Original Article

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Radiology Section

Brain Diffusion in Brainstem Infarctions and Lesion Segmentation using Fluid-attenuation Inversion Recovery: A Diagnostic Accuracy Study

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ABSTRACT

Introduction: Diffusion can efficiently detect infratentorial and brainstem infarctions. Fluid-attenuation Inversion Recovery (FLAIR) is a widely used Magnetic Resonance Imaging (MRI) technique for the segmentation of brain lesions and strokes.

Aim: To investigate the sensitivity of the Lesion Prediction Algorithm (LPA) within the Lesion Segmentation Tool (LST) in the automated segmentation of acute and subacute brainstem infarctions.

Materials and Methods: This study was a retrospective diagnostic accuracy study where 24 patients with brainstem infarctions were referred from the Emergency Department to the Department of Radiodiagnosis at Kasr Alainy Hospital, Cairo University, Egypt. The study was conducted from September 2016 to June 2023. It included 24 patients (14 males and 10 females) with acute and subacute brainstem infarctions. MRI of the brain and diffusion were performed on all patients. Automated segmentation of brainstem infarctions using FLAIR was conducted in all cases. Manual and segmented volumes of brainstem infarctions were calculated. Sensitivity and accuracy of the LPA within the LST in automated segmentation of acute and subacute brainstem infarctions were evaluated. Pearson correlation was used to correlate volumes of White Matter Lesion (WML) burden in patients with brainstem infarctions and patients' age.

Results: The mean age of the participants was 51.75±11.95 years. The sensitivity of the LPA in automated segmentation of acute and subacute brainstem infarctions was 63.6% and 76.9%, respectively. An insignificant correlation (r=0.08; p-value=0.68) between the volumes of WML burden in patients with brainstem infarctions and patients' age was noted.

Conclusion: The sensitivity of the automated method in the segmentation of subacute brainstem infarctions was higher than that in acute brainstem infarctions.

Keywords: Automated segmentation, Infratentorial, Magnetic resonance imaging, Strokes

INTRODUCTION

Brainstem strokes are relatively uncommon. Many studies have demonstrated the validity of brain diffusion in the identification of acute infratentorial and brainstem infarctions [1-4]. Diffusion can efficiently differentiate between acute and chronic brain infarctions [5]. Cerebral infarctions, also known as ischaemic strokes, cause serious disabilities and mortalities [6,7]. On MRI of the brain, several semi-automated procedures have been designed for the localisation and segmentation of brain strokes [8,9]. Automated segmentation provides rapid lesion demarcation. FLAIR is a widely used MRI technique for brain lesion segmentation [10-13]. Multimodal automated methods designed through machine learning approaches have been applied for the segmentation of acute and subacute brain infarctions [14-16]. LST is an automated method for lesion segmentation, including WML, strokes, and other brain diseases. LPA is a subset of LST that requires the FLAIR sequence for lesion segmentation [10,17-19]. Although some researchers have discussed the utility of automated methods in the segmentation of cerebral infarctions, studies focusing on the segmentation of brainstem infarctions have been rare [20]. Recently, automated deep learning procedures have been developed for the segmentation of acute ischaemic cerebral and infratentorial infarctions [21-23]. Thus, the present study aimed to explore the accuracy of LPA within LST in the automated segmentation of acute and subacute brainstem infarctions.

MATERIALS AND METHODS

This study was a retrospective diagnostic accuracy study where 24 patients with brainstem infarctions were referred from the Emergency Department to the Department of Radiodiagnosis at Kasr Alainy Hospital, Cairo University, Egypt. The study was conducted during the period from September 2016 to June 2023. The study was approved by the Institutional Research Ethical Committee of the Faculty of Medicine, Cairo University, with registration number (N-42-2016). The requirement for patient consent has been waived.

Inclusion criteria:

- Patients with acute and subacute brainstem infarctions (ischaemic strokes).
- Patients with brainstem infarctions and associated brain lesions.

Exclusion criteria:

- Chronic brainstem infarctions.
- Haemorrhagic strokes, demyelinating brain disease, brain tumours, inflammation, and head trauma.
- Children, individuals with metallic implants, and postoperative cases.

Study Procedure

The initial diagnosis of brainstem infarctions was based on the clinical presentation of the acute onset of hemiplegia, nystagmus, dysarthria, and MRI brain, including diffusion images.

Image acquisition: Imaging was performed on a 1.5 Tesla MRI superconducting scanner (Intera; Philips Medical Systems, Best, the Netherlands). Images were obtained using a phased-array head coil. MRI of the brain was performed, including axial T1-weighted Images (T1WI) with Repetition Time (TR)/Echo Time (TE)=477 ms/15s, axial T2WI, coronal, and sagittal images with TR/TE=3659 ms/100s, and axial FLAIR images with TR/TE/Time of Inversion (TI): 4948 ms/120s/2000. A slice thickness of 6 mm, with an intersection gap of 1.5 mm, sections were acquired with a 240 mm×240 mm Field Of View (FOV) and image matrix of 256×256. Diffusion-weighted Images (DWI) were acquired in the axial plane using a single-shot Echoplanar imaging-spin echo pulse sequence with the following parameters: TR/TE=3909/95, FOV=24 cm×24 cm, slice thickness=5.5 mm, interslice gap=1 mm, matrix size of 128×128. ADC maps were generated from the DWIs (b=1000 s/mm^2).

Manual measurement of volumes of brainstem infarctions: Volumes of brainstem infarctions were manually measured from FLAIR images using Radiant Digital Imaging and Communications in Medicine (DICOM) Viewer. The volume of brainstem infarction=area of infarction in maximum dimensions×number of slices with brainstem infarctions×slice thickness [24-26].

Preprocessing and automated segmentation: FLAIR images were realigned, co-registered, smoothed, and spatially normalised to Montreal Neurological Institute (MNI) template space using the Statistical Parametric Mapping (SPM12) software package (www.fil.ion.ucl.ac.uk). The output FLAIR images were fed into the LST toolbox (LST) (version 2.0.15) implemented in (SPM12) running in MATLAB R2017a (The MathWorks, Inc., Natick, MA). LPA within the LST toolbox was operated on all cases with a kappa value of 0.3. Automated segmentation and volumetry for brain WML burden, including brainstem infarctions and associated WML, were performed on all patients, generating coloured overlaid FLAIR output images. Volumes of segmented brainstem infarctions were calculated from each slice. The volumes of the segmented brainstem infarctions obtained by the automated method were compared to the original manual volumes. 'Incomplete segmentation' means that less than 70% of the original volume of the brainstem infarction was segmented by the automated method, and 'near complete segmentation' means that more than or at 70% of the original volume of the brainstem infarction was segmented by the automated method. True positives (complete or near-complete segmentation) and false negatives (completely unsegmented or incomplete segmentation) for the automated method (LPA) were calculated.

STATISTICAL ANALYSIS

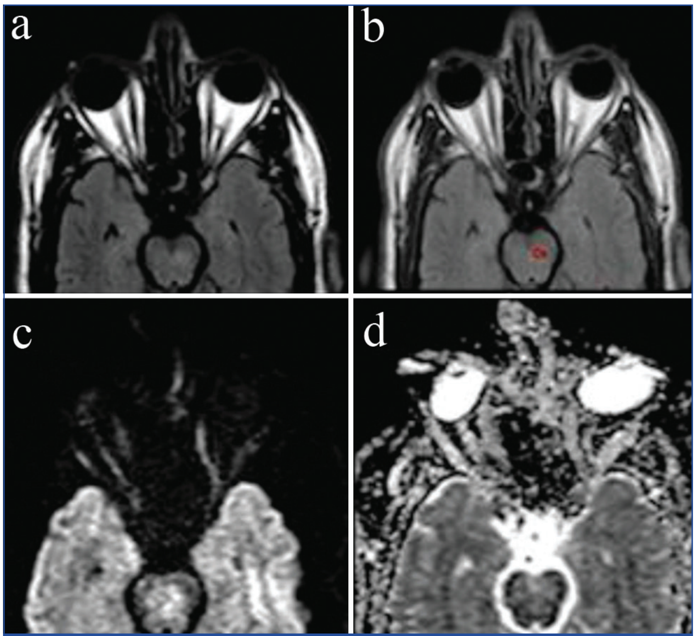
Sensitivity, accuracy, and Dice Similarity Coefficient (DSC) of segmentation of acute and subacute brainstem infarctions using LPA were obtained. Pearson's correlation was used to correlate the volumes of WML burden in patients with brainstem infarctions and the patients' age. Continuous data were expressed as mean (range)±SD (Standard deviation). Statistical analysis was performed using the International Business Machines (IBM) Statistical Package for the Social Sciences (SPSS) software version 22.0 (IBM, Armonk, NY, USA). A p-value <0.05 was considered significant.

RESULTS

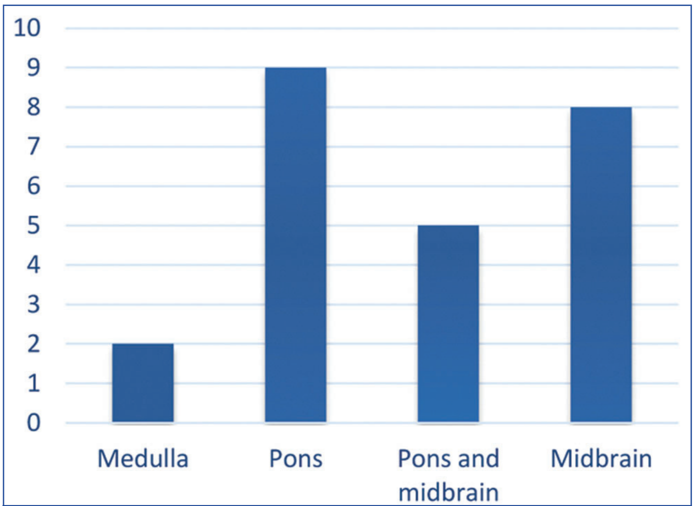
The current study included 24 cases with acute and subacute brainstem infarctions, with a mean age of 51.75±11.95 years.

Image interpretation: The initial diagnosis of acute and subacute brainstem infarctions was established using diffusion and ADC maps. Acute brainstem infarctions were hyperintense in T2, FLAIR, DWI, and hypointense in the ADC map (indicating restricted diffusion). Subacute brainstem infarctions were hyperintense in T2, FLAIR, DWI, and ADC map [Table/Fig-1a-d]. Pontine infarctions were the most common site for brainstem infarctions [Table/Fig-2]. Brainstem infarctions were more common on the left-side (62.5%) compared to the right-side (37.5%).

Patients with brainstem infarctions were associated with brain WMLs showing hyperintense signals in T2 and FLAIR [Table/Fig-3].



[Table/Fig-1]: A 49-year-old male patient with left midbrain infarction. MRI brain a) Axial FLAIR; b) Segmented image of brainstem infarction by lesion prediction algorithm; c) DWI; and d) ADC map. Left deep midbrain hyperintense lesion in FLAIR, DWI, and ADC map denoting subacute infarction. A 99% of the brainstem infarction detected in FLAIR (a) was segmented by lesion prediction algorithm (b).



[Table/Fig-2]: Distribution and locations of cases with acute and subacute brainstem infarctions.

Category	n (%)
Age mean±SD (years)	51.33±11.72
Gender, M:F	14: 10
Hypertensives n (%)	13 (54.16%)
Diabetics n (%)	7 (29.16%)
Total cases with brainstem infarctions	**24**
Acute brainstem infarctions n (%)	11 (45.83%)
Subacute brainstem infarctions n (%)	13 (54.16%)
Manual volumes of brainstem infarction (in FLAIR) (mm^3) mean (range)±SD	
Total cases with brainstem infarctions	113.063 (8.9- 480)±140.02
Acute brainstem infarctions	171.3 (20.28- 480)±173.30
Subacute brainstem infarctions	63.78 (8.9- 277)±82.525
Volumes of segmented brainstem infarctions by LPA (mm^3) mean (range)±SD	
Total cases with brainstem infarctions	86.68 (0-478)±111.89
Acute brainstem infarctions	125.8 (0-478)±145.098
Subacute brainstem infarctions	53.55 (6- 177)±62.13
Total WML burden volumes (mL) in patients with brainstem infarctions mean (range)±SD	10.45 (0.308-61.27)±14.12

[Table/Fig-3]: Demographic and imaging characteristics of patients with brainstem infarctions (N=24).

Evaluation of automated segmentation of brainstem infarctions using LPA: True positives and sensitivity of LPA in automated segmentation of brainstem infarctions were higher in subacute infarctions than in acute infarctions [Table/Fig-4,5]. Complete unsegmentation by the automated method (LPA) was noted in one case with acute brainstem infarction [Table/Fig-3]. An insignificant correlation between volumes of WML burden in patients with brainstem infarctions and patients' age was noted [Table/Fig-6]. Results of the segmentation of brain strokes from the current study and other studies were summarised in [Table/Fig-7] [27-30].

Items	True positives n (%)	False negatives n (%)
Total brainstem infarctions (N=24)	17 (70.8)	7 (29.16)
Acute brainstem infarctions (n=11)	7 (63.6)	4 (36.36)
Subacute brainstem infarctions (n=13)	10 (76.9)	3 (23.07)

[Table/Fig-4]: True positives and false negatives of segmented brainstem infarctions using LPA.

Items	Sensitivity	Accuracy	DSC
Total brainstem infarctions (N=24)	70.8	70.8	82.9
Acute brainstem infarctions (n=11)	63.6	63.6	77.7
Subacute brainstem infarctions (n=13)	76.9	76.9	86.9

[Table/Fig-5]: Sensitivity, accuracy and DSC of segmentation of brainstem infarctions using LPA.

Item	Patients' age	
Total WML burden volumes	Pearson's correlation (r)	p-value*
	0.08	0.68

[Table/Fig-6]: Correlation between total WML burden volume and patients' age in total cases with brainstem infarctions.
*p-value <0.05 was considered significant

Feng C et al., investigated a multispectral automated method using multiple MRI sequences, including FLAIR, to segment subacute brain infarctions and reported a DSC of 0.55±0.3 for the automated method, which aligns with the current results [29]. In the current study, the sensitivity of LPA using FLAIR was higher in subacute brainstem infarctions than in acute infarctions, possibly due to insufficient or faint signal intensity in FLAIR images for lesion mapping in early acute infarctions.

A hybrid semi-automated method was proposed by Rajinikanth V and Satapathy SC to segment Ischaemic Stroke Lesions (ISL) using axial FLAIR with a sensitivity of 0.99 which was slightly higher than that obtained by the current study in segmentation of ischaemic brainstem strokes [30]. Recent studies have utilised diffusion in the automated segmentation of cerebral and brainstem infarctions due to the high detectability of acute infarctions [33,34]. Earlier studies have shown comparable DSC between manual and semi-automated segmentation of acute brain strokes when applying diffusion and FLAIR datasets separately in lesion segmentation, reflecting the expanded use of the FLAIR sequence [28,30]. WMLs depicted in FLAIR commonly co-exist with brain infarctions due to shared vascular risk factors [35-37].

In a study led by Guerrero R et al., multiple automated methods were initiated to segment WMLs and accompanying ischaemic brain strokes in FLAIR and found a significant association between automated volumes of WMLs obtained by LPA and patients' age, which contradicted the current study, likely due to different sample populations and small-sized brainstem infarctions [38]. The current research could contribute to the literature by primarily addressing automated segmentation of brainstem infarctions using the FLAIR sequence.

Study	Zhu H et al., 2021 [27]	De Haan B et al., 2015 [28]	Feng C et al., 2016 [29]	Rajinikanth V and Satapathy SC 2018 [30]	Current study	
Type of strokes	Acute cerebral and infratentorial strokes	Acute brain strokes	Subacute strokes	Ischaemic brain strokes	Acute ischaemic brainstem strokes	Subacute ischaemic brainstem strokes
Method of segmentation	Multimodal automated method	Semi-automated clustering method	Multispectral automated method	Hybrid semi-automated method	Automated method	Automated method
MRI sequence	FLAIR	FLAIR	Multiple MRI sequences including FLAIR	Axial FLAIR	FLAIR	FLAIR
Sensitivity	0.561	-	-	0.99	0.63	0.76
Specificity	0.999	-	-	0.73	-	-
Dice Similarity Coefficient (DSC)	0.647	0.85±0.1	0.55±0.3	0.84	0.77	0.86

[Table/Fig-7]: Summary of results of stroke segmentation from current study and other studies using FLAIR [27-30].

DISCUSSION

In the current study, the pons was the most common location for brainstem infarctions, which is consistent with studies concerned with brainstem strokes [31,32].

In line with the current study, Zhu H et al., proposed a multimodal automated approach to segment acute cerebral and infratentorial strokes, with a DSC of 0.64 and sensitivity of 0.561 [27]. De Haan B et al., conducted a study on the segmentation of acute brain strokes using the FLAIR sequence and found a reasonable agreement between manual and semi-automated methods in segmenting brain strokes, with a slightly higher DSC than that obtained in the current study, likely due to the presence of large supratentorial infarctions in the former study [28].

Limitation(s)

Limitations of the study included a small sample size, small-sized infarctions, the retrospective nature of the research, and a scarcity of literature reports.

CONCLUSION(S)

The LPA within the LST was capable of automated segmentation of acute and subacute brainstem infarctions with high accuracy, particularly in subacute infarctions.

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