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RESEARCH

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Role of arterial spin labeling magnetic resonance perfusion in acute ischemic stroke

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Abstract

Background Arterial spin labeling (ASL) is a recently used magnetic resonance imaging (MRI) perfusion technique in acute cerebrovascular stroke conditions; it can detect the hypo perfused areas on basis of qualitative and quantitative measurements and also identify the area at risk known as penumbra by detecting the diffusion/perfusion mismatch. The purpose of this study was to assess the role of ASL perfusion technique in management of acute ischemic stroke and its ability to predict the clinical outcome of acute stroke patients. The study was prospectively carried out on 33 patients clinically presented with acute stroke from the first of August 2020 till the first of August 2021. All cases were clinically assessed by stroke consultant followed by brain imaging including conventional MRI and ASL perfusion technique, based upon which management was established. These imaging data were correlated with the clinical outcome after 3 months using Modified Rankin Scale.

Results Sixteen cases (48.48%) showed ischemic penumbra with diffusion perfusion mismatch with three cases presenting within the first 4 h managed by intravenous thrombolytic therapy and 13 cases presenting later than 4 h, 10 of whom were managed by endovascular intervention. The group with ischemic penumbra showed significant positive correlation with favorable clinical outcome while the group without ischemic penumbra showed significant positive correlation with poor clinical outcome. Quantitative ASL values were statistically significantly higher ($p \leq 0.05$) in patients with favorable clinical outcome than those with poor clinical outcome. The estimated cut off values of ASL absolute cerebral blood flow and relative cerebral blood flow to predict favorable or poor outcome using ROC curve analysis were 19 ml/100gm/min and 74% compared to the contralateral side respectively.

Conclusion The use of MRI as a primary diagnostic tool in arterial ischemic stroke with the application of non-contrast ASL perfusion sequence allows precise detection of perfusion deficit and diffusion perfusion mismatch (penumbra) and provides a reliable insight into outcome prediction.

Keywords Arterial spin labeling, Modified Rankin scale, Acute ischemic stroke, Penumbra

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Background

Cerebrovascular stroke is one of the leading causes of death and disability all over the world; its acute attacks known as acute ischemic strokes (AIS) are usually presented by focal neurological deficits [1]. Rapid management of AIS is very important to maintain the integrity of cerebral tissues which explains the importance of accurate imaging diagnosis of these cases [2]. Although CT is the mainstay emergency imaging tool to rule out hemorrhagic stroke, yet diffusion weighted images (DWI) is still considered the standard MRI technique in acute stroke cases due to its high sensitivity and specificity for identifying ischemic areas [3].

Until recently, the only effective reperfusion therapy in patients with AIS was intravenous recombinant tissue plasminogen activator (IV-rTPA) administered within 4.5 h after onset of manifestations. Yet, considerable number of patients present usually after this time window especially in wake up strokes which makes IV-rTPA less usefull with high risk for post thrombolytic complications [4]. To overcome this problem, endovascular thrombectomy (EVT) became the golden management decision for patients with large-vessel occlusion in the anterior circulation depending on other factors including presence of salvageable brain tissue known as penumbra as well as states of collaterals [5].

Previous randomized controlled trials provided evidence that patients of acute ischemic stroke showing mismatch between the infarcted and hypoperfused brain volume known as the penumbra might get benefit and be rescued from long lasting disability by reperfusion of the occluded cerebral vasculature even when such reperfusion was done 6–24 h from onset of manifestations [6, 7].

For years, contrast based techniques like CT perfusion (CTP) and dynamic susceptibility contrast (DSC) MRI perfusion have been the modalities of choice for detection of such perfusion mismatch in order to identify the ischemic penumbra [8, 9]. Yet, both techniques are contrast based which may result in acute kidney injury or nephrogenic systemic fibrosis rendering them contraindications in considerable number of old aged patients presenting with acute stroke [10].

ASL perfusion is a non-invasive perfusion technique which can assess cerebral blood flow based on magnetically labeling blood water protons with no usage of contrast material or ionizing radiation. This enables safety for renal patients and patients with hypersensitivity to contrast agents [11].

The aim of the current study was to assess the role of ASL perfusion in management plan of acute ischemic stroke and its ability to predict the clinical outcome of acute stroke patients.

Methods

Approval for this cross-sectional prospective study was obtained from the local human research ethics committee. All study procedures were carried out in accordance with the Declaration of Helsinki regarding research involving human subjects [12]. Written informed consent was obtained from all patients.

Study population

This study was conducted in the time interval from August 2020 to August 2021 on adult patients with clinical manifestations of acute cerebrovascular stroke who were referred from Neurology department at Alexandria University hospital and specialized stroke centers to the Radiodiagnosis Department, Alexandria, Egypt. Patients were included if they showed clinical suspicion of arterial ischemic stroke (AIS), and brain MR imaging was done within 24 h after the onset of symptoms. Patients were excluded if they showed hemorrhagic stroke, posterior circulation stroke, venous infarctions, stroke mimics as tumors as well as absolute contraindications to MRI such as metallic devices and pacemakers.

Pre-imaging clinical assessment

The clinical examination of the cases was done by neurology consultant with 5 years' experience in stroke management during the day of initial clinical presentation. Clinical assessment was performed using the National Institutes of Health Stroke Scale (NIHSS) which is a clinical scoring consisting of 11 elements including level of consciousness, best gaze, visual field, facial affection, motor arm affection, motor leg affection, limb ataxia, sensory abilities, language abilities, dysarthria as well as extinction and inattention. Finally, the cases were categorized according to NIHSS scale into 5 grades which are: 0 = no stroke symptoms, 1–4 = mild stroke, 5–15 = moderate stroke, 16–20 = moderately severe stroke and 21–42 = severe stroke.

MRI imaging protocol

MRI examinations were done using 3 Tesla Magnet MRI scanner (Discovery MR750 w 3.0 T, General Electric (GE), Milwaukee, USA). The images of MRI sequences were acquired with the following protocols:

- *Conventional MRI non contrast sequences* of the brain including axial T1-weighted spin echo (repetition time (TR) = 600 ms, echo time (TE) = 15 ms), axial, sagittal and coronal T2-weighted turbo spin echo (TR = 4000 ms, TE = 100 ms), axial FLAIR (TR = 11,000 ms, TE = 140 ms, inversion time (TI) = 2200 ms), Diffusion weighted imaging (DWI) with diffusion gradient b values of 0 and 1000 s\mm^2, along three orthogonal axes (x, y and z directions) over (TR = 5072; number of sections = 16–22) and Susceptibility Weighted Images; SWI (TR 38.5 ms, TE 22.9 ms, 320 × 224 acquisition matrix, field of view 240 × 192 mm, slice thickness 3 mm and a gap of 0.2 mm).

- *ASL MR perfusion sequence* using combined pseudo continuous arterial spin labeling [PCASL], and three dimensional [3D] fast spin echo acquisition techniques. The imaging parameters were as follows: TR = 4712 ms /TE = 12 ms, TI = 2025 ms, flip angle = 40°, FOV = 250 × 250 cm, matrix = 512 × 8, slice thickness/gap = 4/0.0 mm, number of dynamics = 30. The total acquisition time was 4 min with the labeling slab thickness positioned at the level of the upper cervical region.

Data analysis and image evaluation

The imaging assessment was done by 2 separate expert neuro-radiologists with 15 years and 10 years' experience according to the following steps:

1. *Detection of acute stroke* was done by DWI; the territorial involvement of the ischemic core on DWI sequence was determined using the Alberta Stroke Program Early CT score (ASPECTS) involving a ten-point topographic scoring system. According to this system, the MCA irrigation area is divided into 10 zones, and 1 point is subtracted from the initial score of 10 for every region involved [11]. (Fig. 1)
2. *Detection of perfusion deficit* was done by ASL perfusion: ASL data processing was done on General Electric workstation using Functool Brain stat software (ADW4.7 GE workstation). Visual assessment of diffusion perfusion mismatch was done to assess the presence of penumbra. Quantitative assessment of ASL was also done for prediction of the final outcome. The aCBF values were determined by drawing regions of interest (ROIs) within the ischemic area, avoiding the regions of vessels and cystic changes. The rCBF values were determined by drawing ROIs over the contralateral normal appearing areas.
3. *Detection of hemorrhagic stroke* was done by SWI (patients were excluded if showed hemorrhagic lesions).
4. *Detection of stroke mimics* was done by T2 and FLAIR sequences (patients were excluded if showed stroke mimics lesions).

Post-imaging management

All cases were managed by stroke neuro-consultant. According to the 2018 American Heart Association (AHA)/American Stroke Association (ASA) guidelines [13], the treatment decision depended on the ASPECTS score (interpreted in the current study from DWI) within the first 4 h of manifestations, where intravenous recombinant tissue plasminogen activator (IV-rTPA) was administered if ASPECTS score was more than 7. After the first 4 h, presence of penumbra (interpreted in the current study from ASL/diffusion mismatch) was the main factor upon which endovascular clot removal with stent insertion was the treatment choice.

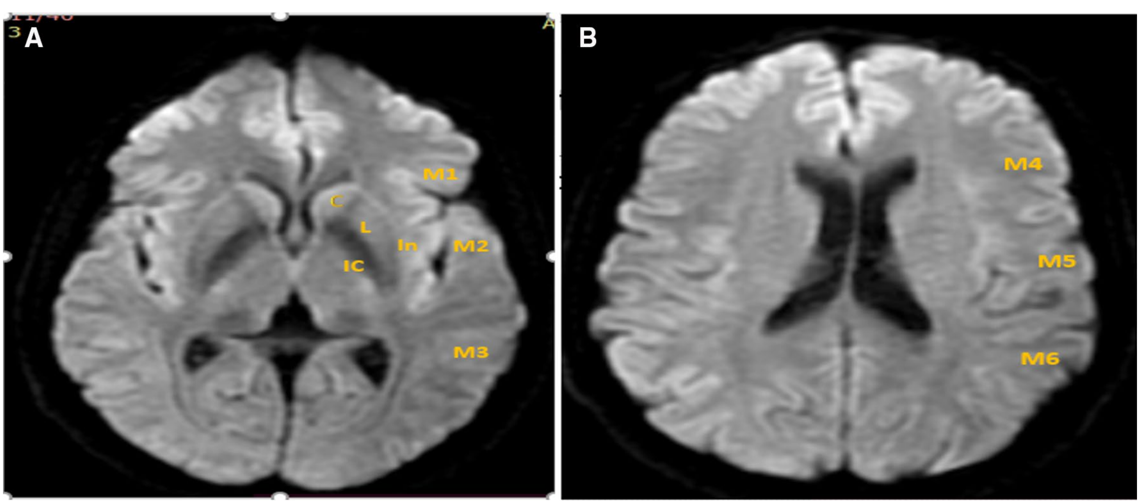

Fig. 1 Alberta Stroke Program Early CT Score (ASPECTS) in diffusion weighted imaging. **A** axial DWI at the level of the basal ganglia showing seven areas assessed in ASPECTS including caudate nucleus (C), insular ribbon (In), internal capsule (IC), lentiform nucleus (L), anterior middle cerebral artery (MCA) cortex (M1), MCA cortex lateral to the insular ribbon (M2), and posterior MCA cortex (M3). **B** Axial DWI at supraganglionic level showing the other three areas assessed in ASPECTS including M4, M5 and M6 which are the anterior, lateral, and posterior MCA territory immediately superior to M1, M2, and M3

Clinical follow up assessment

All cases were reassessed after 3 months using modified Rankin Scale (mRS) which is a commonly used clinical outcome scale for measuring the disability or dependence degree of people who have suffered acute stroke insults. It runs from 0 to 6 starting from perfect health without symptoms to death and categorized into 2 groups according the numerical date of the scale which are: 0–2 = Favorable outcome and 3–6 = poor outcome including the score 6 which considered patient's death.

Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). The Shapiro–Wilk test was used to verify the normality of distribution of variables. Correlation between penumbra status and clinical outcome was assessed using Chi-square test. Student t-test and Spearman coefficient were used for comparison between mRS (representing the clinical outcome) and the imaging data of the studied cases including ASPECT score, ASL aCBF and ASL rCBF. Receiver operating characteristic curve (ROC) was used to predict the expected stroke outcome (mRS favorable or poor), and was generated by plotting sensitivity (TP) on Y axis versus 1-specificity (FP) on X axis at different cut off values. The area under the ROC curve denotes the diagnostic performance of the test. Area more than 50% gives acceptable performance and area about 100% is the best performance for the test. Significance of the obtained results was judged at the 5% level.

Results

Demographic data

The study was carried out on 33 adult patients presenting by acute ischemic stroke, ranging in age from 33 to 94 years with mean age 64.45 ± 14.74 years. Within the study group 17/33 (51.52%) cases were males and the remaining 16/33 cases (48.48%) were females.

Clinical data at the time of initial presentation

Some patients were presenting by more than one complaint. The most common clinical presentation within the study group was motor affection (hemiparesis) presenting in 29 patients (87.88%) followed by sensory affection which was present in 19 patients (57.58%). Other less common symptoms were dysphasia, visual symptoms and disturbed level of consciousness; however, the least common one was apraxia which was present in only 2 cases. Right sided weakness was predominant seen in 21 patients (63.64%).

Average pre-diagnostic time interval was estimated for all cases, where five patients presented within the first 4 h after start of manifestations while the rest of 28 patients presented after 4 h up to 24 h. The mean time was 11.73 ± 1.46 h (lowest is 2 h and highest is 24 h).

NIHSS scale was assessed and according to which the cases were classified into 4 groups: 1–4 = mild stroke included 3 patients, 5–15 = moderate stroke included 19 patients, 16–20 = moderately severe stroke included 6 patients and 21–42 = severe stroke which included 5 patients. The median NIHSS scale for the study group was 14 and the interquartile ratio (IQR) was 5 (Table 1).

Imaging data

I-patients presenting within the first 4 h

All five cases presenting within the first 4 h showed diffusion restriction with 3 cases showing ASPECT score more than 7, yet with diffusion-perfusion mismatch. The three cases received IV-rTPA and showed favorable outcome in follow up after three months. Two cases showed low ASPECTS score (less than 7) with no evidence of DWI-ASL mismatch, and they didn't receive IV-rTPA. These last two cases showed poor follow up clinical outcome.

II-patients presenting after 4 h up to 24 h

The remaining 28 cases presenting after 4 h were further divided into two groups according to the presence of diffusion–perfusion mismatch:

Group IIA: patients with DWI-ASL mismatch

13 cases presented with DWI-ASL mismatch, 10 of them showed ASPECTS score more than 7 and thus underwent endovascular clot removal (Fig. 2), while the remaining three showed low ASPECTS score and didn't receive endovascular intervention. All 10 patients who underwent endovascular intervention showed favorable outcome after 3 months, while the remaining three patients showed poor outcome.

Group IIB: patients with No DWI-ASL mismatch

15 cases presented after 4 h yet with no DWI-ASL mismatch indicating absence of penumbra and thus didn't undergo any neurovascular intervention. ASPECTS score was low in all patients and 14/15 of them showed poor outcome after 3 months while the remaining case showed favorable outcome (Fig. 3).

Figure 4 represents a flow chart showing different acute stroke cases groups (groups I, II A, IIB) and their management and outcome.

Table 1 Demographic data of the studied acute stroke patients ($n = 33$)

Demographic data			No. of cases	%
Sex				
Male			17	51.52
Female			16	48.48
Age (years)				
30–≤ 39			2	6.06
40–≤ 49			3	9.09
50–≤ 59			6	18.18
60–≤ 69			10	30.30
70–≤ 79			9	27.27
80–≤ 89			1	3.03
90–≤ 99			2	6.06
Mean and SD			64.45 ± 14.74 years	
Pre-diagnostic time interval			No. of cases	%
First 4 h			5	15.15
After 4 h till 24 h			28	84.84
Mean and SD			11.73 ± 1.46 h	
Clinical presentation			No	%
Site of presentation				
Right sided			21	63.64
Left sided			10	30.30
Other presentations			2	6.06
Clinical presentation (Some cases showed more than 1 presentation)				
Motor weakness			29	87.88
Sensory affection			19	57.58
Dysphasia			7	21.21
Visual symptoms (visual field defect, blurred vision)			5	15.15
Disturbed level of consciousness			4	12.12
Apraxia			2	6.06
	Group A	**Group B**	**Group C**	**Group D**
NIHSS categories				
Finding	Mild stroke	Moderate stroke	Moderately severe stroke	Severe stroke
No. of cases	3 (9.09%)	19 (57.56%)	6 (18.18%)	5 (15.15%)
Median NIHSS	14			
IQR NIHSS	5 (minimum 12, maximum 17)			

IQR Interquartile ratio, *NIHSS* National Institutes of Health Stroke Scale, *No.* Number, *SD* standard deviation

Clinico-imaging correlation after 3 months

It was done by stroke consultant using mRS scale; the studied cases were categorized into 2 groups; 0–2 points = favorable outcome which included 14 cases (42.42%) and 3–6 points = poor outcome which included 19 cases (57.58%) considered that 6 points means death.

Positive significant statistical correlation was proved between presence of penumbra (detected as diffusion/ASL perfusion mismatch) and mRS clinical outcome. Detection of ischemic penumbra was significantly correlated with late favorable outcome and its absence was significantly correlated with poor outcome ($p \leq 0.05$) (Table 2).

Positive significant statistical correlation was also proved between ASL perfusion data and mRS using student t-test. The quantitative ASL perfusion imaging

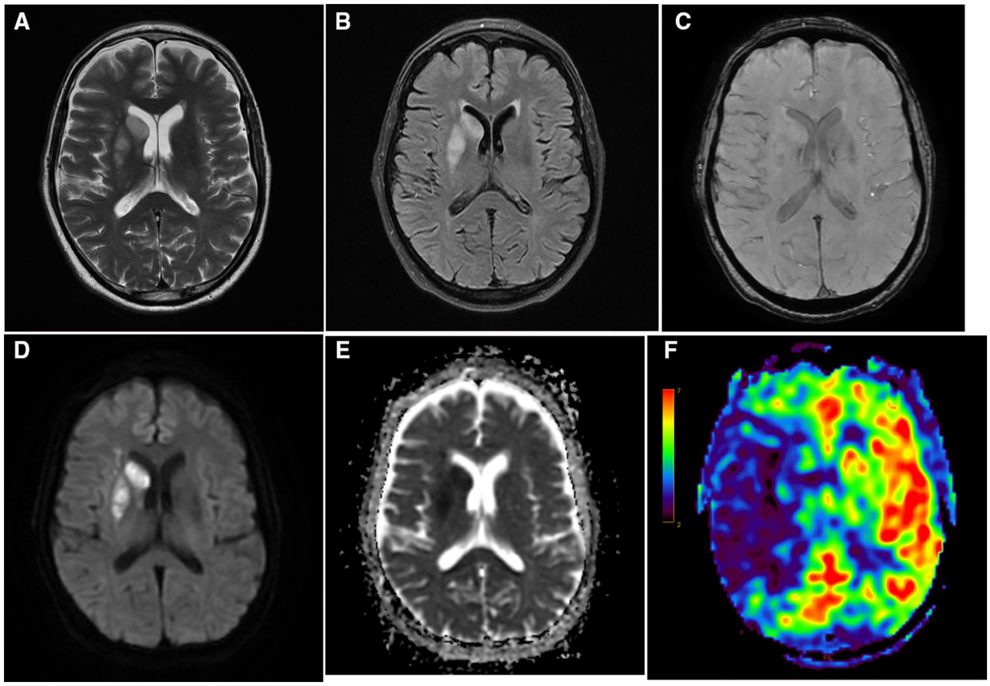

Fig. 2 Acute infarction with ischemic penumbra: 78 years old male patient complaining of left hemiplegia since 8 h. **A** T2WI, **B** FLAIR, **C** SWI, **D** DWI, and **E** ADC map show acute ischemic infarct at the right basal ganglia. ASPECTS score was 8/10. **F** ASL perfusion at 1.5 s shows larger area of hypo perfusion (diffusion perfusion mismatch) reflecting large area of ischemic penumbra, aCBF = 14 mL/gm 100/min—rCBF = 65% to contralateral side. *aCBF* absolute cerebral blood flow, *ADC* apparent diffusion coefficient, *ASL* arterial spin labeling, *ASPECT* Alberta Stroke Program Early CT Score, *DWI* diffusion weighted image, *rCBF* relative cerebral blood flow, *SWI* susceptibility weighted image

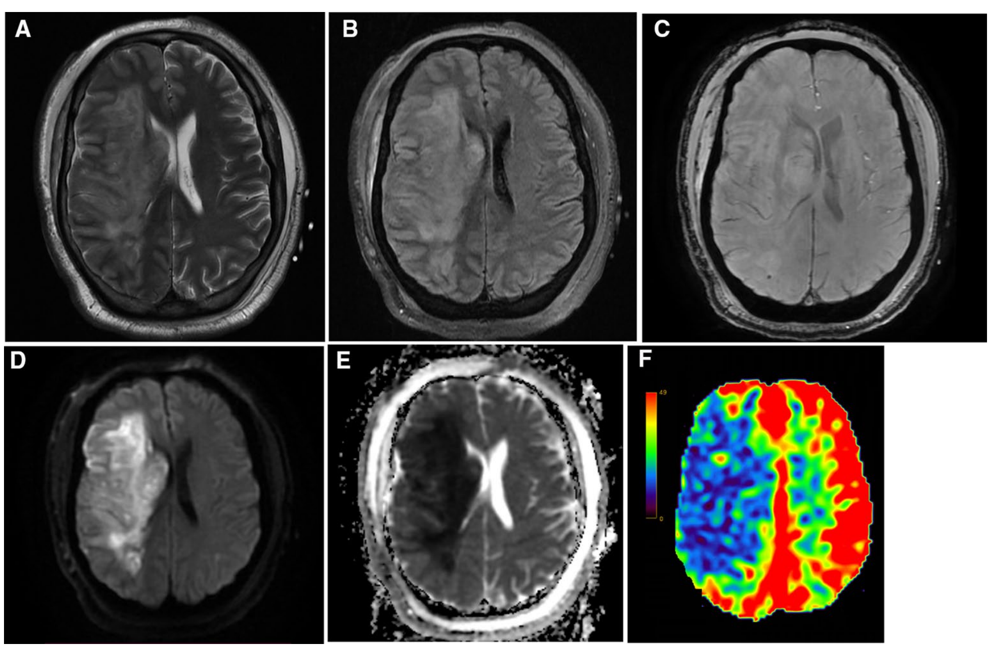

Fig. 3 Acute infarction with no ischemic penumbra: 75 years old female patient complaining of left hemiplegia since 10 h. **A** T2WI, **B** FLAIR, **C** SWI, **D** DWI, and **E** ADC map show acute ischemic infarct at the right frontoparietal region along the territory of the right MCA. ASPECTS score was 3/10. **F** ASL perfusion at 1.5 s shows corresponding area of hypo perfusion (no diffusion perfusion mismatch) without ischemic penumbra, aCBF = 11 mL/gm 100/min—rCBF = 62% to contra lateral side. *aCBF* absolute cerebral blood flow, *ADC* apparent diffusion coefficient, *ASL* arterial spin labeling, *ASPECT* Alberta Stroke Program Early CT Score, *DWI* diffusion weighted image, *rCBF* relative cerebral blood flow, *SWI* susceptibility weighted image

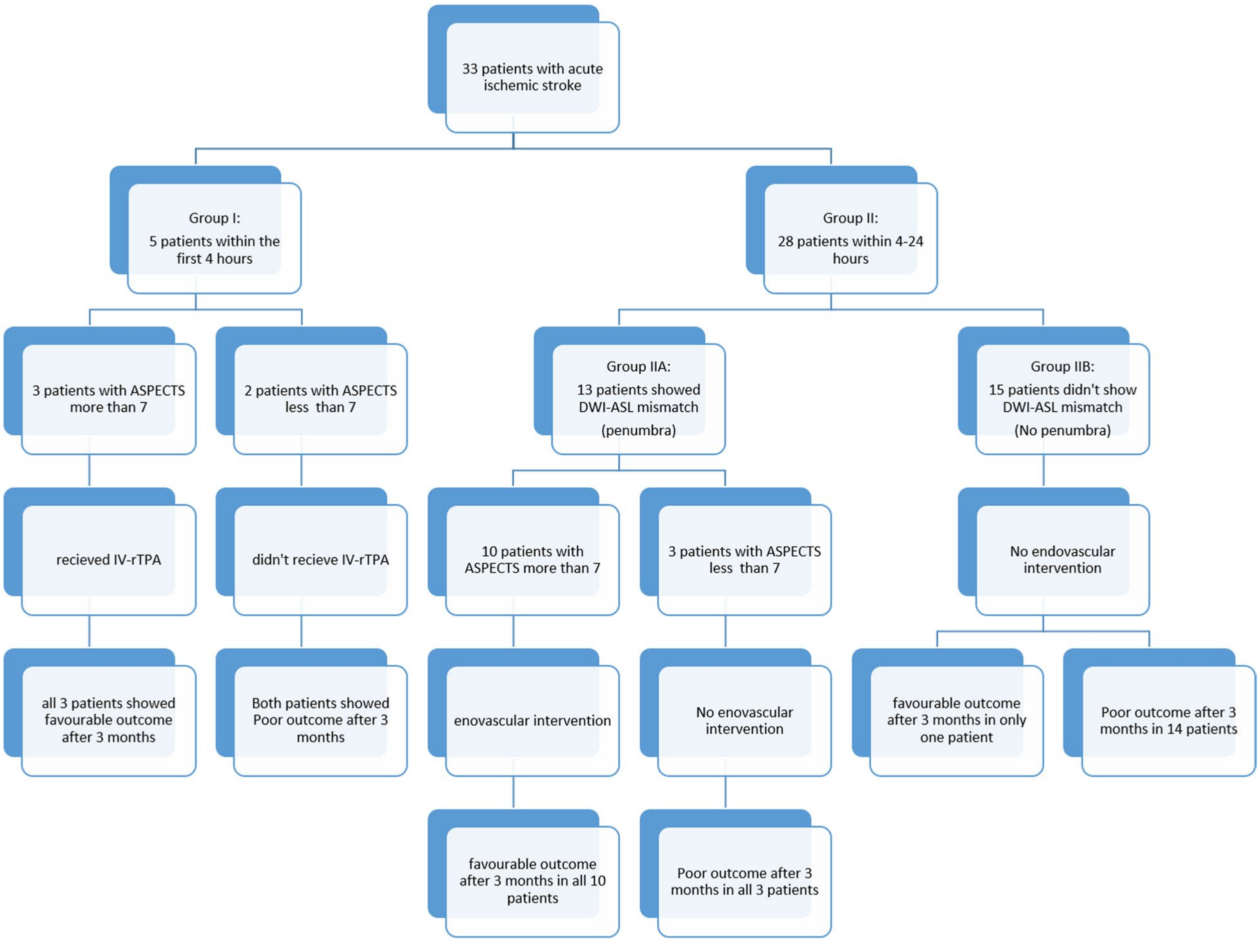

Fig. 4 Flow chart showing different acute stroke cases categories and their management and outcome (groups I, II A, IIB)

Table 2 Correlation between penumbra status (diffusion/ASL mismatch) and clinical outcome after 3 months (modified Rankin score) in acute stroke patients ($n = 33$)

	Diffusion/ASL mismatch (Penumbra) ($n = 16$)	No diffusion/ASL mismatch (No penumbra) ($n = 17$)	χ^2	p
Favorable outcome ($n = 14$)	13	1	19.1677*	< 0.001*
Poor outcome ($n = 19$)	3	16		

ASL arterial spin labeling, χ^2 Chi square test

*Statistically significant at $p \leq 0.05$

findings were significantly higher in patients with mRS favorable outcome compared with patients with poor outcome ($p \leq 0.05$) (Table 3).

ROC curve analysis showed ASL relative CBF ≤ 74% as compared to normal appearing brain to have higher accuracy than absolute CBF ≤ 19 ml/100gm/min in predicting poor stroke outcome (84.21% sensitivity, 78.57% specificity, 84.2% positive predictive value and 78.6% negative predictive value as compared to 78.95%, 71.43%, 78.9% and 71.4% respectively). Figure 5 and Table 4.

Table 3 Correlation between imaging data (ASPECTS and ASL) and clinical outcome (modified Rankin score) in acute stroke patients

Imaging data	mRS category		t	*p*
	Favorable ($n=14$)	Poor ($n=19$)		
ASPECT				
Mean ± SD	8.21 ± 0.43	5.68 ± 2.31	4.666*	< 0.001*
Median (Min.–Max.)	8 (8–9)	7 (0–8)		
ASL aCBF				
Mean ± SD	20.29 ± 4.32	15.79 ± 4.04	3.070*	0.004*
Median (Min.–Max.)	21.5 (10–25)	14 (8–22)		
ASL rCBF				
Mean ± SD	79.14 ± 4.24	67 ± 8.55	4.876*	< 0.001*
Median (Min.–Max.)	79.5 (73–89)	69 (42–79)		

aCBF absolute cerebral blood flow, *ASL* arterial spin labeling, *ASPECT* Alberta Stroke Program Early CT Score, *mRS* modified Rankin score, *p* p value for comparing between mRS class and radiological data, *rCBF* relative cerebral blood flow, *SD* Standard deviation, *t* Student t-test

*Statistically significant at $p \leq 0.05$

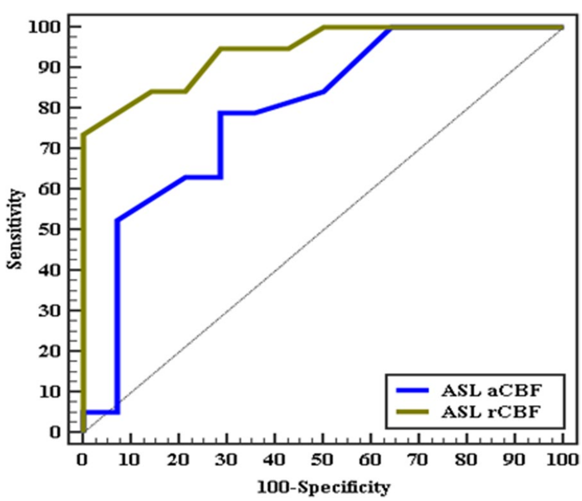

Fig. 5 ROC curve for ASL absolute CBF (aCBF) and relative CBF (rCBF) to predict the expected stroke outcome (mRS favorable or poor)

Discussion

Cerebrovascular acute ischemic stroke (AIS), predominantly if it is produced by a large-vessel occlusion (LVO), is a severe and life-threatening disease. New developments in neuroimaging have demonstrated a great benefit of endovascular thrombectomy (EVT) if patients were properly triaged based on clinical and imaging features [14, 15].

Endovascular therapy after imaging evaluation for AIS trials represent a paradigm shift in management, moving from the previously strictly accepted time-based decision to a more physiologic based decision depending on the advanced neuroimaging findings suggestive of salvageable brain tissue [16–18].

In addition to confirming the presence of AIS and identifying occluded vessels, different imaging techniques are used for detection of core infarcts and penumbras. They accurately separate core infarct from reversible ischemic tissue at risk, thus indicating the potential benefits of mechanical thrombectomy [19, 20].

Based on both DWI and perfusion; the area at risk which is called ischemic penumbra can be identified representing the ongoing parenchyma to be irreversibly infarcted and can be potentially salvageable if the adequate treatment succeeds to reperfuse it within a window period [21, 22].

The current study tried to assess the role of ASL perfusion sequence in management of acute stroke patients based on penumbra detection and its ability to predict the clinical outcome status relying on its quantitative values.

Can ASL perfusion aid in management of acute stroke patients? Was the first question we tried to answer. The current study showed that ASL succeeded in detection of ischemic penumbra as three cases out of five presenting within the first four hours showed diffusion perfusion mismatch and more importantly 13/28 cases presenting within the latter time window of 4–24 h showed such mismatch, depending on which these cases were treated with endovascular clot removal and showed favorable outcome.

Table 4 Validity (AUC, sensitivity, specificity) of ASL aCBF and rCBF to assess the expected stroke outcome (favorable or poor mRS)

	AUC	*p*	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV
ASL aCBF	0.793	0.004*	0.631–0.955	$\leq 19^{\#}$	78.95	71.43	78.9	71.4
ASL rCBF	0.942	< 0.001*	0.869–1.014	≤ 74	84.21	78.57	84.2	78.6

ASL arterial spin labeling, *aCBF* absolute cerebral blood flow, *AUC* Area Under a Curve, *CI* Confidence Intervals, *NPV* Negative predictive value, *p value* Probability value, *PPV* Positive predictive value, *rCBF* relative cerebral blood flow

*Statistically significant at $p \leq 0.05$

[#] Cut off was choose according to Youden index

Such findings were in agreement with the previous study of Dongmei et al. [10], who studied the role of diffusion perfusion mismatch based on ASL in 12 patients with wake up stroke; defined as stroke occurring during sleep. All patients in such study showed mismatch and 11/12 patients showed reduced NIHSS score at their discharge with 8/12 patients (66.7%) showing favorable mRS at 90 days follow up.

Can ASL perfusion predict the clinical outcome of acute ischemic stroke? Was the second question we tried to answer. The current study proved significant statistical correlation between presence of penumbra detected by DWI/perfusion mismatch and clinical outcome using mRS; detection of ischemic penumbra was significantly correlated with favorable outcome and its absence was significantly correlated with poor outcome ($p \leq 0.05$).

The current study also proved significant statistical correlation between quantitative assessment using absolute and relative ASL CBF values and clinical outcome using mRS. Significant correlation was proved between higher ASL CBF values and favorable clinical outcome which is explained by presence of collateral blood flow supplying these areas and maintaining its functional and metabolic activities. By using ROC curve, our study showed good prognostic characteristics of ASL aCBF and rCBF cut-off values of 19 ml/100gm/min and 74% compared to the contralateral side respectively in predicting clinical outcome.

Such findings were in agreement with the previous study of Trenkic et al. [23], who studied the prognostic role of ASL perfusion in 205 patients with acute ischemic stroke and concluded that the determination of CBF values in patients with AIS is a significant prognostic factor for assessing a favorable outcome following an appropriate reperfusion therapy. This was explained as drop in CBF is one of the first of many sequential events finally resulting in brain damage. Autoregulation mechanisms that preserve the tissue viable become exhausted over time subsequently resulting in a drop in CBF values. When the drop reaches a certain threshold, cerebral tissue becomes irreversibly injured, consequently causing a poorer functional outcome.

As regards quantitative assessment using ROC curve, our study showed nearly similar cut off value for absolute CBF (19 ml/100gm/min in both studies) in predicting the outcome, yet relative CBF was different (74% in our study compared to 49.7% in the study of Trenkic et al. [23]). Such difference may be explained by the larger study group of their study which included 205 patients but our study included only 33 cases [23]. Another cause may be the region of interest or normal appearing brain selection as we selected contralateral normal appearing white matter while they have selected contralateral grey matter to compare with.

Points of strength The current study was done at a high magnetic field of 3 T with a higher signal to noise ratio (SNR) and all the cases were clinically assessed from the start of the clinical manifestations till the end of the treatment and these clinical data were correlated with the imaging data.

Limitations of the study The main limitation of the current study was the relatively smaller number of patients included in the study which explains the difference in quantitative role of ASL perfusion as mentioned. Another limitation was doing single phase ASL technique with no usage of multi delay ASL technique. The multi delay technique allows detection of adequate collaterals via pial arteries and hence delayed improvement of ASL perfusion values on delayed phases. The last limitation was absence of comparative study between ASL perfusion and the more established dynamic susceptibility contrast (DSC) brain perfusion technique or CT perfusion which are more established techniques in detection of brain penumbra; as no contrast was given to the included patients; such comparison would have added value to the role played by ASL in acute stroke management.

Conclusions

The use of MRI as a primary diagnostic tool in arterial ischemic stroke with the application of up-to-date non-contrast ASL perfusion sequence allows precise detection of perfusion deficit and diffusion perfusion mismatch renovating the management paradigm from a firm time-based approach to a more flexible imaging based approach tailored to save acute stroke patient presenting beyond the first 4 h as well as providing a reliable insight into outcome prediction.

Abbreviations

aCBF	Absolute cerebral blood flow
AIS	Acute ischemic strokes
ASL	Arterial spin labeling
ASPECTS	Alberta Stroke Program Early CT score
DWI	Diffusion weighted imaging
EVT	Endovascular thrombectomy
IV-rTPA	Intravenous recombinant tissue plasminogen activator
mRS	Modified Rankin scale
NIHSS	National Institutes of Health Stroke Scale
rCBF	Relative cerebral blood flow

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Author contributions

AB and MH drafted the manuscript. MH and HK collected the data. AY and AN edited the images. AH performed the clinical assessment and management for the patients. All authors read and approved the final manuscript.

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Availability of data and materials
The data sets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved by the Department of Radiology, Benha Faculty of Medicine Research Ethics Committee, University of Benha, Egypt (ethics committee reference number is not available). A written consent was obtained from each patient involved in this research before performing the study.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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