



Radio-Diagnosis

A DESCRIPTIVE STUDY TO ASSESS THE DIAGNOSTIC ROLE OF ARTERIAL SPIN LABELING MAGNETIC RESONANCE PERFUSION IMAGING IN INTRA-AXIAL BRAIN LESIONS

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ABSTRACT ASL MRI is invaluable in evaluating patients with intra axial brain lesions. It is non-invasive, fast and easy to perform. The addition of an ASL sequence to routine brain MRI in a hospital setting provides additional findings compared with conventional brain MRI at the cost of only a few minutes. It enabled us in detection of intra axial neoplastic lesions and distinguishing neoplastic brain lesions from non neoplastic brain lesions and derived the cut offs for the same. From the findings of our study, we concluded that the ASL MRI has high sensitivity, specificity, PPV, NPV and diagnostic accuracy in detecting intra axial neoplastic lesions.

KEYWORDS : Arterial spin labeling, neoplastic lesions, intra- axial brain lesions, mean cerebral blood flow lesion, mean cerebral blood flow perilesional edema, metastases, micro vascular density, normalized cerebral blood flow lesion, normalized cerebral blood flow perilesional edema.

INTRODUCTION

Intra-axial brain tumors are responsible for significant morbidity and mortality and Imaging plays an integral role in their management. Magnetic resonance imaging (MRI) is method of choice to evaluate location and preoperative anatomic delineation of the tumors; however, morphologic pulse sequences lack the diagnostic accuracy to grade brain tumors [1-2]. Diffusion parameters and Proton spectroscopy also overlap between benign and aggressive lesions [3-7]. Contrast enhancement (CE) depicts blood-brain barrier (BBB) impairment, so every lesion that shows CE is not a high grade neoplasm and vice versa [8]. Perfusion weighted imaging (PWI) serves as a useful adjunct to conventional MRI and overcomes these limitations by estimating tumor neoangiogenesis, which helps in tumor grading. Dynamic susceptibility contrast (DSC), routinely used with PWI, uses an exogenous contrast agent. Arterial spin labeling (ASL) is noninvasive PWI method that provides absolute quantification of cerebral blood flow (CBF) in absence of exogenous contrast, thus has advantages of non-invasiveness, simple operation, and repeatable inspection and makes ASL a promising technique for studying perfusion in patients with allergies, renal failure, difficult intravenous access, repetitive follow-ups, pregnant women and children. With this background, our study was conducted to evaluate the diagnostic role of ASL MR perfusion imaging in intra-axial brain lesions.

The objectives of this study were:

1. To find out sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of ASL MR perfusion imaging to diagnose neoplastic intra-axial brain lesions.
2. To establish a cut off value of ASL MRI data to distinguish neoplastic and non neoplastic intra axial brain lesions.

METHOD-

The study population consisted of all age groups, gender patients with untreated intra axial brain lesions. Exclusion criteria was; patients who refused to give consent, poor general conditions not permitting the study, claustrophobic, patients with metallic implants, MRI incompatible pacemakers and prosthetic heart valves, extra axial brain lesions, prior specific surgical treatment of the lesion.

A total of 80 patients were taken. MRI was performed on a 3 tesla MRI scanner (Signa Pioneer, Wipro, GE, USA) and a 32- channel head-neck-spine coil including routine imaging protocols of axial T1WI [TR, 1,750 ms; TE, 24ms; section thickness, 4 mm; inter-slice gap = 0 mm; field of view (FOV), 240 × 240 mm²; matrix, 320 × 256], T2WI (TR, 3,976 ms; TE, 92 ms; section thickness, 5mm; inter-slice gap = 1.5 mm; FOV, 240 × 240 mm²; matrix size, 512 × 512), FLAIR (TR, 8,400 ms; TE, 145 ms; section thickness, 5 mm; inter-slice gap = 1.5 mm; FOV, 240 × 240 mm²; matrix size, 160 × 256), DWI (b value = 0 and 1000 mm²/sec) and whole-brain three-dimensional

pseudo continuous ASL (3D PCASL) [(TR, 4,320 ms; TE, 54.5ms); postlabeling delay, 1025 msec for pediatric age groups and 2025 msec for adults; 80 axial partitions; field of view, 240 × 240 mm; section thickness, 4 mm; acquisition matrix, eight spiral arms in each three-dimensional partition with 512 points per arm; acquisition time, 4 to 5 minutes; Bandwidth, 62.5].

Analysis of images was performed by using medical image viewer (Ready view 14.0, Ext.8). Four ASL MRI parameters [mean cerebral blood flow values from lesion (mCBFL), perilesional edema (mCBFPE) and normalized CBF values from lesion (nCBFL), perilesional edema (nCBFPE) were recorded. The conventional MR sequence assessed the lesion localization, characterization and perilesional edema (PE) on T2 FLAIR. Cerebral blood flow CBF values were calculated by positioning three circular region of interests (ROIs) (5–10 mm²) over the lesions showing highest perfusion signal as visually determined from the CBF maps and from the PE (within 1 cm from the lesion) excluding necrotic, cystic and hemorrhagic areas. To minimize measurement errors of CBF analysis, uniformly sized ROIs were kept and targeted to the maximal abnormalities within the lesion. An average of three CBF measurements was taken and in case of multiple lesions, the larger lesion with maximum perfusion value was targeted for measurements. For normalization to avoid individual patient variation, three similar ROIs were placed on the corresponding normal contralateral white matter (CWM) and averaged to obtain mean CWM CBF values. All of these patients were followed up to correlate the ASL MRI findings with final histopathological and clinico-radiological diagnosis. Analysis was performed to obtain CBFL, CBFPE and normal CWM. Normalized (n) CBF ratio was obtained by dividing the mean CBFL and mean CBFPE by the mean CBF value of CWM. Clinico-radiological diagnoses were determined by a combination of provided clinical history, typical imaging findings, biochemical, culture and post-treatment follow-ups in patients. Histopathologic analysis-Tumor samples were analyzed by two experienced pathologists who were blinded to ASL data and used hematoxylin-eosin staining and immunohistochemistry panel.

Statistical Analysis-

Linear variables were summarized as mean and standard deviation whereas nominal/categorical variables were shown as proportions (percentage). Ordinal variables were presented as median and interquartile range. Unpaired t-test, Pearson correlation coefficient and ROC curve analysis was done for linear variables while Chi square test and Fischer exact test were used for nominal (categorical) variables. p-value < 0.05 was taken as statistically significant.

RESULTS

A total of 80 patients were taken, 40 in neoplastic group (male: female

1.6, Age range 8-78 years) and 40 non neoplastic (male: female 2.63, Age range 15-75 years). In contrast to the study conducted by Soni et al [9] where the age range was 38–66 years in the neoplastic group and 18–46 years in the non-neoplastic group, our study also included the pediatric population.

Out of 40 patients (50%) with non neoplastic lesions, 15 were tuberculomas (18.75%), 13 abscesses (16.25%) [figure-1], 5 tumefactive demyelination (6.25%) [figure-2], 5 neurocysticercosis (6.25%) and 2 fungal granulomas (2.5%) based on final histopathology and clinico radiological diagnosis.

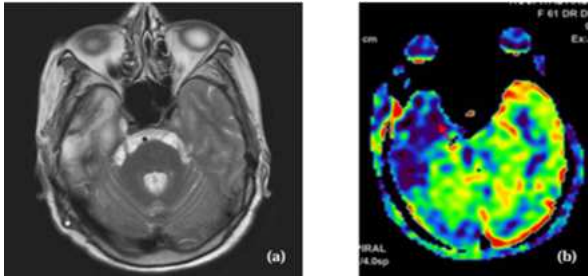


Figure 1: Cerebritis with evolving brain abscess (a) Axial T2-WI shows an ill defined lesion with a high-signal intensity and extensive peripheral vasogenic edema in the right temporal region. (b) ASL MRI showing blue hue in the region indicating hypoperfusion (red arrow).

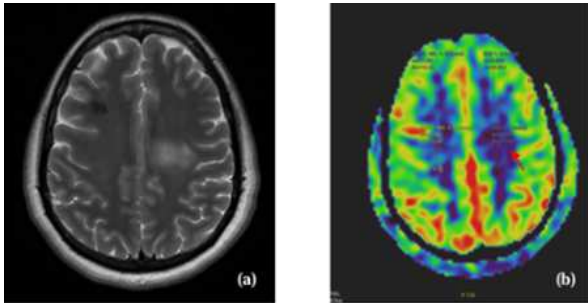


Figure 2: Tumefactive demyelination. (a) Axial T2-WI shows a hyper intense lesion with perilesional edema in the left frontal centrum semiovale region. (b) Hypoperfusion is seen within the lesion on ASL perfusion map (red arrow).

Accuracy and characteristics of ASL MRI indices for detecting Intra axial neoplastic lesions- Parameters derived from ASL MRI, including mCBFL (114.31 ± 59.98 versus 11.94 ± 4.72 ; Mean $\pm$ SD in neoplastic versus non-neoplastic groups, respectively), mCBFPE (51.73 ± 25.92 versus 14.66 ± 6.36 ; Mean $\pm$ SD in neoplastic versus non-neoplastic groups, respectively), nCBFL (3.79 ± 2.35 versus 0.77 ± 0.23 ; Mean $\pm$ SD in neoplastic versus non-neoplastic groups, respectively), nCBFPE (1.35 ± 0.55 versus 0.85 ± 0.21 ; Mean $\pm$ SD in neoplastic versus non-neoplastic groups, respectively) were significantly higher in neoplastic group ($p > 21.4, > 25, > 1.43$ and > 1.07 , respectively).

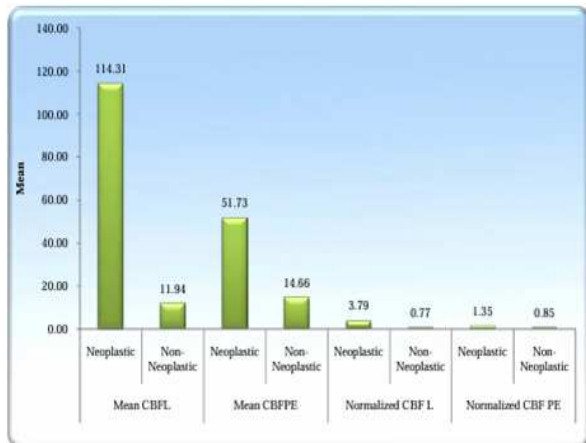


Figure 3: Comparison of ASL MRI parameters with respect to groups

It was found that for distinguishing intra axial neoplastic lesions from non neoplastic lesions, the cut off value of mCBFL, mCBFPE, nCBFL and

nCBFPE was $> 21.4, > 25, > 1.43$ and > 1.07 , respectively (Figure 4 (a-d)).

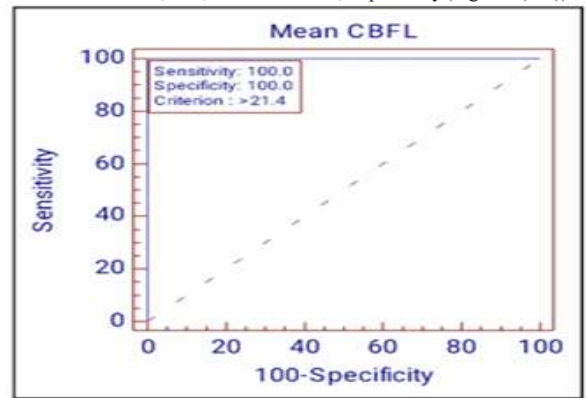


Figure 4 (a) ROC curve representing the discriminatory capability of mCBFL in distinguishing neoplastic lesions from non-neoplastic lesions with area under the curve. ROC: receiver operating characteristic.

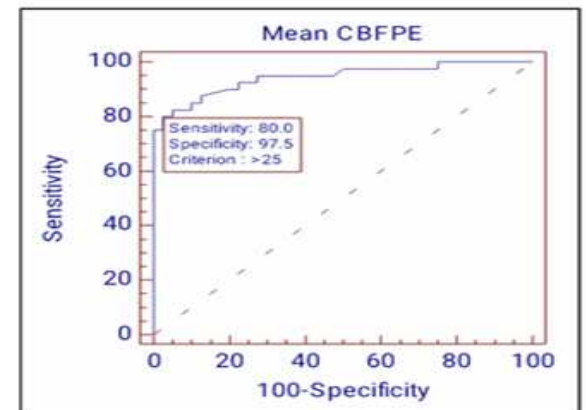


Figure 4 (b) ROC curve representing the discriminatory capability of mCBFPE in distinguishing neoplastic lesions from non-neoplastic lesions with area under the curve.

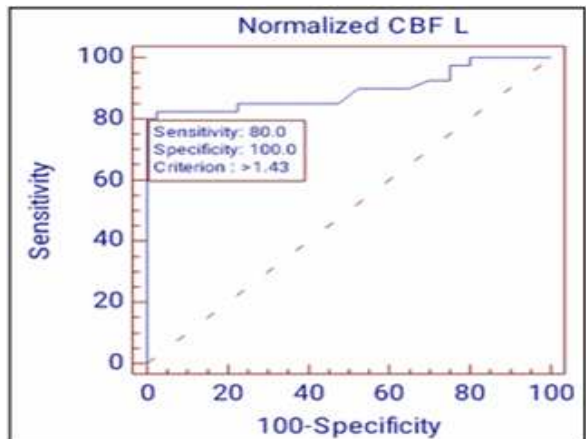


Figure 4 (c) ROC curve representing the discriminatory capability of nCBFL in distinguishing neoplastic lesions from non-neoplastic lesions with area under the curve.

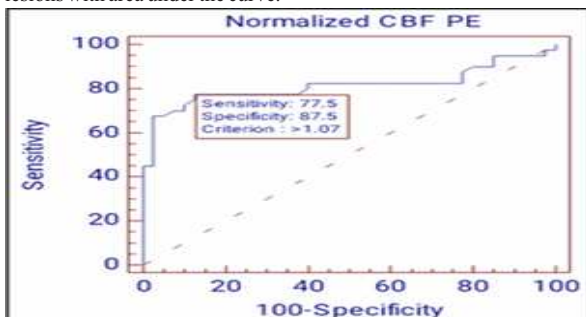


Figure 4 (d) ROC curve representing the discriminatory capability of nCBFPE in distinguishing neoplastic lesions from non-neoplastic lesions with area under the curve.

nCBFPE in distinguishing neoplastic lesions from non-neoplastic lesions with area under the curve.

The AUC for mCBFL, mCBFPE, nCBFL and nCBFPE was 1.000, 0.944, 0.894 and 0.814, respectively.

In our study, the sensitivity of mCBFL, mCBFPE, nCBFL and nCBFPE for diagnosing intra axial neoplastic lesions was 100.00%, 80.00%, 80.00% and 77.50%, respectively, whereas the specificity was 100%, 97.5%, 100% and 87.5%, respectively.

The positive predictive values of mCBFL, mCBFPE, nCBFL and nCBFPE for diagnosing intra axial neoplastic lesions were 100.00, 96.97, 100.00 and 86.11, respectively, whereas the negative predictive values were 100.00, 82.98, 83.33 and 79.54, respectively.

The diagnostic accuracy of mCBFL, mCBFPE, nCBFL and nCBFPE for diagnosing intra axial neoplastic lesions was 100.00, 88.75, 82.50 and 82.50, respectively.

DISCUSSION

ASL MRI is invaluable in evaluating patients with intra axial brain lesions. It is non-invasive, fast and easy to perform. The addition of an ASL sequence to routine brain MRI in a hospital setting provides additional findings compared with conventional brain MRI at the cost of only a few minutes. It enabled us in detection of intra axial neoplastic lesions and distinguishing neoplastic brain lesions from non neoplastic brain lesions. Neoplastic brain lesions display higher CBF than non neoplastic brain lesions.

In our study, Mean $\pm$ SD value of mCBFL was 114.31 $\pm$ 59.98 in neoplastic lesions which was comparable to the study conducted by Hu et al [10] where it was 114.59 $\pm$ 40.83. Mean $\pm$ SD value of mCBFL was 11.94 $\pm$ 4.72 in our study for non-neoplastic lesions which was lower than the values in the study by Hu et al [10]. In our study, the Mean $\pm$ SD value of mCBFPE was 51.73 $\pm$ 25.92 in neoplastic lesions while that of non-neoplastic lesions it was 14.66 $\pm$ 6.36. The Mean $\pm$ SD value of nCBFL was 3.79 $\pm$ 2.35 in neoplastic lesions while that of non-neoplastic lesions it was 0.77 $\pm$ 0.23 in our study which was lower as compared to the study by Soni et al [9] where nCBFL of neoplastic lesions was 6.65 $\pm$ 4.07 and that of non-neoplastic lesions was 1.68 $\pm$ 0.80. This result may be attributed to the fact that neoplastic lesions could induce angiogenesis, leading to increase in blood perfusion. Mean $\pm$ SD value of nCBFPE was 1.35 $\pm$ 0.55 in neoplastic lesions while that of non-neoplastic lesions it was 0.85 $\pm$ 0.21 in our study. In study by Soni et al [9], nCBFPE of neoplastic lesions was 1.86 $\pm$ 1.43 which was higher and of non-neoplastic lesions it was 0.74 $\pm$ 0.21 which was similar to our study.

In our study, on deriving the appropriate cut off values to differentiate neoplastic lesions from non neoplastic lesions, it was found that cut off value of mCBFL was >21.4 , mCBFPE was >25 , nCBFL was >1.43 and of nCBFPE was >1.07 . While Soni et al [9] found nCBFL cutoff value of 1.89 and nCBFPE value of 0.76.

The sensitivity of mCBFL, mCBFPE, nCBFL and nCBFPE was 100.00% (95% CI, 91.2-100.0), 80.00% (95% CI, 64.4-90.9), 80.00% (95% CI, 64.4-90.9) and 77.50% (95% CI, 61.5-89.2), respectively, whereas the specificity was 100% (95% CI, 91.2-100.0), 97.5% (95% CI, 86.8-99.9), 100% (95% CI, 91.2-100.0) and 87.5% (95% CI, 73.2-95.8), respectively to distinguish intra axial neoplastic lesions from non-neoplastic.

Parameters derived from ASL MRI, including mCBFL (114.31 $\pm$ 59.98 vs 11.94 $\pm$ 4.72), mCBFPE (51.73 $\pm$ 25.92 vs 14.66 $\pm$ 6.36), nCBFL (3.79 $\pm$ 2.35 vs 0.77 $\pm$ 0.23), nCBFPE (1.35 $\pm$ 0.55 vs 0.85 $\pm$ 0.21) were significantly higher in neoplastic group ($p < 0.001$) than non neoplastic group with a good ability of ASL to define neoplastic lesions when mCBFL of 21.4 and nCBFL of 1.43 was considered as the cutoff value (sensitivity 100% and 80%, respectively and specificity 100% and 100%, respectively) and mCBFPE of 25 and nCBFPE of 1.07 was considered as the cutoff value (sensitivity 80% and 77.50% and specificity 97.50% and 87.50%, respectively).

Summary

In this study we concluded that parameters derived from ASL MRI, including mCBFL (114.31 $\pm$ 59.98 vs 11.94 $\pm$ 4.72), mCBFPE (51.73 $\pm$ 25.92 vs 14.66 $\pm$ 6.36), nCBFL (3.79 $\pm$ 2.35 vs 0.77 $\pm$ 0.23), nCBFPE (1.35 $\pm$ 0.55 vs 0.85 $\pm$ 0.21) were significantly higher in neoplastic

group ($p < 0.001$) than non neoplastic group with a good ability of ASL to define neoplastic lesions when mCBFL of 21.4 and nCBFL of 1.43 was considered as the cutoff value (sensitivity 100% and 80%, respectively and specificity 100% and 100%, respectively) and mCBFPE of 25 and nCBFPE of 1.07 was considered as the cutoff value (sensitivity 80% and 77.50% and specificity 97.50 % and 87.50%, respectively).

From the findings of our study, we concluded that the ASL MRI has high sensitivity, specificity, PPV, NPV and diagnostic accuracy in detecting intra axial neoplastic lesions. mCBFL and nCBFL showed highest PPV to diagnose intra axial neoplastic lesions. mCBFL showed highest NPV; rest 3 parameters (mCBFPE, nCBFL and nCBFPE) showed good and comparable NPV to diagnose intra axial neoplastic lesions.

Therefore, ASL parameters are very useful in discriminating non-neoplastic from neoplastic lesions, thus preventing misdiagnosis.

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