

Comparative Study Between Brain MRI Perfusion and Diffusion Weighted Including Apparent Diffusion Coefficient Value in Assessment of Brain Penumbra and Infarction Core in Acute Cerebral Infarction

Riyadh W. AL. Esawi¹, Zahraa Ayad Jaber², Zaid Raad Kadhem³

^{1,2,3}Faculty of Medicine, University of Kufa, Dept. of Radiology. E_mail:
riyadh.alisawi@uokufa.edu.iq

Cite this paper as: Riyadh W. AL. Esawi, Zahraa Ayad Jaber, Zaid Raad Kadhem (2024) Comparative Study Between Brain MRI Perfusion and Diffusion Weighted Including Apparent Diffusion Coefficient Value in Assessment of Brain Penumbra and Infarction Core in Acute Cerebral Infarction . *Frontiers in Health Informatics*, 13 (4), 1110-1125

Abstract:

Rapid and precise identification of the penumbra is important for decision-making in acute stroke. The perfusion weighted imaging/diffusion weighted imaging PWI/DWI mismatch region may exceed the true penumbral area and is usually much larger than the final size of the infarct. These limitations led us to investigate the value of an ADC quantitative assessment of early tissue changes, especially in the mismatch area.

Early detection of decrease in apparent diffusion coefficient (ADC) within infarcted area which eventually evolve toward infarction may help to identify diffusion/perfusion (DWI/PWI) mismatch. Perfusion imaging can identify patients who benefit from reperfusion beyond the conventional time window or in whom time of symptom onset is unknown.

The Aim of The Study:

The aim of this study is to evaluate apparent diffusion coefficient (ADC) value in assessment of area of penumbra and infarction core in acute cerebral infarction and this may replace using of brain perfusion study.

Patients and methods:

A prospective study include 30 patients with acute cerebral infarction were examined with MRI 1.5 T. performing perfusion brain study and DWI/ADC concentrating on area of penumbra assessing ADC value in relation to PW (CBF ,CBV, TTP)

This study carried out in the Middle Euphrates Neuroscience Center in AL-Sadir Medical City from February 2023 till November 2023 in AL-Najaf AL-Shraf.

Results:

Total of 30 patients were included in this study which were divided into subgroups based on age, gender and BMI groups

Mean age (63.8 ± 8.7 years) and BMI (27.4 ± 3.5).

The apparent diffusion coefficient (ADC) mean value in the central area of infarction was

($0.47 \pm 0.11 \times 10^{-6}$ mm²/s), peripheral area of infarction ($0.66 \pm 0.15 \times 10^{-6}$ mm²/s), penumbra area ($0.81 \pm 0.07 \times 10^{-6}$ mm²/s) and the normal brain area ($0.94 \pm 0.16 \times 10^{-6}$ mm²/s) which was of significant difference P-value=0.001.

Regarding perfusion, the time to peak (TTP) mean value in the center of infarction was 56.6 ± 28.6 s and in the periphery of infarction 70.5 ± 36.5 s, 60.2 ± 31.9 s in penumbra and in normal area was 59.9 ± 35.1 s, the difference was insignificant, P-value = 0.4.

The cerebral blood flow (CBF) mean value were different among different regions of infarction without significance difference P-value=0.9. In the center of infarction was 15.57 ± 24.6 mL/100 g/min and in the periphery of infarction 14.1 ± 23 mL/100 g/min, 16.8 ± 27.2 mL/100 g/min in penumbra and in normal area was 14.5 ± 21.3 mL/100 g/min.

The cerebral blood volume (CBV) mean value in the center of infarction was 24.7 ± 34.7 mL/100g and in the periphery of infarction 40.5 ± 46.5 mL/100g, 72 ± 86.1 mL/100g in penumbra and in normal area was 59.5 ± 85.7 mL/100g this difference was significant (P-value= 0.04).

Conclusion:

- 1) The only CBV perfusion parameter was of significant difference in different areas of infarction.
- 2) ADC value was rapid and easy to be measured with significant difference among different regions of infarction.
- 3) The perfusion parameter TTP was of no significant difference in different areas of infarction.
- 4) The perfusion parameter CBF was of no significant difference in different areas of infarction.

Key word: acute infarction, MRI perfusion, Apparent diffusion coefficient (ADC).

1.1 Introduction:

Strokes are one of the global leading causes of physical or mental impairment and second leading cause of death worldwide, associated with focal CNS injury of vascular origin which precipitates neurological deficit ⁽¹⁾. Fundamentally, strokes are classified into hemorrhagic and embolic ischemic strokes (ISs). ISs happen when a thrombus blocks or plugs an artery and interrupts or reduces blood supply to the brain tissue. Strokes resulting from an acute decline of vascular supply to the brain comprise a notable portion of 80% of all strokes. Factors such as hypertension increase susceptibility to hemorrhagic strokes, but also brings about an indirect surge in ischemic strokes that result from atherosclerosis. Moreover, hyperlipidemia, atrial fibrillation, diabetes and smoking are risk factors for intracranial and extra cranial vessel atherosclerosis-originated strokes and cardio embolic strokes, respectively ⁽²⁾.

Computed tomography scans play a crucial role in diagnosing and evaluating ischemic strokes. Although other imaging modalities like DWI can offer greater sensitivity and additional information that is beneficial in later stages, the high availability, cost-effectiveness and rapid image acquisition of CT scans make them particularly suitable for the early phases of the disease ^(3,4). This is especially important given that treatment options like thrombolytic therapy are most effective within the first few hours of stroke onset ⁽⁵⁾. It should be noted that differentiation between ischemic and hemorrhagic strokes through CT is not troublesome due to the fact that hemorrhagic strokes present as hyper dense collections of blood ⁽¹⁾.

1.2 Cerebral MRI

Although MRI is more specific and sensitive than CT, it is not commonly used for the initial

diagnosis of an acute ischemic stroke. MRI is a less frequently used option as a primary imaging modality, mostly due to its greater price, extended scan time, lack of availability and more difficult workflow. The use of MRI in the initial assessment of acute ischemic strokes is limited and reserved only for unique indications. However, after the emergency setting, brain MRI can give more precise diagnostic information to improve further care ⁽⁶⁾.

Specific parts of the brain are visualized using different MRI sequences ⁽⁷⁾. T1- and T2-weighted imaging (T1WI and T2WI) are the two MRI sequences that are most frequently used ⁽⁸⁾. These two conventional MRI sequences, together with non-contrast CT, represent a standard imaging protocol in the imaging of a stroke and have been used mainly to exclude hemorrhages ⁽⁹⁾. Diffusion-weighted MR imaging (DWI) is a sequence that recognizes the movement of water molecules ⁽⁷⁾. It is frequently used in the diagnosis of acute brain infarctions because of its ability to reveal cytotoxic edema ⁽¹⁰⁾. Ischemic brain tissue appears as a bright area or a spot on the image as a result of restricted water movement in the cells ⁽⁸⁾. The apparent diffusion coefficient (ADC) quantitatively expresses the degrees of diffusion, and its lowered values indicate a restriction in diffusion ^(9,10). DWI may be, at times, incapable of identifying small infarcts and can misidentify reversible injuries as irreversible. To improve image accuracy, DWI is frequently used in conjunction with perfusion-weighted imaging (PWI). PWI measures perfusions of the cerebrum using the evaluation of hemodynamic parameters like mean transit time, cerebral blood flow and cerebral blood volume ⁽⁷⁾. The DWI/PWI mismatch concept has been used to define the presence of hypoperfused ischemic penumbra in PWI and the infarct core in DWI ^(7,11,12). It has been tested as a thrombolysis selection marker and can also provide a prediction of the final infarct area, which can be used to reduce variability between cases in studying the treatment outcome ⁽¹³⁾. Analyzing the intensities of the signal in different sequences (DWI, ADC and FLAIR) can help to differentiate between different stages of ischemic strokes ⁽¹⁴⁾.

2. Patients and Methods

2.1 Study design & population:

A prospective cross sectional study carried out in the Middle Euphrates Neuroscience Center in AL-Sadir Medical City from February 2023 to November

2023 in Al-Najaf Al-Ashraf. Thirty patients with acute stroke were enrolled in this study, after taking their verbal and written consent. 15 patients were females and 15 males, and their ages ranged between 50 –80 year.

2.2 Inclusion criteria. Patients with clinical acute ischemic stroke, with positive MRI findings.

2.3 Exclusion criteria

1-Patients with hemorrhagic stroke. 2-Patients with brain tumor. 3-Patients with abnormal renal function tests. 4- Small infarction which can't give clear perfusion images. 5- Inconclusive images due to motion artifacts. 6- Unconscious patients with large infarction.

2.4 Data collection:

Clinical data: including age, gender, time of insult, presentation, body mass index history of smoking, hypertension and diabetes mellitus.

History of medicine, past surgical operation,.

renal function tests (blood urea and serum creatinine), lipid profile, hemoglobin level.

2.5 Methods:

All patients were examined by MRI 1.5 TESLA, Philips Achieva Machine, close type, manufactured in the Netherlands.

All patients were examined according to the following protocol

1- Axial T2 sections. 2- Axial T1. 3- Coronal FLAIR. 4-Diffusion weighted Image

5-ADC. 6-Perfusion weighted (dose of contrast, 0.1 ml/kg of gadolinium + 10 ml of normal saline)

and waiting for 8 seconds, then the study performed.

2.5.1 Image interpretation:

The examination was reviewed and measured in an expanded workstation.

The Infarcted area is determined by DWI (b1000).

The parameters of perfusion (CBV, CBF and TTP) are determined and calculated by draw ROI at the center of Infarcted area, its periphery, within the penumbra and in the adjacent normal brain tissue.

The diffusion/perfusion mismatch done by 1) mismatch alignment, 2) mark the seed point.

Then the ADC value measured at same ROI of the perfusion.

All data were collected in paper form then transformed into a Microsoft excel format sheet and sent for statistical analysis to obtain the results.

3. Results

A total of 30 patients were included in this study, which were divided into subgroups based on age, gender, and BMI groups which summarized in Table (3.1).

Table 3.1. Descriptive of the demographic characteristics of patients

Variables		Frequency	Percent%
Age	50-60 years	12	40
	61-70 years	11	36.7
	71-80 years	7	23.3
Gender	Male	15	50
	Female	15	50
BMI	Normal weight	9	30
	Overweight	11	36
	Obesity	10	34
Presentation	limb weakness	21	70
	headache	20	66.6
	Dysphasia and slurred speech	17	56.6
	Ophthalmoplegia, ptosis	2	6.3
History of DM	Yes	17	59
	No	13	41
History of HTN	Yes	19	59.4
	No	11	39.6
History of medication	Aspirin	6	18.8
	No aspirin	24	81.3
History of smoking	Yes	4	12.5
	No	26	87.6

Table 3.2. Mean difference of ADC value and perfusion (TTP, CBV, CBF) among different areas in cerebral tissue.

Variables		Means \pm SD	Lower bound	Upper bound	P-value
ADC(in $10^{-6}\text{mm}^2/\text{s}$)	Center of infarcted area	0.47 ± 0.11	0.42	0.51	0.001 (S)
	Periphery of infarcted area	0.66 ± 0.15	0.61	0.72	
	Penumbra area	0.81 ± 0.07	0.78	0.84	
	Normal area	0.94 ± 0.16	0.88	1.0	
TTP (in second)	Center of infarcted area	56.6 ± 28.6	45.9	67.3	0.4 (NS)
	Periphery of infarcted area	70.5 ± 36.5	56.9	84.2	
	Penumbra Area	60.2 ± 31.9	48.2	72.1	
	Normal area	59.9 ± 35.1	46.8	73.0	

CBV ml/ 100 mg	Center of infrected area	24.7 ± 34.7	11.7	37.7	0.04(S)
	Periphery of infrected area	40.5 ± 46.5	23.1	57.9	
	Penumbra Area	72 ± 86.1	39.8	104.2	
	Normal area	59.5 ± 85.7	27.5	91.6	
CBF ml/ 100 mg/min	Center of infrected area	15.5 ± 24.6	6.62	25.0	0.9 (NS)
	Periphery of infrected area	14.1 ± 23.93	5.2	23.0	
	Penumbra Area	16.8 ± 27.2	6.67	27	
	Normal area	14.5 ± 21.3	6.51	22.4	

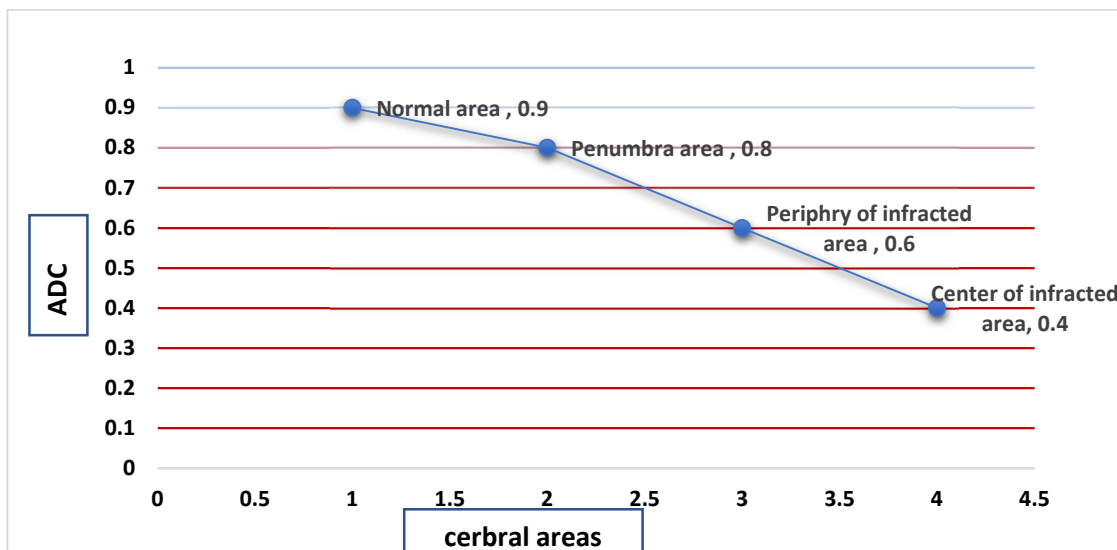


Figure 3.1. Regression line of distribution of ADC mean value among different cerebral area.

As show in figure above, ADC value gradually increase from center of infrected area to normal area.

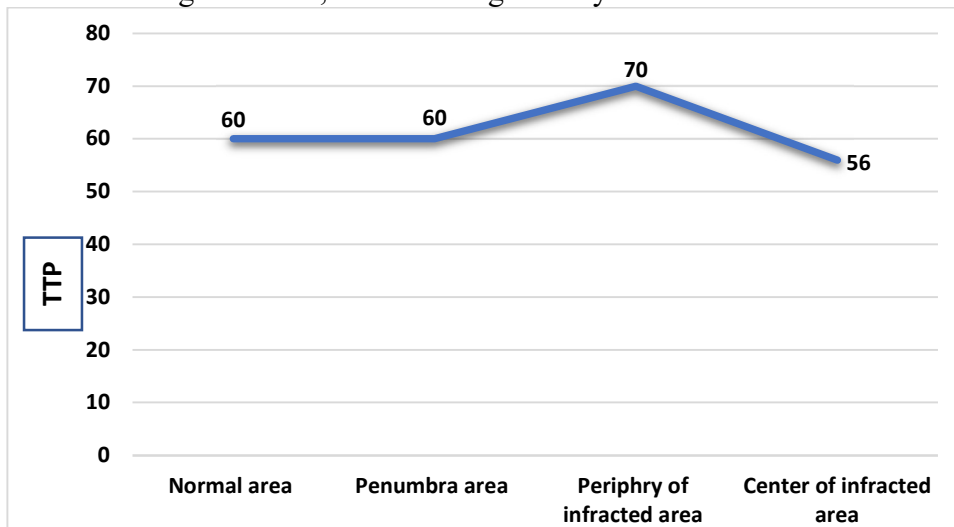


Figure 3.2. Regression line of distribution of TTP mean value among different cerebral area.

This figure show the periphery of infrected area was the highest TTP among different cerebral area, and the center of infrected area was the lowest TTP.

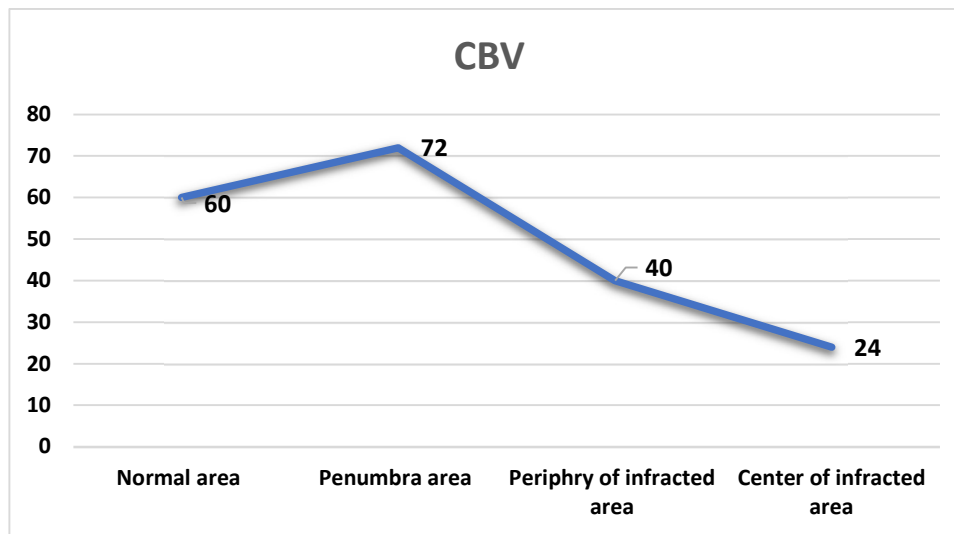


Figure. 3.3. Regression line of distribution of CBV mean value among different cerebral area .As notes in this figure. penumbra area with the highest value of CBV, while the center of infarcted area was the lowest.

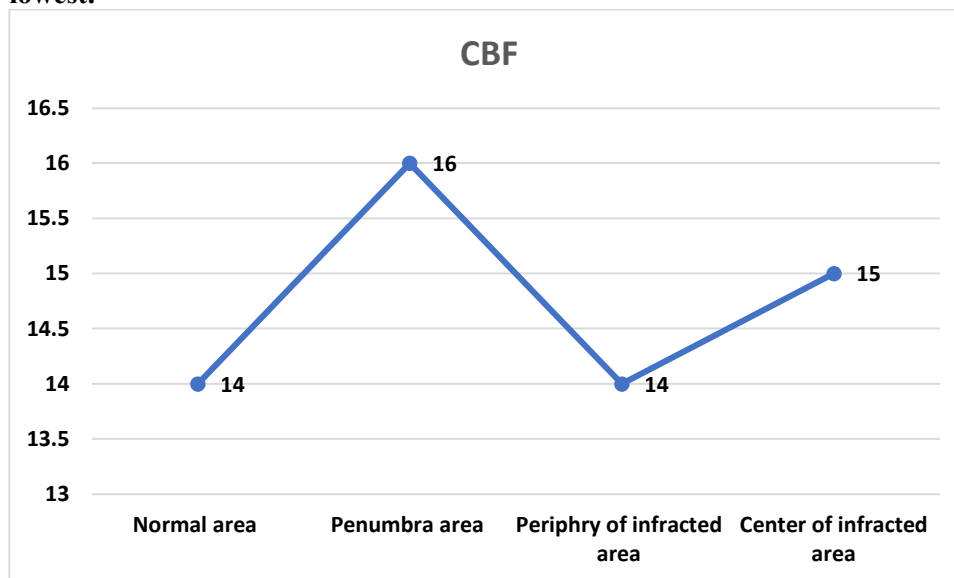
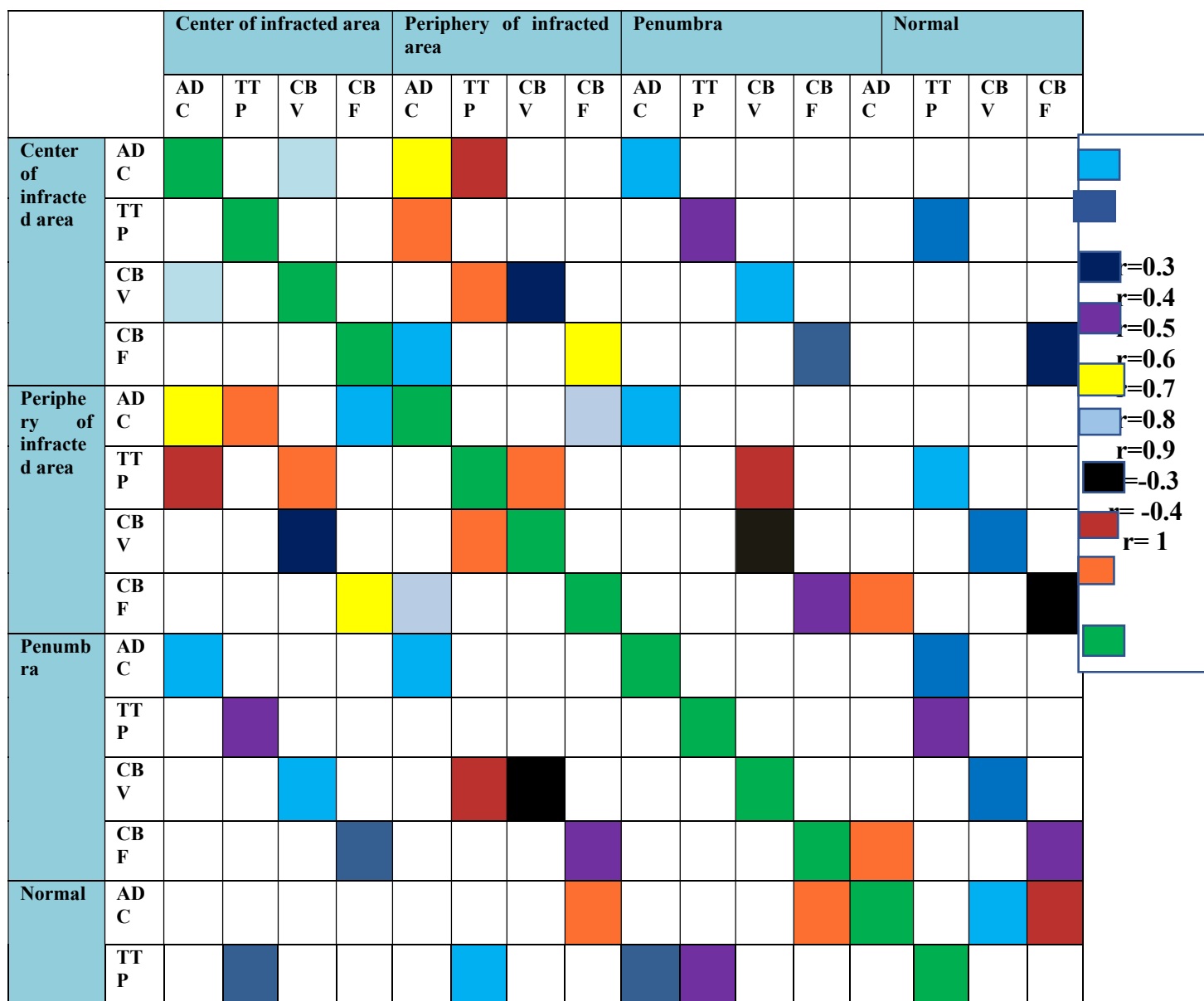


Figure. 3.4. Regression line of distribution of CBF mean value among different cerebral area.

Table. 3.3. Mean differences of ADC and perfusion (TTP, CBV, CBF) among age groups.

Variables		Means \pm SD			P-value
		Age groups			
		(50-60) years	(61-70) years	(71-80) years	
Center of infarcted area	ADC	0.50 \pm 0.13	0.47 \pm 0.13	0.42 \pm 0.06	0.2 (NS)
	TTP	63.9 \pm 27.5	51.3 \pm 34.4	52.5 \pm 20.6	0.7 (NS)
	CBV	29.9 \pm 32.6	9.8 \pm 10.2	39.2 \pm 54.8	0.001 (S)
	CBF	12.7 \pm 29.2	13.1 \pm 17.3	25.2 \pm 27.0	0.5 (NS)
Periphery of infarcted area	ADC	0.70 \pm 0.22	0.65 \pm 0.09	0.62 \pm 0.06	0.5 (NS)
	TTP	66.0 \pm 23.9	80.3 \pm 49.2	62.9 \pm 32.8	0.3 (NS)
	CBV	52.0 \pm 43.0	14.7 \pm 17.9	61.2 \pm 67.5	0.001 (S)
	CBF	12.4 \pm 27.3	16.4 \pm 23.9	13.3 \pm 20.6	0.6 (NS)

Penumbra Area	ADC	0.80 ± 0.04	0.82± 0.1	0.82 ± 0.08	0.1 (NS)
	TTP	66.5 ± 32.4	58.4 ± 39.3	52.1 ± 16.2	0.5 (NS)
	CBV	97.5 ± 89.5	26.3 ± 21.2	100 ± 120	0.008 (S)
	CBF	11.7 ± 17.3	18.5 ± 31.1	22.9 ± 36.2	0.2 (NS)
Normal area	ADC	0.95 ± 0.18	0.92 ± 0.17	0.94 ± 0.13	0.7 (NS)
	TTP	60.3 ± 29.5	60.6 ± 44.1	58.3 ± 33.3	0.4 (NS)
	CBV	82.4 ± 112	22.3 ± 25	78.5 ± 85	0.004 (S)
	CBF	12.4 ± 19.1	17.8 ± 25.7	12.6 ± 19.8	0.2 (NS)
ANOVA test was significant at P-value ≤ 0.05. SD: Stander Deviation, S: Significant, NS: Non- Significant.					



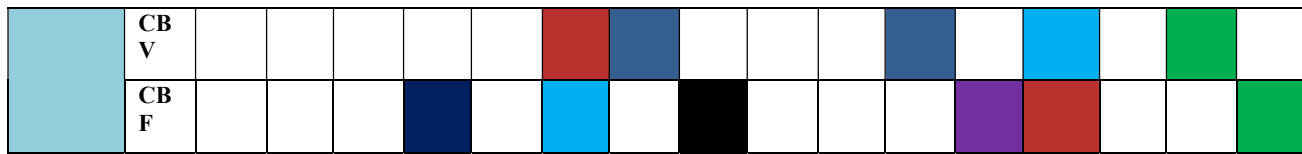
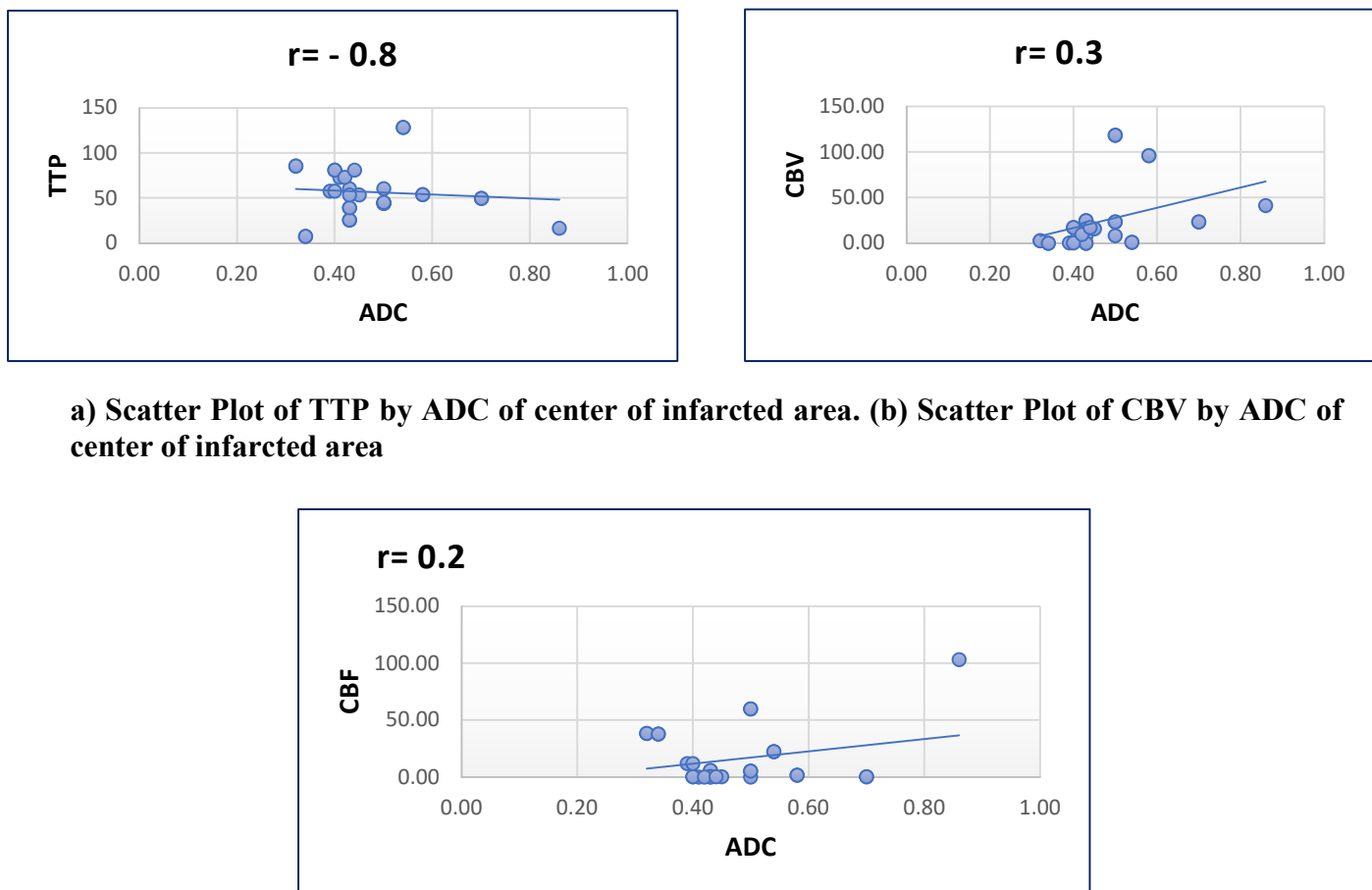


Figure 3.5. a. Heatmap chart of the Spearman rank test analysis, white boxes indicate a lack of correlation ($p > 0.05$) while coloured boxes reported statistically significant direct and indirect correlations, respectively. The intensity of the colour indicates the following above box.

3.1. Correlation

The Spearman rank test analysis was used to analyze the response relationship between parameters. The correlation study shows many significant correlations among the measured parameters, (figure 3.5). The correlation coefficient was used for determining linear relationships between ADC of center of infarcted area and TTP, CBV, CBF of center of infarcted area in patients with acute cerebral infarction. The results showed that there was relationship and significant positive correlation between ADC and CBV of center of infarcted area ($p \geq 0.05$), there are significant negative association between ADC of and TTP, as shown in (fig. 3.6.a,b,c).



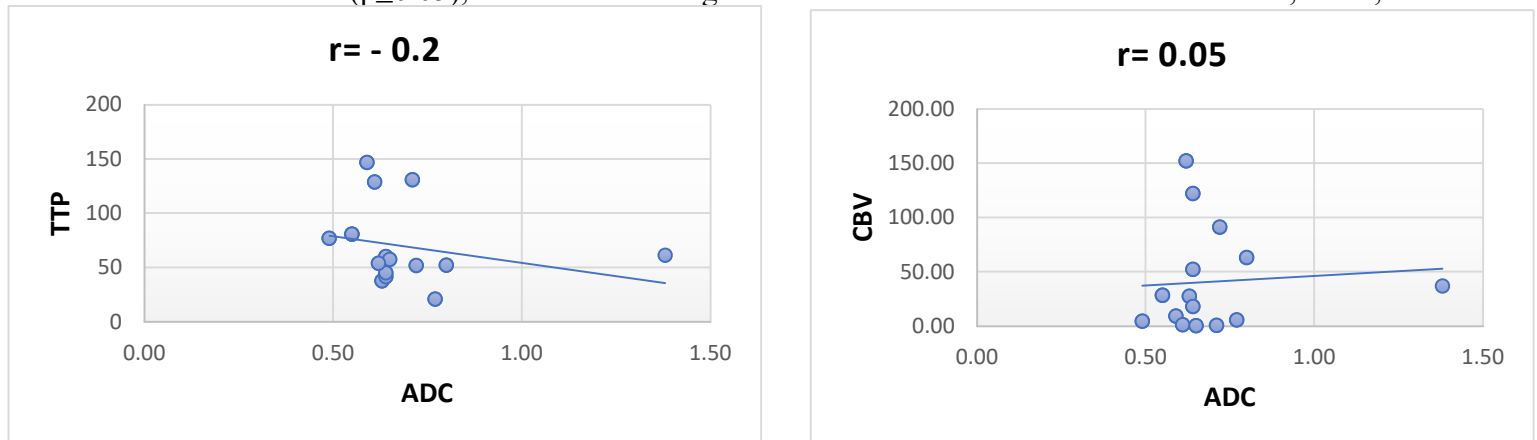
a) Scatter Plot of TTP by ADC of center of infarcted area. (b) Scatter Plot of CBV by ADC of center of infarcted area

c) Scatter Plot of CBF by ADC of center of Infarcted area

Fig.3.6. Simple linear regression of ADC with TTP, CBV, CBF of center of infarcted area for

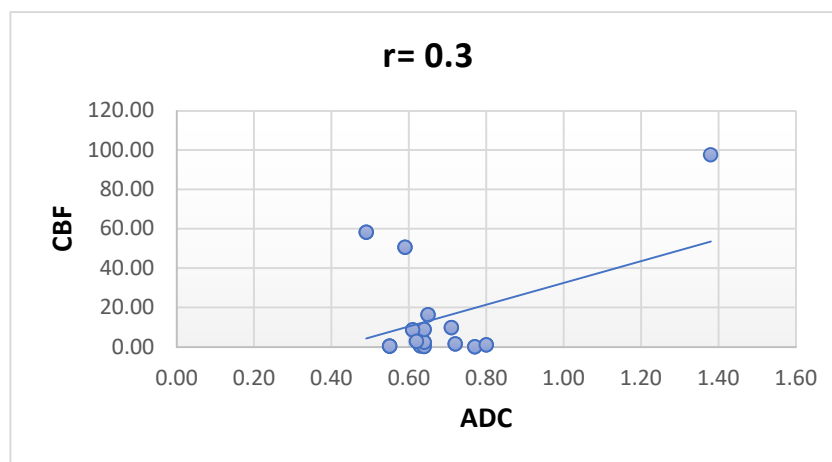
acute cerebral infraction.

The correlation coefficient was used for determining linear relationships between ADC and TTP, CBV, CBF of periphery of infarcted area in patients with acute cerebral infraction. The results showed that there were relationship and significant positive correlation between ADC and CBF of periphery of infarcted area ($p \geq 0.05$), there were no significant association between ADC and TTP, CBV, as



a) Scatter Plot of TTP by ADC of Periphery of infarcted area
ADC of Periphery of infarcted area

b) Scatter Plot of CBV by



c) Scatter Plot of CBF by ADC of Periphery of infarcted area

Fig.3.7. Simple linear regression of ADC with TTP, CBV, CBF of periphery of infarcted area for acute cerebral infraction.

The correlation coefficient was used for determining linear relationships between ADC of penumbra area in patients with acute cerebral infraction. The results showed that there was no relationship and no significant correlation between ADC and TTP, CBF, CBV ($p \geq 0.05$), as shown in (fig. 3.8.a,b,c).

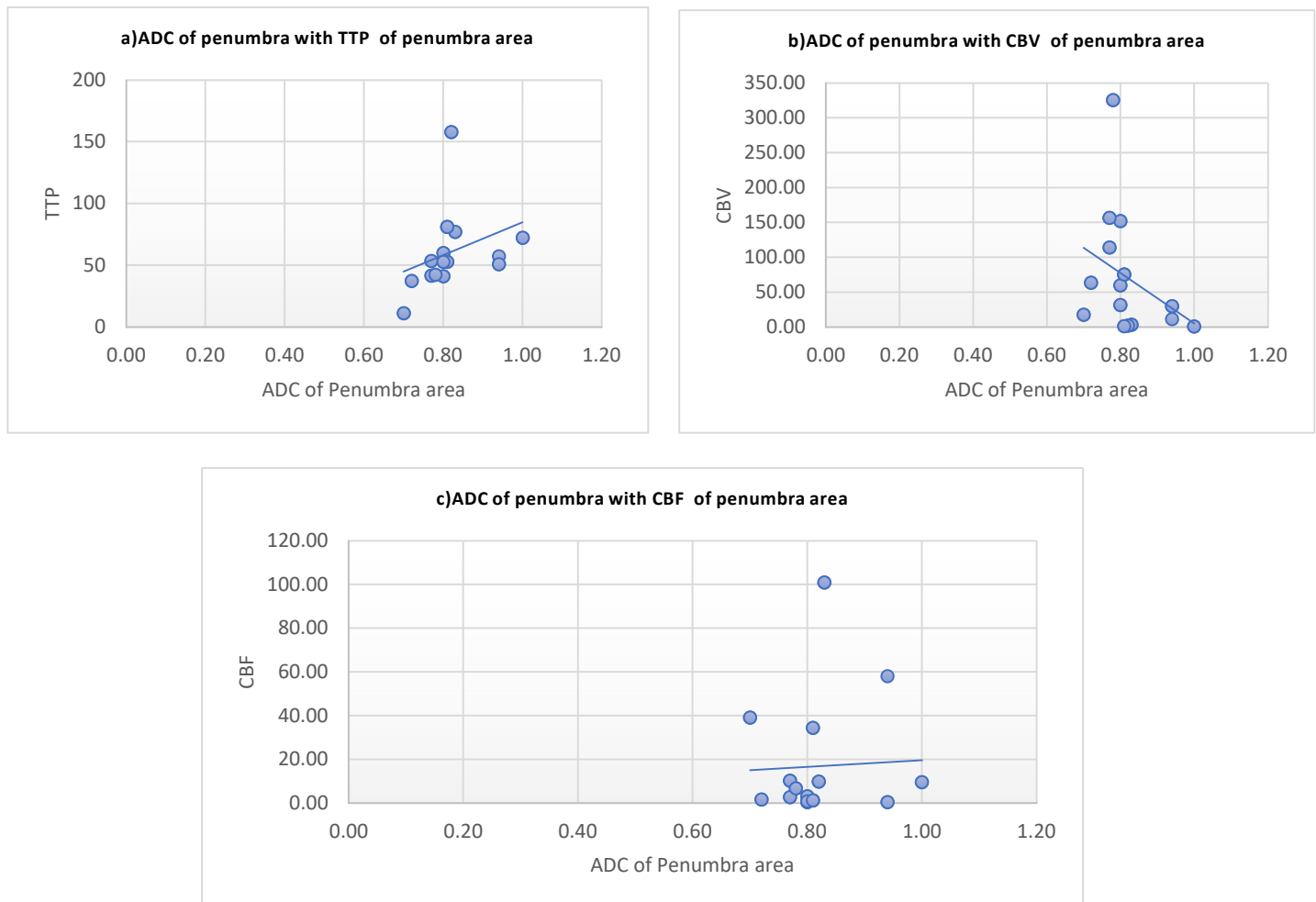
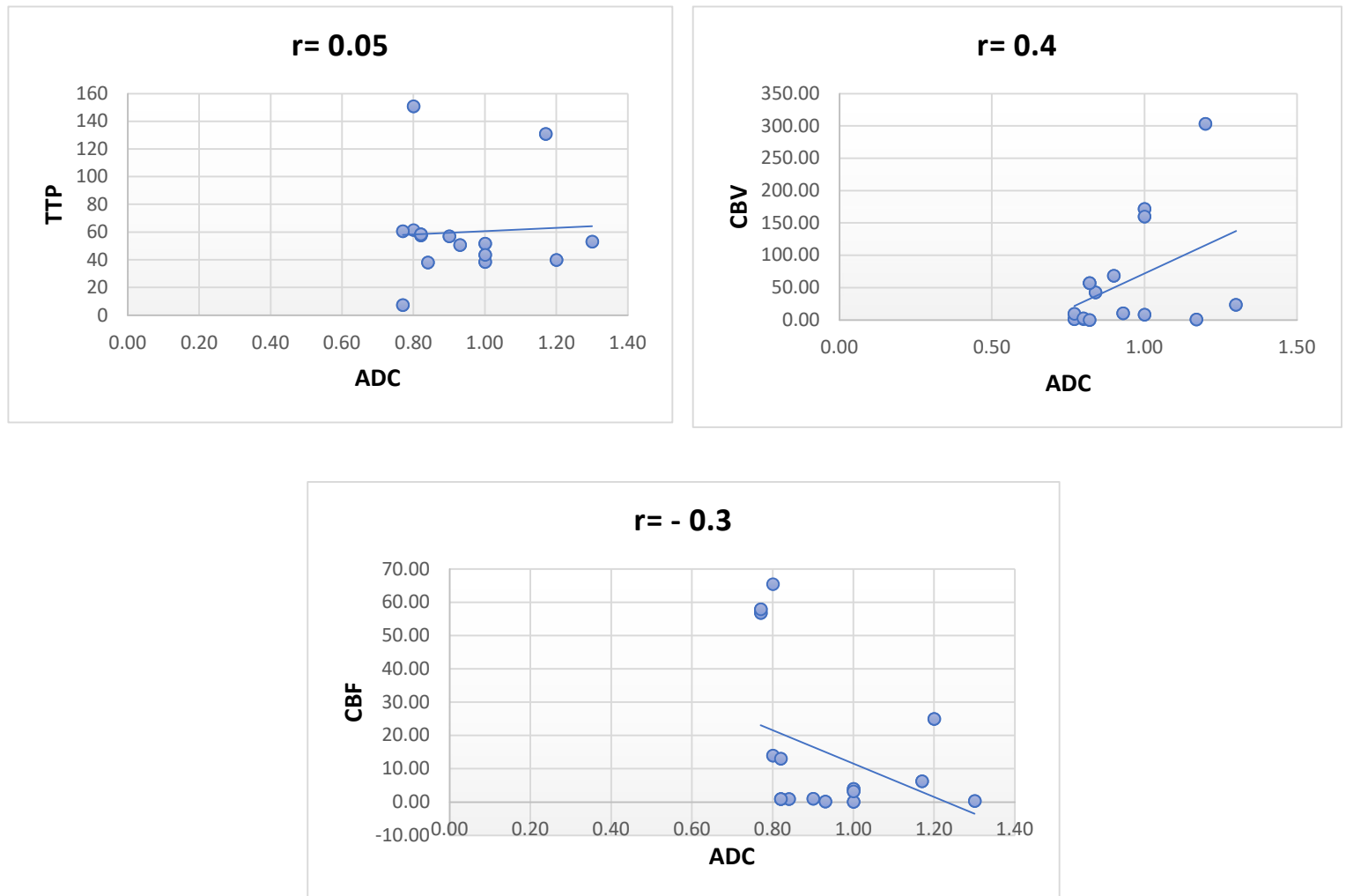


Fig.3.8. Simple linear regression of ADC of penumbra area with TTP, CBV, CBF of the same area for acute cerebral infraction.

The correlation coefficient was used for determining linear relationships between ADC and TTP, CBV, CBF OF normal area in patients with acute cerebral infraction. The results showed that there was no relationship and no significant correlation between ADC and TTP of normal area ($p \geq 0.05$), there was significant positive association between ADC and CBV, but there was negative association between ADC and CBF, as shown in (fig. 3.9.a,b,c).



a) Scatter Plot of TTP by ADC of Normal area

b) Scatter Plot of CBV by

ADC of Normal area. c) Scatter Plot of CBF by ADC of Normal area.

Figure.3.9. Simple linear regression of ADC of penumbra area with ADC, TTP, CBV, CBF of normal area for acute cerebral infarction.

4. Discussion

MRI can detect an ischemic stroke within a few hours of its onset. Multimodal imaging provides information for the diagnosis of ischemic stroke, patient selection for thrombolytic therapy, and prognosis estimation⁽¹⁵⁾.

The ADC value is higher when water molecules are rapidly diffusion and vice versa.

This difference in the value of ADC is due to the rapid spread of water molecules in the brain after infarction, in acute infarction, the speed of propagation of water molecules is low, so the ADC value is lower at the infarction center⁽¹⁶⁾.

They found that sodium accumulates intracellular while water out produces swelling. This makes the diffusion of water molecules slower in the center, and gives a lower value to the ADC concentrate⁽¹⁷⁾. YousufuddinM, *et al.*, 2019⁽¹⁸⁾ states that aging is the most robust non-modifiable risk factor for

incident stroke, which doubles every 10 years after age 55 years. Approximately three-quarters of all strokes occur in persons aged ≥ 65 years. As the number of people aged ≥ 65 years is projected to grow, the number of incident strokes in older adults is expected to rise, presenting major challenges for clinicians and policy makers in the foreseeable future⁽⁵⁹⁾. This is consistent with the current study where the mean \pm SD for age (63.8 ± 8.7).

The BMI of enrolled patient was $27.4 \pm (3.5)$, which considered over weight, this finding comparable with Shiozawa M. *et al.*, 2021⁽¹⁹⁾ whom states that overweight and obesity were associated with a greater incidence of stroke and ischemic stroke in both men and women.

Incidence of hypertension among stroke patients was 59.4 % and diabetes mellitus was 59%, these findings were comparable with Chekol, *et al.*, 2023⁽²⁰⁾ states that Diabetes mellitus was a common comorbidity among stroke patients and that accounted for 86.49%, followed by uncontrolled hypertension (85.58%). Regarding biomarkers, 69.37%, 78.38%, 66.67%, and 63.96% of stroke patients had high levels of LDL, triglycerides, HDL, and total cholesterol, respectively. This current study showed that the cholesterol level was of upper normal limit in most of the patients.

Shah RS, *et al.*, 2010⁽²¹⁾ studies performed across various ethnicities and populations demonstrate a strong association between smoking and stroke risk, with current smokers having at least a two- to fourfold increased risk of stroke compared with lifelong nonsmokers or individuals who had quit smoking more than 10 years prior. In one study, the risk increased to sixfold when this population was compared with nonsmokers who had never been exposed to environmental tobacco smoke (i.e., second-hand smoke), this study was different from the current study where the percentage of nonsmoker was 87.6%, and this difference mostly due to small sample volume.

The enrolled patients 81.3% were no aspirin, while 18.7 % using aspirin, many literature mentioned favorable benefits of aspirin in decreasing occurrence of stroke and decreasing size of stroke, Ryu WS, *et al.*, 2021⁽²²⁾ states that the pre-stroke aspirin use (vs nonuse) was significantly related to a reduced infarct volume (by 30%), particularly in large artery atherosclerosis stroke (by 45%). In cardio embolic stroke, pre-stroke aspirin use was associated with a ~50% lower incidence of early neurological deterioration (END) (adjusted difference = -5.4%, 95% confidence interval [CI] = -8.9 to -1.9). Thus, pre-stroke aspirin use was associated with ~30% higher likelihood of favorable outcome (3 month modified Rankin Scale score < 3), particularly in large artery atherosclerosis stroke and cardio embolic stroke.

In the current study the most common clinical presentation was limb weakness 70 % , dysphasia and slurred speech 56.6 % , headache percentage was 66.6% this is consistent with Fekadu, G. *et al.*, 2019⁽²³⁾ that states the most common clinical presentation was headache complained by 87 (75.0%) patients followed by aphasia 70 (60.3%) and hemiparesis 62 (53.4%).

The current study showed that the mean value of ADC in the central area of infarction was the lowest = $0.47 \pm 0.11 \times 10^{-6} \text{ mm}^2/\text{s}$, while the periphery of infarction = $0.66 \pm 0.15 \times 10^{-6} \text{ mm}^2/\text{s}$, the penumbra area = $0.81 \pm 0.07 \times 10^{-6} \text{ mm}^2/\text{s}$ and it was the highest value in the normal brain tissue = $0.94 \pm 0.16 \times 10^{-6} \text{ mm}^2/\text{s}$ ($P = 0.001$). These findings were consistent with Leigh, R. *et al.*, 2018⁽¹⁶⁾ found that the ADC value was the lowest in the center, and highest value in the normal area, the ADC values were (center 0.53 ± 0.15 - penumbra 0.76 ± 0.1 - normal 0.84 ± 0.1).

These findings also consistent with Lopez-Mejia, *et al.*, 2016⁽²⁴⁾ their study on 75 patients with acute brain infarction, their results showed that the mean of ADC gradually increases from the infarction center to the periphery and then the penumbra until it is the highest value in the normal brain area with significant difference $P \leq .001$.

Regarding perfusion

Time-to-peak (TTP) is the time at which contrast concentration reaches its maximum. ⁽²⁵⁾.

The TTP mean value in the center of infarction was 56.6 ± 28.6 s and in the periphery of infarction 70.5 ± 36.5 s, 60.2 ± 31.9 s in penumbra and in normal area was 59.9 ± 35.1 s, the difference was insignificant, P-value = 0.4, this finding was incomparable with Moon WJ, *et al.*, 2005⁽²⁶⁾ were mean value of the TTP showed a significant difference, with the lower value being observed for the less ischemic area and the higher value being observed for the more ischemic area ($p < 0.001$).

Cerebral blood flow (CBF) is one of the parameters generated by perfusion techniques. CBF is defined as the volume of arterial blood delivered to brain tissue per unit of time ⁽²⁷⁾.

In this study The CBF mean value were different among different regions of infarction without significance difference $P=0.9$. In the center of infarction was 15.57 ± 24.6 mL/100 g/min and in the periphery of infarction 14.1 ± 23 mL/100 g/min, 16.8 ± 27.2 mL/100 g/min in penumbra and in normal area was 14.5 ± 21.3 mL/100 g/min, these finding were close to Ma X, *et al.*, 2022⁽²⁹⁾, the mean values of CBF in the infarct core (16.42 mL/100 g/min) were lower than those in the ischemic penumbra (21.54 mL/100 g/min). other study done by Seiler, *et al.*, 2019⁽²⁹⁾, disagree with our results, they found different values of CBF in different regions of infarction with a significant difference. **Cerebral blood volume (CBV)** is defined as the volume of blood in a given amount of brain tissue, ⁽³¹⁾.

In this study The CBV mean value in the center of infarction was 24.7 ± 34.7 ml/100gm and in the periphery of infarction 40.5 ± 46.5 ml/100gm, 72 ± 86.1 ml/100gm in penumbra and in normal area was 59.5 ± 85.7 ml/100gm this difference was significant ($p = 0.04$). This agree with Ma X, *et al.*, 2022⁽²⁸⁾. In the current study there was no significant difference in the ADC value of different regions of infarction related to the age as well as TTP and CBF p value > 0.05 , only the CBV show significant difference in regions of infarction related to patient age (p value = 0.001, Elschot E.P, *et al.*, 2024⁽³¹⁾) agree with our findings in all parameters except CBV whom found there is no significant difference in CBV according to patient age ($p = 0.498$).

In the current study the relationship between ADC and CBV is significant with positive correlation in central area of infarction and in normal brain area while the correlation is negative in peripheral area and penumbra,

And the relationship between ADC and CBF is significant and positive correlation in peripheral area, while the correlation is negative in central area of infarction, penumbra and in normal area. these findings are consistent with Yoshie T, *et al.*, 2020⁽³²⁾, showed that in ischemic core ADC regions, were associated with more highly abnormal perfusion parameters CBF: Spearman correlation, $r = -0.22$, $P = .005$, CBV: $r = -0.41$, $P < .001$

Liu J, *et al.*, 2021⁽³³⁾, found that there is a negative correlation between CBF and ADC and a positive correlation between ADC and CBV. with a $P \leq 0.001$. This result almost matches the results of our study where the association between ADC and CBF is negative.

Huang, H. T, *et al.*, 2021⁽³⁴⁾, have observed that ADC and CBF at the center of the infarction area, has lower value..

In the current study the relationship between ADC and TTP is insignificant in all brain areas. Moon WJ, *et al.*, 2005⁽²⁶⁾, agree with our study, found that in the penumbral area the ADC ratios displayed significant negative correlation with the TTP ratios ($p < 0.001$).

Our comments, we found that the parameters of perfusion includes TTP, CBF of no significant difference in different areas of infarction and only the CBV shows significant difference.

As we know that perfusion study is time consuming, costly with hazards of contrast to the patient while the ADC measurement is simple with short time, free of hazards, low cost to the patient and more accurate in determining different regions of infarction.

References:

1. Sacco R.L., Kasner S.E., Broderick J.P., *et al.* An updated definition of stroke for the 21st century: A statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2013;44:2064–2089.
2. Boehme A.K., Esenwa C., Elkind M.S. Stroke Risk Factors, Genetics, and Prevention. *Circ. Res.* 2017;120:472–495.
3. Allen L.M., Hasso A.N., Handwerker J., Farid H. Sequence-specific MR imaging findings that are useful in dating ischemic stroke. *Radiographics*. 2012;32:1285–1297.
4. Potter C.A., Vagal A.S., Goyal M., *et al.* CT for Treatment Selection in Acute Ischemic Stroke: A Code Stroke Primer. *Radiographics*. 2019;39:1717–1738.
5. Powers W.J., Derdeyn C.P., Biller J., *et al.* American Heart Association Stroke Council. 2015 American Heart Association/American Stroke Association Focused Update of the 2013 Guidelines for the Early Management of Patients with Acute Ischemic Stroke Regarding Endovascular Treatment: A Guideline for Healthcare Professionals from the American Heart Association/American Stroke Association. *Stroke*. 2015;46:3020–3035.95,
6. Lee H, Yang Y, Liu B, Castro SA, Shi T. Patients With Acute Ischemic Stroke Who Receive Brain Magnetic Resonance Imaging Demonstrate Favorable In-Hospital Outcomes. *J Am Heart Assoc.* 2020 Oct 20;9(20):e016987.
7. Kakkar P, Kakkar T, Patankar T, Saha S. Current approaches and advances in the imaging of stroke. *Dis Model Mech.* 2021 Dec 1;14(12):dmm048785..
8. Tedyanto EH, Tini K, Pramana NAK. Magnetic Resonance Imaging in Acute Ischemic Stroke. *Cureus.* 2022 Jul 25;14(7):e27224.
9. Wey H.-Y., Desai V.R., Duong T.Q. A review of current imaging methods used in stroke research. *Neurol. Res.* 2013;35:1092–1102.
10. Ulu E., Ozturk B., Atalay K., Okumus I.B., Erdem D., Gul M.K., Terzi O. Diffusion-Weighted Imaging of Brain Metastasis: Correlation of MRI Parameters with Histologic Type. *Turk. Neurosurg.* 2022;32:58–68.
11. Xu K, Gu B, Zuo T, Xu X, Chen YC, Yin X, Feng G. Predictive value of Alberta stroke program early CT score for perfusion weighted imaging - diffusion weighted imaging mismatch in stroke with middle cerebral artery occlusion. *Medicine (Baltimore).* 2020 Dec 11;99(50):e23490.
12. Heo HY, Tee YK, Harston G, Leigh R, Chappell MA. Amide proton transfer imaging in stroke. *NMR Biomed.* 2023 Jun;36(6):e4734.
13. Mandeville E.T., Ayata C., Zheng Y., Mandeville J.B. Translational MR Neuroimaging of Stroke and Recovery. *Transl. Stroke Res.* 2017;8:22–32.
14. Lin M.P., Liebeskind D.S. Imaging of Ischemic Stroke. *Continuum.* 2016;22:1399–1423.
15. Tedyanto EH, Tini K, Pramana NA. Magnetic resonance imaging in acute ischemic stroke. *Cureus.* 2022 Jul;25:14(7).
16. Leigh, R., Knutsson, L., Zhou, J., & van Zijl, P. C. Imaging the physiological evolution of the ischemic penumbra in acute ischemic stroke. *Journal of Cerebral Blood Flow & Metabolism*, 2018; 38(9):1500-1516.
17. Yu XW, Zhang Z, Yang J, Zhang YL, Wang R, Niu G, Guo YM. [Quantitative evaluations of ischemic stroke based on meta-analysis]. *Zhonghua Yi XueZaZhi.* 2011 Nov 22;91(43):3066-70.
18. Yousufuddin M, Young N. Aging and ischemic stroke. *Aging (Albany NY).* 2019 May 1;11(9):2542-2544.
19. Shiozawa M, Kaneko H, Itoh H, Morita K, Okada A, Matsuoka S, Kiriyaama H, Kamon T, Fujiu K, Michihata

- N, Jo T, Takeda N, Morita H, Nakamura S, Node K, Yasunaga H, Komuro I. Association of Body Mass Index with Ischemic and Hemorrhagic Stroke. *Nutrients*. 2021 Jul 9;13(7):2343.
- 20.Chekol YM, Merid MW, Tesema GA, Tesfie TK, Tebeje TM, Gelaw NB, Gebi NB, Seretew WS. Development and Validation of a Risk Prediction Model to Estimate the Risk of Stroke Among Hypertensive Patients in University of Gondar Comprehensive Specialized Hospital, Gondar, 2012 to 2022. *DegenerNeurolNeuromuscul Dis*. 2023;13:89-110.
- 21.Shah RS, Cole JW. Smoking and stroke: the more you smoke the more you stroke. *Expert Rev Cardiovasc Ther*. 2010 Jul;8(7):917-32.
- 22.Ryu WS, Schellingerhout D, Hong KS, Jeong SW, Kim BJ, Kim JT, et al. Relation of Pre-Stroke Aspirin Use With Cerebral Infarct Volume and Functional Outcomes. *Ann Neurol*. 2021 Nov;90(5):763-776.
23. Fekadu, G., Chelkeba, L. &Kebede, A. Risk factors, clinical presentations and predictors of stroke among adult patients admitted to stroke unit of Jimma university medical center, south west Ethiopia: prospective observational study. *BMC Neurol*.2019;19:187.
24. Lopez-Mejia, M., & Roldan-Valadez, E. Comparisons of apparent diffusion coefficient values in penumbra, infarct, and normal brain regions in acute ischemic stroke: confirmatory data using bootstrap confidence intervals, analysis of variance, and analysis of means. *Journal of Stroke and Cerebrovascular Diseases*,2016; 25(3):515-522.
- 25.Thapa G, Murphy A, Hacking C, et al. Time to peak (TTP). Reference article, Radiopaedia.org (Accessed on 28 Mar 2024) .
- 26.. Moon WJ, Na DG, Ryoo JW, Roh HG, Byun HS, Jeon YH, Chung EC. Assessment of Tissue Viability Using Diffusion- and Perfusion-Weighted MRI in Hyperacute Stroke. *Korean J Radiol*. 2005 Apr-Jun;6(2):75-81.
- 27.Proisy M, Mitra S, Uria-Avellana C, Sokolska M, Robertson NJ, Le Jeune F, Ferré JC. Brain Perfusion Imaging in Neonates: An Overview. *AJNR Am J Neuroradiol*. 2016 Oct;37(10):1766-1773.
28. Ma X, Wang Y, Wang M, Zhang M, Meng N, Zhang L, Zhang J, Dou S, Wang M. Evaluation of infarct core and ischemic penumbra by absolute quantitative cerebral dynamic susceptibility contrast perfusion magnetic resonance imaging using self-calibrated echo planar imaging sequencing in patients with acute ischemic stroke. *Quant Imaging Med Surg*. 2022 Aug;12(8):4286-4295.
- 29.Seiler A, Blockley NP, Deichmann R, et al. The relationship between blood flow impairment and oxygen depletion in acute ischemic stroke imaged with magnetic resonance imaging. *Journal of Cerebral Blood Flow & Metabolism*. 2019;39(3):454-465.
- 30.Petrella JR, Provenzale JM. MR perfusion imaging of the brain: techniques and applications. *AJR Am J Roentgenol*. 2000 Jul;175(1):207-19.
- 31.Elschot, E.P.; Backes, W.H.; van den Kerkhof, M.; Postma, A.A.; Kroon, A.A.; Jansen, J.F.A. Cerebral Microvascular Perfusion Assessed in Elderly Adults by Spin-Echo Dynamic Susceptibility Contrast MRI at 7 Tesla. *Tomography* 2024, 10, 181-192. <https://doi.org/10.3390/tomography10010014>.

32. Yoshie T, Yu Y, Jiang H, Honda T, Trieu H, Scalzo F, Saver JL, Liebeskind DS; UCLA Reperfusion Therapy Investigators. Perfusion Parameter Thresholds That Discriminate Ischemic Core Vary with Time from Onset in Acute Ischemic Stroke. *AJNR Am J Neuroradiol*. 2020 Oct;41(10):1809-1815.
33. Liu J, Lin C, Minuti A, Lipton M. Arterial spin labeling compared to dynamic susceptibility contrast MR perfusion imaging for assessment of ischemic penumbra: A systematic review. *J Neuroimaging*. 2021 Nov;31(6):1067-1076.
34. Huang, H. T., Tung, T. H., Lin, M., Wang, X., Li, X., Liang, K., ... & Chen, P. E. Characterizing spatiotemporal progression and prediction of infarct lesion volumes in experimental acute ischemia using quantitative perfusion and diffusion imaging. *Applied Radiation and Isotopes*, 2021;168: 109