of bias based on QUADUS-2, sensitivity & specificity of the CT versus MRI at 95% confidence interval (CI) and summary of key findings were recorded on the evidence table.

Data Analysis and Synthesis

Accuracy based on data of comparative sensitivity and specificity of the CT versus MRI (95% CI) in detecting acute ischaemic and haemorrhagic strokes in the emergency setting was extracted and recorded in a 2 by 2 contingency table as the number of true and false positive or negative stroke diagnosis cases. Based on the tabulated data, the percentage sensitivity and specificity of MRI and CT scans in detecting acute stroke was calculated at 95% CI. The relative specificity and sensitivity of T2-GRE-MRI and DW-MRI in detecting ICH and acute ischaemia, respectively, were also compared.

RESULTS

The initial electronic searches from MEDLINE, AMED, CINAHL and EMBASE returned a total of 157 hits as shown on the PRISMA diagram (Fig. 1). Upon systematic removal of apparently irrelevant articles and duplicates based on titles, the search results narrowed down to120 potentially relevant citations. Manual bibliographic hand searches led to the identification of one potentially relevant citation. Upon further screening of the 121 abstracts, 107 citations were disqualified because they were obviously irrelevant. At this point, the 107 citations were ineligible because some were reviews, commentaries and merely compared technical aspects of CT versus MRI or did not directly compare diagnostic accuracy of MRI (DWI or T2-weighted GRE) with CT in acute stroke diagnosis. Fourteen (14) full-text articles were considered for further eligibility evaluation where 10 articles were excluded. At this point, three (3) articles were excluded because clinical diagnoses of stroke were performed in the non-emergency setting (>6 hours after onset of stroke-like symptoms). Four (4) articles were disqualified because acute stroke diagnoses were either performed in mixed (emergency and non-emergency settings) or unclear clinical settings. Two (2) articles were ineligible because they compared the diagnostic accuracy of CTP or the multimodal CTP/CTA with the noncontrast CT or MRI (but with no clear comparator test) in evaluating acute stroke patients. The remaining one (1) article was disqualified because MRI was performed as the comparator test of CT/CTA. Therefore, four (4) articles fulfilled the inclusion criteria and were finally included in the systematic review. [11, 13, 17, 18]

The four selected diagnostic test accuracy studies included a total of 780 patients with suspected acute/hyperacute stroke or transient ischaemic attack (TIA) presented in the emergency department. Three of the four selected studies were prospective,[11,13,18] while the remaining one study was retrospective.[17] One study directly compared diagnostic test accuracy between DWI and non-contrasted CT for the detection of acute/hyperacute ischaemic brain lesions,[18] while two studies compared T2-weighted GRE-MRI and non-contrasted CT for the detection of acute intracerebral haemorrhage.[13,17] One study compared diagnostic test accuracy between MRI sequences and non-contrasted CT for the detection of both acute haemorrhagic and ischaemic brain lesions.11 Therefore, two studies,[11,18] contributed data for the evaluation of acute ischaemic stroke and three studies contributed data for evaluation of acute haemorrhagic stroke.[11,13,17] Study characteristics are as summarised in the table 1.

The methodological quality of the selected studies in terms of risk of bias and applicability concerns was evaluated based on the QUADAS-2 tool.[24] Three studies[11,17,18] were considered of good methodological quality while one study Kidwell et al, (2004)[13] was of poor quality. High risk of bias with respect to patient selection was evident in one study [13] while in two studies[11,18] with respect to index test. Three studies[11,17,18] had some risk of bias due to unclear flow and timing of brain imaging while one study (Kidwell et al, 2004)[13] exhibited high risk of bias. Kidwell et al. (2004)[13] presented applicability concerns with respect to patient selection and index test while Chalela et al. (2007)[11] had applicability concern regarding patient selection (Fig. 2 & 3).

Three studies contributed diagnostic test data that directly compared noncontrast CT with bi-modal or multimodal MRI for the detection of acute haemorrhagic stroke within 6 hours of ictus of stroke-like symptoms in the same patient population).[11,13,17] The three diagnostic accuracy reports involved a total of 680 participants with sample size range of 124 to 356. The combined mean age (range) of 324 patients from two studies[13,17] was 72.32 years while the 356 participants in Chalela et al. (2007)[11] study had a median age of 76 years. The overall age range of all the 680 participants was 21-100 years. Based on the NIHSS score, median stroke severity of the participants recruited in the three studies was 3, 6 and 9.5, respectively; [11,13,17] with overall NIHSS score range of 0-37. All studies evaluated patients with DWI and T2-weighted GRE-MRI followed by non-contrast CT. Table 2 presents a summary of basic demographic data of three studies contributing data on the diagnosis of acute haemorrhagic stroke.

Two studies [11,18] contributed data that directly compared non-contrasted CT with DW-MRI (with a b value of 1000 s/mm^2) for the detection of acute ischaemic brain injury within 3 hours of stroke symptom ictus in the same patient population. The two diagnostic test accuracy reports included a total of 456 participants; 100 and 256 participants from Barber et al. (2005)[18] and Chalela et al. (2007),[11] respectively. The two studies included adult participants with comparable age. The mean age of participants from Barber et al. (2005)[18] was 68 yrs with SD of 13.9 yrs while participants in Chalela et al. (2007)[11] had a mean age of 76 yrs with age range of 21–100 years. Barber et al. (2005)[18] reported the proportion of men as 69% while Chalela et al. (2007)[11] did not report the proportion of men to women included in the study. This clearly points to possible risk of bias in patient selection process in Chalela et al. (2007) study.[11] Both studies clearly reported stroke severity based on NIHSS score. Table 3 presents a summary of basic demographic data of two studies contributing data on the diagnosis of acute haemorrhagic stroke.

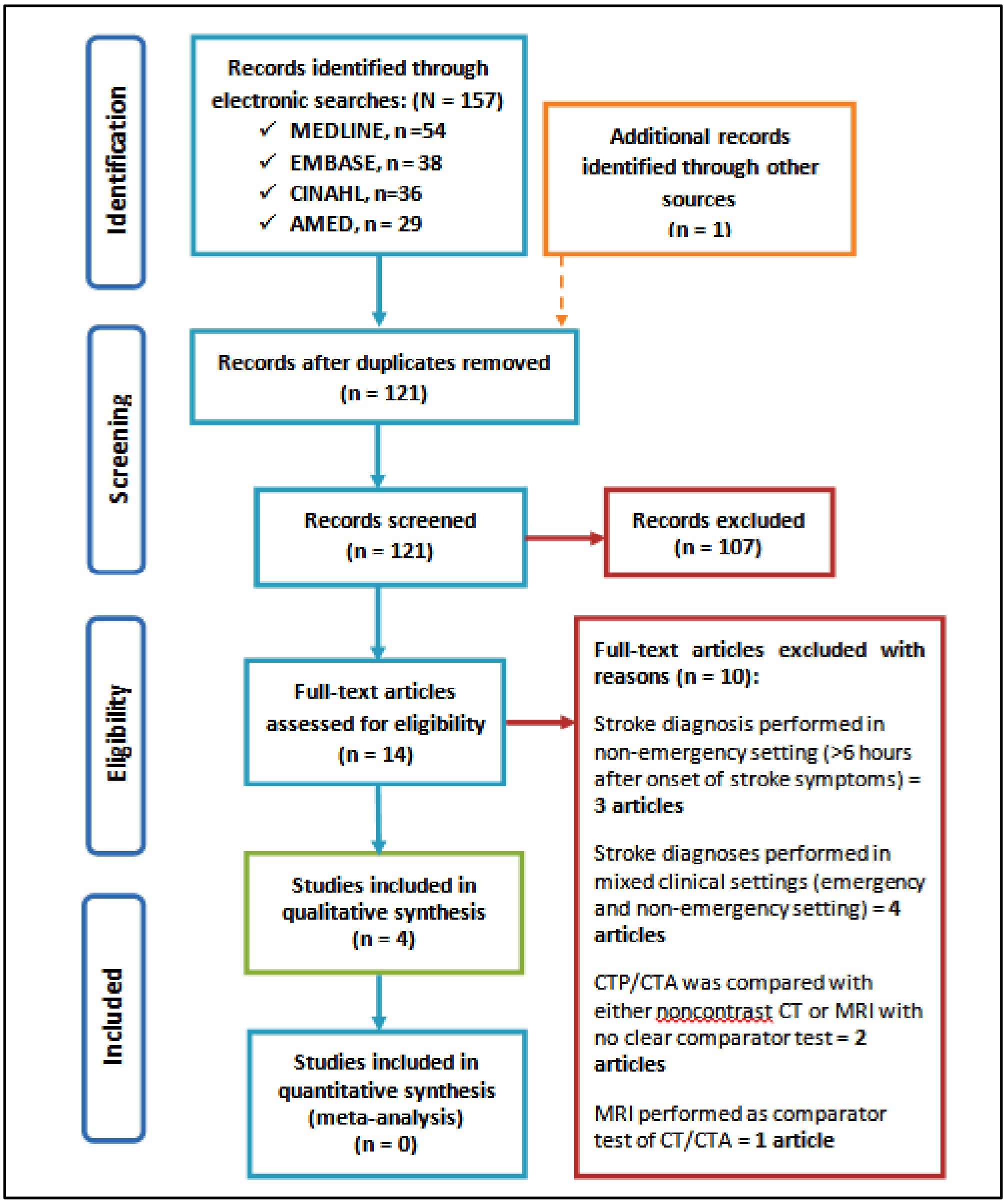

Figure 1: PRISMA flow diagram (Moher et al, 2009) showing electronic and manual hand search results, eligibility screening and the included studies

Table1: Evidence table of diagnostic test accuracy reports for diagnosis of acute haemorrhagic and ischaemic stroke in patients with suspected stroke in the emergency setting.

Author	Study Design & Sample size	Patient characteristics	Type of clinical condition(s) & diagnostic tests	Reference standard	Study quality (QUADUS-2)	Sensitivity & specificity (95% CI)	Summary of key Findings
Fiebach et al. (2004)	Prospective design N=124 patients n =31 (25%) women	Mean age: 65.5 yrs Mean baseline stroke severity of 9.5 (range, 4-31) scored on the NIHSS	Acute intracerebral haemorrhage (ICH) and ischaemic infarction 62 patients with ICH (experimental) and 62 patients with suspected ischaemic stroke (control) received both DWI and T2-weighted GRE-MRI (as the index test) and noncontrast CT (as the comparator test). All MRI sequences were performed using1.5-T scanners. DWI performed with b value of 1000 mm/s^2 The scans were acquired in either order within the first 6 hrs after the onset of stroke-like symptoms	Clinical diagnosis coupled with CT served as the 'gold standard' (reference standard)	Low risk of bias on patient selection, index test, reference standard and diagnostic flow/timing	CT as the gold standard had a 100% accuracy for ICH Multimodal MRI sensitivity was 100% (95% CI: 97 -100) with overall specificity of 95.5%	Hyperacute ICH exhibited characteristic imaging pattern on stroke MRI. Therefore, stroke MRI can rule out ICH in patients suspected with hyperacute stroke in the emergency stetting
Kidwell et al. (2004)	Retrospective design N=200 n =110 (55%) women	Patients with acute ischaemic stroke. Mean age of 75 (range 25-99) yrs: Median baseline NIHSS: 6 (range: 0-33)	Acute ICH Patients underwent brain MRI sequences (T2-weighted GRE-MRI and DW) followed by non-contrasted CT within 6 hours of onset of stroke-like symptoms. All MRI sequences were performed using1.5-T scanners. DWI was performed with b value of 1000 mm/s^2	Clinical diagnosis coupled CT imaging findings	Low risk of bias on index test and reference standard: Being retrospective there is high risk of patient selection bias and diagnostic flow/timing.	CT, which was the 'gold standard' showed a 100% accuracy for ICH GRE-MRI sensitivity was also 100% accurate	MRI and CT exhibited equivalent accuracy (96%) in detecting acute haemorrhages, suggesting that MRI is as accurate as CT for the diagnosis of acute haemorrhagic stroke in patients with suspected focal stroke-like symptoms
Barber et al. (2005)	Prospective design N=100 patients n = 69 (69%) men	Patients suspected with acute ischaemic stroke. Mean (SD) age of 68 (13.9) yrs Median baseline NIHSS score was 9 (range 0–32).	Acute ischaemic stroke Patients received either noncontrast CT scans (within 6 hrs of onset of symptoms) or DW-MRI (within 7 hrs of stroke-like symptoms) or both in either order DW-MRI was performed using 3.0 T MRI scanners DW-MRI was performed with a b value of 1000 s/mm^2	Baseline and follow up CT and DW-MRI images read based on Alberta Stroke Program Early CT Score (ASPECTS)	Low risk of bias on patient selection, index test, reference standard and diagnostic flow/timing	Sensitivity of CT versus DWI ASPECTS at acute stage = 54/67 (0.81) = 81% Specificity of CT versus DW-MRI ASPECTS at acute stage = 29/33 (0.88) = 88%	The sensitivity difference between CT and DW-MRI in visualizing early ischaemic infarction was small based on ASPECTS and therefore, comparable. CT was faster and more accessible than MRI, therefore convenient for diagnosis of suspected acute stroke in emergency setting.

Chalela et al. (2007)	Prospective design with blind comparison N=356 patients	Patients with suspected acute ischaemic or haemorrhagic stroke Age range; 21–100 yrs (median age 76 yrs). Median baseline score on NIHSS = 3 (range 0-37)	Both acute ischaemic and haemorrhagic stroke. All patients received DW-MRI for detection of ischaemic stroke or MRI sequences (DW and GRE) for the detection of haemorrhagic stroke and non-contrasted CT as the comparator test. All MRI sequences were performed using 1.5 T MRI scanners. DWI performed with b values of 0 and 1000 s/mm² Both MRI and CT were performed within 3 hrs, and between 3–12 hrs of onset of acute stroke-like symptoms	Final diagnosis based on all available clinical evidence coupled with acute and follow-up imaging, which is the 'current best practice'.	Low risk of bias on patient selection, index test, reference standard and diagnostic flow/timing but high risk of bias on index test.	DW-MRI for acute ischaemic stroke: sensitivity of 0.73(CI; 0.5-0.8) and specificity of 0.92 (CI; 0.80-0.98) CT for ischaemic stroke: sensitivity 0.12 (CI; 0.04-0.26) and a specificity of 1.00 (CI. 0.93-1.00) DW-MRI and GRE MRI for ICH: sensitivity of 0.83 (CI; 0.52-0.98) and a specificity of 1.00 (CI 0.95-1.00)	MRI was highly sensitive (83%) as compared to CT (26%). Diagnostic specificity of the two imaging modalities for acute ischemic stroke detection was similar (96-97%).

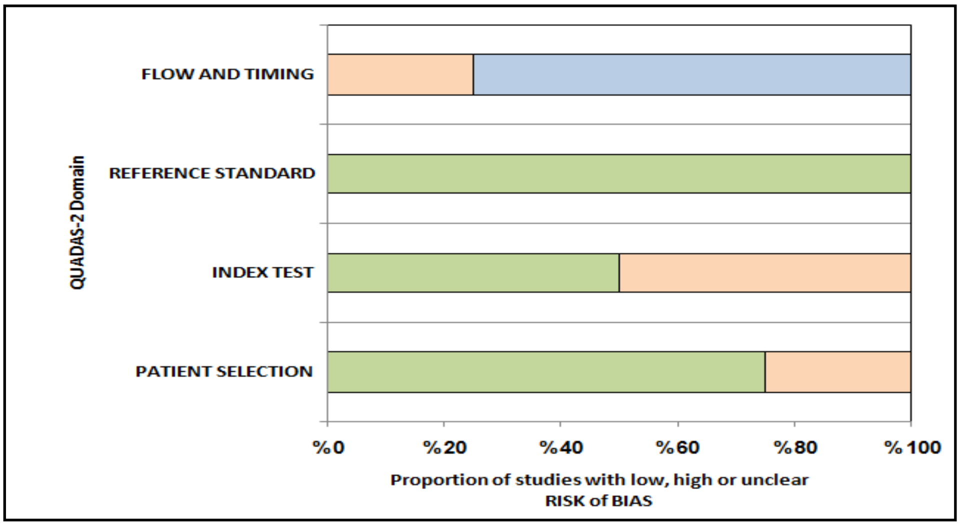

Figure 2: Bar charts presenting proportion of studies (%) with high, low or unclear risk of bias based on QUADAS-2 rating.

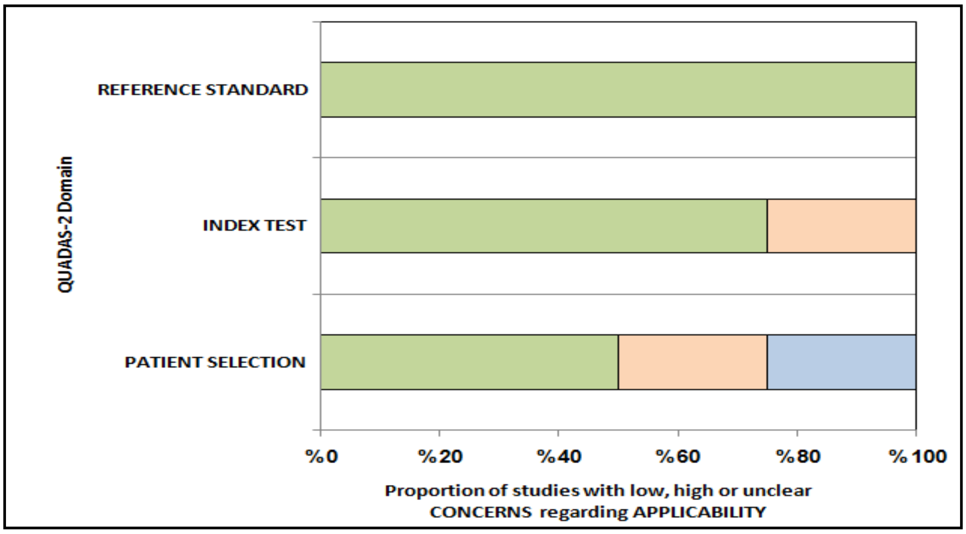

Figure 3: Bar charts presenting proportion of studies (%) with high, low or unclear applicability concerns based on QUADAS-2 rating.

Table 2: Demographics of studies contributing data on acute haemorrhagic stroke diagnosis

Authors	N	Age	Proportion of women (%)	NIHSS scores
Fiebach et al. (2004)	**124**	Mean (SD) age 68 (13.9) yrs	25%	Median NIHSS score was 9.5 (range, 4-31)
Kidwell et al. (2004)	**200**	75 (25-99)	55%	Median NIHSS score was 6 (range: 0-33)
Chalela et al. (2007)	**256**	Mean age 76 yrs; age range of 21–100 yrs	Not reported	Median NIHSS score = 3 (range: 0-37)

Table 3: Demographics of studies contributing data on acute ischaemic stroke diagnosis

Authors	N	Age	Proportion of women (%)	NIHSS scores
Barber et al. (2005)	100	Mean (SD) age 68 (13.9) yrs	69%	Median NIHSS score was 9 (range 0–32)
Chalela et al. (2007)	256	Mean age 76 yrs; age range of 21–100 yrs.	Not reported	Median NIHSS score = 3 (range 0-37)

Table 4: A summary of GRE-MRI accuracy in detecting acute hemorrhagic stroke

Authors	% sensitivity (95% CI)	% specificity (95% CI)
Fiebach et al. (2004)	100% (0.97-1.00)	95.5%
Kidwell et al. (2004)	100%	100%
Chalela et al. (2007)	83 % (0.52-0.98)	100% (0.95-1.00)

Table 5: A summary of DW-MRI accuracy in detecting acute ischaemic stroke

Authors	% sensitivity (95% CI)	% specificity (95% CI)
Barber et al. (2005)	81% (0.72-0.88): based on ASPECTS	88% based on ASPECTS
Chalela et al. (2007)	73% (0.5-0.8)	92% (0.80-0.98)

Fiebach et al. (2004)[17] showed a sensitivity of 100% (95% CI: 0.97-1.00) with an overall specificity of 95.5% in detecting ICH for the GRE-MRI in patients assessed within 6 hours of onset of stroke-like symptoms. This was comparable to that demonstrated by Kidwell et al. (2004) study,[13] which showed that MRI sensitivity and specific of 100%. Similarly, Chalela et al. (2007)[11] showed a GRE-MRI sensitivity of 0.83 (95% CI; 0.52-0.98) and a specificity of 1.00 (95% CI; 0.95-1.00) based on only 12 out of 90 (13%) patients scanned within 3 hours of onset of stroke-like symptoms who were found to have acute ICH (table 4).

Based on ASPECTS, Barber et al. (2005)[18] demonstrated sensitivity of 54/67 (81%) and specificity of 29/33 (88%) for CT versus DW-MRI in detecting ischaemic infarction in the acute stage. Similarly, Chalela et al. (2007)[11] demonstrated a sensitivity of 0.12 (95% CI; 0.04-0.26) and a specificity of 1.00 (95% CI. 0.93-1.00) for CT compared to 0.73 (95% CI; 0.5-0.8) and specificity of 0.92 (95% CI; 0.80-0.98) for DW-MRI in detecting acute ischaemic stroke (table 5). The two studies clearly demonstrated that DW-MRI is superior over CT in the detection acute ischaemic infarction in the acute stage. However, according to data from Chalela et al. (2007), [11]although CT had poor sensitivity (12%) in detecting acute ischaemic infarction; CT had better specificity (100%) when compared with DW-MRI (92 %).

DISCUSSION

Reperfusion (thrombolytic) therapies are the first-line clinical interventions for patients with confirmed diagnosis of ischaemic brain lesions but totally contraindicated in patients with haemorrhagic brain lesions.[3] Given that thrombolysis can worsen existing intracranial haemorrhages, safe treatment of acute stroke requires accurate differential diagnosis of ischemic and haemorrhagic brain lesions.[3,7,8]

Equally important, timely differential diagnosis of acute ischaemic stroke in patients presented in the emergency department with symptoms of acute stroke within 3-6 hours of onset is critical for timely initiation of thrombolytic therapies, which have relatively narrower therapeutic window of effectiveness than those for myocardial infarction.[7,9] Therefore, an ideal neuroimaging technique should offer rapid differential diagnoses of haemorrhagic and non-haemorrhagic brain lesions.[7,8] Owing to its sensitivity in detecting intracranial haemorrhages, the noncontract CT is still extensively used as the basic differential diagnostic technique for patients with suspected acute stoke to aid in therapeutic decision-making on administration of thrombolytic therapies.[3,9] However, MRI is increasingly being used for acute stroke diagnosis owing to its putative sensitivity in detecting ischaemic brain lesions, which are often missed on CT.[11]

Therefore, the present diagnostic test accuracy review, systematically reviewed the current best available evidence on the comparative sensitivity and specificity of CT versus MRI in acute stroke diagnosis in same patients presented with stroke-like symptoms in the emergency setting.

A total of four diagnostic test accuracy studies were reviewed;[11,13,17,18] where three studies contributed data for evaluation of haemorrhagic stroke while two studies contributed to evaluation of ischaemic stroke. Data from these studies strongly indicate that the multimodal MRI has generally higher sensitivity than CT in detecting both acute ischaemic and haemorrhagic stroke. It appears that the two imaging modalities have comparable specificity. However, the quality of evidences presented in the four studies reviewed has important methodological and applicability concerns worth highlighting.

It is extensively documented that DW-MRI has excellent sensitivity in detecting acute ischaemic brain lesion but poor in detecting acute intracerebral haemorrhage (ICH).[15, 16] However, emerging evidence suggest that MRI with DW-MRI and GRE sequences could detect acute stroke within 6 hours after the onset of acute stroke-like symptoms.[11,13,17]

In general data from these studies strongly affirm that the noncontrast CT is 100% sensitive in detecting acute haemorrhagic stroke in the emergency setting. This is highly consistent with the literature, where the noncontrast CT is basically used as the 'gold standard' for deferential diagnosis of acute ICH in patients with suspected stroke.[12,14] By this account, two studies clearly employed the non-contrast CT coupled with final clinical diagnoses of acute stroke as the reference standard for haemorrhagic stroke detection. This is the best practice for acute stroke diagnoses.[13,17] On the other hand, GRE-MRI exhibited a good sensitivity in detecting ICH (83-100%, 95% CI) therefore, affirming the emerging evidence on the preferential use of MRI over CT for evaluation of patients with suspected acute stroke in the emergency setting. [11,13,17,27]

Consequently, while the limited data presented in the present review study suggest that MRI is equally sensitive as CT and even more sensitive in the diagnosis of acute ICH in the emergency setting, evidence presented is insufficient and generally not reliable for any sound conclusive verdict on this clinical question.

Data from the two studies evaluating the diagnostic accuracy of MRI versus CT in the detection of acute ischaemic stroke, clearly demonstrated that DW-MRI is superior over CT.[11,17]

Barber et al. (2005)[18] used ASPECTS for ischaemic grading using CT and DW-MRI where the two imaging modalities were found to have comparable sensitivity in visualising early ischaemic infarction. However, ASPECTS is designed for topographic CT scan rather than DWI. Therefore, using ASPECTS on DWI could have invalidated findings from Barber et al. (2005).[18] Next, it has been suggested that DW-MRI is so sensitive that it can even detect relatively small ischaemic lesions following sub-acute ischaemic infarctions in transient ischaemic attack (TIA) or minor stroke.[27] Chalela et al. (2007)[11] included participants with TIA or minor stroke as evidenced by a low NIHSS median score of 3 compared to a NIHSS median score of 6[13] and a NIHSS mean score of 9.5.[17] This clearly indicates that while Chalela et al. (2007)[11] made good attempt to include participants with broader spectrum of acute stroke, inclusion of participants with TIA could have increased the sensitivity of DWI over CT in detecting ischaemic stroke. In this case, Chalela et al. (2007)[11] indicated that patients whose final diagnoses revealed TIA were considered as having final diagnoses of acute ischaemic stroke. This apparently points to incorporation bias that invalidates the overall findings from this study.[24,28] In Chalela et al. (2007)[11] study, the aspect of incorporation bias was evidenced by the index test forming part of the reference standard.[24] Conversely, reference standard review and clinical review biases are also other biases possible in Chalela et al. (2007)11 study because it appears the index and reference standard tests were interpreted with knowledge of ether index tests or clinical results.[24,28] Data from the evaluated diagnostic accuracy studies give some evidence that MRI is more sensitive that CT for the detection of acute ischaemic stroke and has good sensitivity in detecting acute ICH.[11,13,17,18] Given that ischaemic stroke accounts for about 80-85% of all stroke cases,[2] direct detection of ischaemic lesions with DW-MRI could enhance accuracy in clinical decision-making regarding the administration of thrombolytic therapies. However, applicability of MRI for routine diagnoses of acute stroke in the emergency setting is currently marred by aspects of patient diagnostic throughput and cost-effectiveness. CT is generally inexpensive to acquire commercially and requires less specialised personnel to operate as compared to MRI.[18]

Importantly, CT is generally rapid than MRI in neuroimaging and has therefore, remained a preferable imaging modality for evaluating patients with suspected stroke in the emergency setting. Only one of the reviewed study,[18] assessed applicability aspects, where the noncontrast CT was found to be rapid and more accessible than MRI for acute stroke diagnoses in the emergency setting. However, since 2005 neuroimaging technology has changed rapidly and MRI can now be performed much faster than before. For instance, a recent study has demonstrated that a 6-minute multimodal MR protocol is practical for evaluating patients with acute ischaemic stroke with comparable acquisition time as the multimodal CT protocol. Besides, a 6-minute multimodal MR protocol can provide a good diagnostic quality at a significantly reduced acquisition time.[29]

Importantly, unlike CT, MRI has multiple bases for contraindications. Patients with severe acute stroke are often contraindicated to MRI because it is not well-tolerated in such patient groups.[30]

In this case, Chalela et al. (2007)[11] reported to have excluded 49 patients who were contraindicated to MRI on the common criterion that they exhibited severe acute stroke. Furthermore, MRI protocols for patient safety do not allow patients with biomedical or metallic implants such as pacemakers, cochlear (ear) implant, aneurysm clips and cardiac stents, to enter the MR space, because this can result in harmful interaction of patient body with the generated magnetic field.[30]

Equally important, the physiological function of the magnetically sensitive devices can be deactivated or dislocated while in the patient's body.[10,30] However, while an MRI of the brain/head is generally safe for patients with non-head metal implants, the process of masking the body torso (the trunk of the human body) for selective head scanning is time-consuming and likely to derail timely administration of thrombolytic therapies to otherwise eligible ischaemic stroke patients. By this account, further research is warranted to delineate the applicability of MRI in acute stroke diagnosis for health policy makers.

LIMITATIONS

The general limitation of the present diagnostic test accuracy review study is that limited data from only four comparative studies were evaluated. Due to complexities associated with acquisition of translation service for scientific research articles, it was not possible to review potentially relevant articles published in languages other than English. Therefore, the present review study has one aspect of publication bias, which is the major limitation that rendered the inclusion of only a few comparative studies.

Data presented from the four studies generally lack internal and external validity. The evidences presented in the few included comparative studies were apparently marred by lack of adequate sample power, spectrum composition bias of acute stroke patients, methodological inconsistencies, and procedural biases. In general, the evaluated studies recruited participants with narrow spectrum of acute stroke, therefore limiting generalizability of the overall findings to the wider population of acute stroke patients, worldwide.

To conclude, the aims and objectives of the present diagnostic test accuracy review were partially achieved due to limitations highlighted and discussed in the preceding chapter. Hence, the quality and quantity of the summarised evidence does not meet threshold for making any decisive conclusions. Furthermore, the applicability of findings to the evidence-based clinical practice was not presented in a majority of the evaluated studies. Based on QUADAS-2 tool, most studies generally demonstrated good applicability of reference standard, but poor applicability with respect to index test and patient selection. Therefore, more comparative diagnostic test accuracy studies are warranted with special consideration of reducing the effect of the highlighted limitations. Future studies should consider using multi-centre trials with standardised technical capabilities of neuroimaging equipments and imaging modalities.

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