

RESEARCH ARTICLE

ÖZGÜN ARAŞTIRMA

**TIME DEPENDENT CALIBRATION OF HEMIPLEGIA AS A SENSITIVE CLINIMETRIC TOOL FOR OCCLUSION
OF M1 SEGMENT OF THE MIDDLE CEREBRAL ARTERY**

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ABSTRACT

INTRODUCTION: Large vessel's occlusion of the brain produces significant disability of speech, mobility and cognition. In this paper, we present a time-dependent clinimetric scale of hemiplegia, denoted as H3H, that's fast and reliable in predicting large segment's occlusion of the middle cerebral artery (MCA). We have also compared its performance to the National Institute of Health Stroke scale (NIHSS), Los Angeles Motor scale (LAMS) and Vision, Aphasia, Neglect scale (VAN).

METHODS: This is a prospective observational study in 170 patients of acute ischemic stroke of MCA. Occlusions of large M1 segment and focal branches of MCA were confirmed on computed tomography (CT) scan of the brain. Predictive accuracy of each scale for M1 segment's occlusion was compared to the brain CT to calculate its sensitivity, specificity and accuracy.

RESULTS: Of the 170 patients, 60% were males and 40% were females. Average age was 63 years \pm 6.1. Forty patients had infarctions of large M1 segment while 130 patients had focal infarctions of MCA. Predictive accuracy of H3H scale (Sensitivity: 100%, Specificity: 86%) exceeded VAN [Sensitivity: 100%, Specificity: 81%] and LAMS [Sensitivity: 100%, Specificity: 77%] and was better than NIHSS [Sensitivity: 100%, Specificity: 72%]. The negative predictive value was 100% for all. It took only 11 \pm 2.7 seconds to conclude H3H scale for a patient.

DISCUSSION AND CONCLUSION: Time- based calibration of hemiplegia gives us a novel H3H scale that has speed and simplicity. Its predictive accuracy for occlusion of M1 segment of MCA is competitive to other scales.

Keywords: Hemineglect, hemiplegia, infarction.

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ORTA SEREBRAL ARTERİN M1 SEGMENT TIKANIKLIĞI İÇİN HASSAS BİR KLİNİMETRİK ARAÇ OLARAK HEMİPLEJİNİN ZAMANA BAĞLI KALİBRASYONU

ÖZ

GİRİŞ ve AMAÇ: Serebral büyük damarlarının tıkanması belirgin derecede konuşma, hareket ve kognisyon yitimine neden olur. Bu araştırmada orta serebral arterin (MCA) proksimal segment oklüzyonunu öngörmeye hızlı ve güvenilir olma potansiyeline sahip H3H olarak adlandırılan hemiplejinin zamana bağlı klinimetrik bir ölçeğini sunulmaktadır. Ek olarak H3H performansı Ulusal Sağlık İnme Ölçeği (NIHSS), Los Angeles Motor Ölçeği (LAMS) ve Vizyon, Afazi, İhmal Ölçeği (VAN) ile karşılaştırılmıştır.

YÖNTEM ve GEREÇLER: Bu çalışma, 170 akut MCA sahası inmesi olan hastada yapılan prospektif ve gözlemsel bir çalışmadır. Proksimal M1 segment ve dal oklüzyonları Bilgisayarlı Beyin Tomografisi (CT) ile takipte doğrulandı. Her bir ölçeğin M1 segmenti oklüzyonu için tahmin doğruluğu, BBT'nin duyarlılık, özgüllük ve doğruluk oranları ile karşılaştırıldı.

BULGULAR: 170 hastanın %60'ı erkek, %40'ı kadındı. Ortalama yaş 63 ± 6.1 yıl idi. Kırk hastada geniş M1 segment enfarktı, 130 hastada ise MCA dal enfarktı vardı. H3H ölçeğinin M1 oklüzyonunu tahmin etmedeki doğruluğu (Duyarlılık: %100, Özgüllük: %86), VAN (Duyarlılık: %100, Özgüllük: %81) ve LAMS (Duyarlılık: %100, Özgüllük: %77)'i geçmiş olup NIHSS'den de daha iyi (Duyarlılık: %100, Özgüllük: %72) bulunmuştur. Negatif prediktif değer tümü için %100 idi. Bir hasta için H3H ölçeğini tamamlamak sadece 11 ± 2.7 saniye sürmüştür.

TARTIŞMA ve SONUÇ: Akut hemiplejinin zamana bağlı kalibrasyonu bize hızlı ve basit olan yeni bir olarak H3H ölçeğini sunmaktadır. H3H'nin MCA'nın M1 segment tıkanıklığının tahmini için doğruluğu diğer ölçeklerle rekabet edebilecek seviyededir.

Anahtar Sözcükler: Hemineglect, hemipleji, enfarkt.

INTRODUCTION

The precedence of speedy management of acute ischemic stroke which is consistently growing for the last three decades has shown promising results for patients with large vessel occlusion (1). Large vessel's occlusion produces instant lose of essential functions like speech, mobility, vision, thinking and intelligence (2). It brings detrimental physical, social and psychological consequences to the patients. Every minute, hundreds of brain's cells die due to ischemia (3). Disability increases with the passage of time and every minute counts for a better prognosis. Therefore, prompt diagnosis and swift action is avidly needed in large vessel's occlusion to disparage the damage and escort the penumbra (4). The significance of early and prompt management of acute ischemic stroke has encouraged the development of important clinical scales to predict the large vessel's occlusion. There are many clinical scales for the assessment of stroke's severity that includes, face, arm, speech test (FAST), National Institutes of Health Stroke Scale (NIHSS), legs, eyes, gaze, speech (LEGS), Los Angeles Motor Scale (LAMS), Ontario Prehospital Stroke Screening (OPSS), Melbourne Ambulance Stroke Screen (MASS), Rapid Arterial occlusion Evaluation Scale (RACE), and vision, aphasia, neglect (VAN) (5-12). Some of these scales i.e. the

VAN, RACE and LAMS are used for the prediction of large vessel's occlusion. All these scales require adequate correspondence of the patient for a score to predict the severity of infarction. However, sometimes it is not feasible to perform adequate examination for a score as in the altered conscious level, aphasia, seizures and irritability. The functions of the two hemispheres are also different. In most patients, the aphasia develops with infarction of the left hemisphere and hemineglect develops with infarction of the right hemisphere. These factors limit the usefulness and precision of the available scales in predicting large vessel occlusion. Therefore, we would always need a simple scale of adequate precision to predict large vessel's occlusion in acute ischemic stroke with less cooperation of the patients. As mentioned earlier, the larger is the caliber of a vessel, substantial would be the damage in the brain, and more rapid would be the onset of weakness. None of the available scales have considered the time of onset of symptoms as an important predictor of the large vessel's occlusion.

In this paper, we present the performance of a novel time-dependent scale of hemiplegia [severity of hemiplegia in the first three hours of symptoms (H3H)] in predicting the occlusions of larger M1 segment and focal branches of the MCA in comparison to the VAN scale, NIHSS of > 6 and the LAMS.

METHODS

This is a prospective, cross sectional observational study, in patients with acute ischemic stroke of the middle cerebral artery (MCA). The study was performed in accordance with Helsinki Declaration. The research was approved from the Ethical Committee of DHQ, Teaching Hospital KDA Kohat (Number: 116/K-17, Date: 11.01.2019). Informed consent was signed by all patients before the enrolment. We examined all patients with absolutely resolved territories of infarctions for the distal focal and proximal M1 segments of the MCA which have peculiar gross appearances on plain images of computed tomography scan (CT). We did time-based calibration of the severity of hemiplegia after its onset and depending upon the speed of onset of severe hemiplegia, occlusion of large M1 segment or focal branch of MCA was predicted. The results were then compared to infarctions which matched in appearance to either focal or large segments' occlusions of MCA on brain CT.

The Novel Time-Dependent Scale:

The vessel most appropriate for finding the relevance of large segment's occlusion to rapid onset of severe weakness in less time, was occlusion of proximal M1 segment of the MCA. Likewise, the distal cortical segment of MCA was expected to produce less severe weakness in several minutes or hours of symptom's progression. This provided a time-dependent calibration for the severity of hemiplegia into two categories that formed the basis for the new scale, denoted as H3H i.e. the severity of hemiplegia in the first three hours. The numerical scoring of the severity of hemiplegia is an integral part of the NIHSS. We have added the time factor to hemiplegia to calibrate its severity instead of scoring it by numerical numbers. It gives speed and simplicity to the scale. The four components of the VAN scale were also derived from the NIHSS and has shown better results on the true negative predictions of large vessels' occlusions than NIHSS. We made it more simpler with time-based calibration of hemiplegia to predict large M1 segment's occlusion. The novel scale depends on motor predominant weakness and was therefore tested on patients with anterior circulation's ischemic stroke. Patients with rapid onset of severe hemiplegia i.e. no power left on the affected side for sliding movements on the bed's surface, in

the first ten to fifteen minutes of symptoms' onset, were considered positive by H3H scale. The scale was considered negative for M1 segment's occlusion if there had been a possibility for either sliding or more purposeful movements on the affected side in less than three hours but beyond the first fifteen minutes of symptoms' onset. The performance of H3H scale was also compared to the NIHSS, LAMS and the VAN scale. The scales were tested only for the territory of the MCA. The method of implementation of H3H scale on patients with acute ischemic stroke is illustrated in Figure 1.

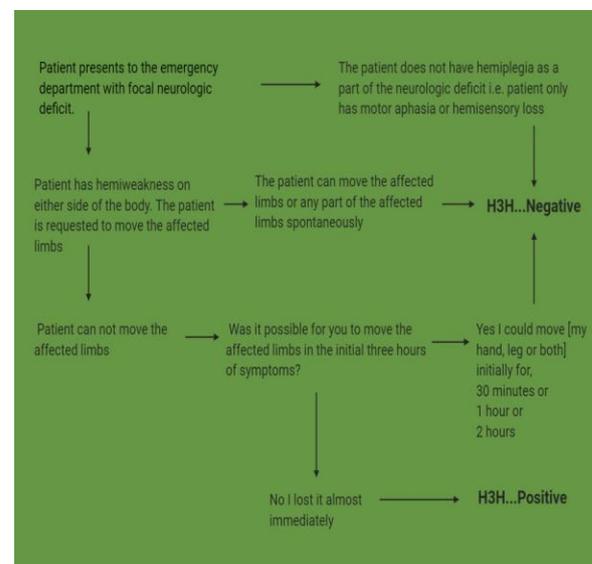


Figure 1. Application of H3H scale on the ischemic stroke patients.

Inclusion Criteria:

- ✓ All patients with new-onset focal neurologic deficit, having no further progression of symptoms and had well defined area of infarction for the territory of MCA on brain CT.
- ✓ Only conscious patients of acute ischemic stroke were enrolled, because VAN scale, NIHSS and LAMS required patient's cooperation for the calculation of scores.
- ✓ Patients who were well aware of the severity of hemiplegia at the time of onset of symptoms.

Exclusion Criteria:

- ✓ Patients with dementia of any cause.
- ✓ Hemorrhagic transformation of the ischemic infarction.
- ✓ Ischemic infarction with surrounding edema.

- ✓ Patients with clinical presentation of homonymous hemianopia with or without partial hemiparesis were excluded. This is because H3H scale depends on motor predominant weakness for its sensitivity and cases of the posterior cerebral artery's (PCA) infarctions of the occipital lobe, which is a sensory predominant area, often causes less severe weakness despite of its large segment's occlusion. Hence, cases of posterior circulation's with partial weakness were clinically excluded. However, patients with rapid onset of severe weakness were considered positive for H3H i.e. represented large vessel occlusion, regardless of the presence of homonymous hemianopia.

Neuroimaging Criteria for Occlusion of M1 Segment and Focal Branches of MCA: The anatomical course of MCA in relation to the deep brain structures and the cerebral cortex is illustrated in Figure 2. The artery instigates from the supraclinoid part of the internal carotid artery. The M1 segment is the initial and larger part of the vessel. It gives lenticulostriate branches to the ipsilateral basal ganglia and the internal capsule and becomes M2 segment which moves across the insula and the peri-insular cortex. Therefore, occlusion of proximal M1 segment will produce simultaneous changes of signal of infarction in the basal ganglia, internal capsule, the insula and the peri-insular cortex. This peculiar pattern of infarction produced by M1 segment's occlusion is shown in Figure 3.

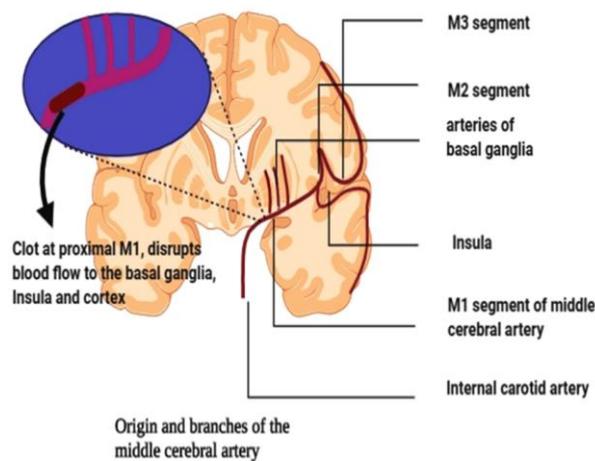


Figure 2. Branches of the middle cerebral artery.

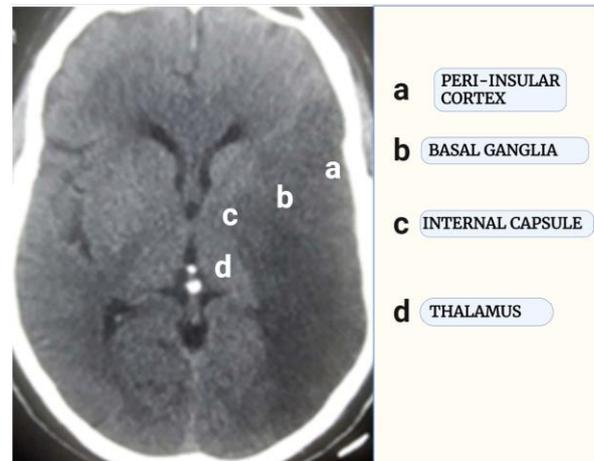


Figure 3. Occlusion of M1 segment of the middle cerebral artery causing infarction of the ipsilateral internal capsule, basal ganglia and peri-insular cortex.

In comparison to M1 segment's occlusion, a focal infarction is produced by occlusion of a small penetrating branch which invokes a focal change of signal of infarction in the outer territory of MCA without concurrent changes at the insula as shown in Figure 4. The two sets of infarctions i.e. of the proximal M1 segment and the penetrating branch of MCA, had unique configurations on plain images of the brain CT in patients with static non-progressive neurological deficits. Therefore, further evaluation by CT angiography was unnecessary and non-productive in the present study. The results of the CT scan for occlusions of focal branches and M1 segment of MCA, were compared to the predictions of each clinical scale to determine its sensitivity, specificity, positive predictive value and accuracy. The statistical methods used in our study are defined in Table 1.

RESULTS

We examined 170 patients of acute ischemic stroke of the territory of the MCA between 15-01-2019 and 28-06-2021. Average age was 63 years \pm 6.1. Of the 170 patients, 60% were males and 40% were females. There were 40 patients who had infarctions of M1 segment of the MCA on brain CT and the remaining 130 patients had infarctions of focal non-M1 segments of the MCA. The H3H scale, NIHSS, LAMS and the VAN scale showed a sensitivity of 100% and correctly detected the occlusion of M1 segment in all patients. The H3H scale was positive in 57 patients. It took only 11 \pm 2.7 seconds on average to decide the H3H scale for

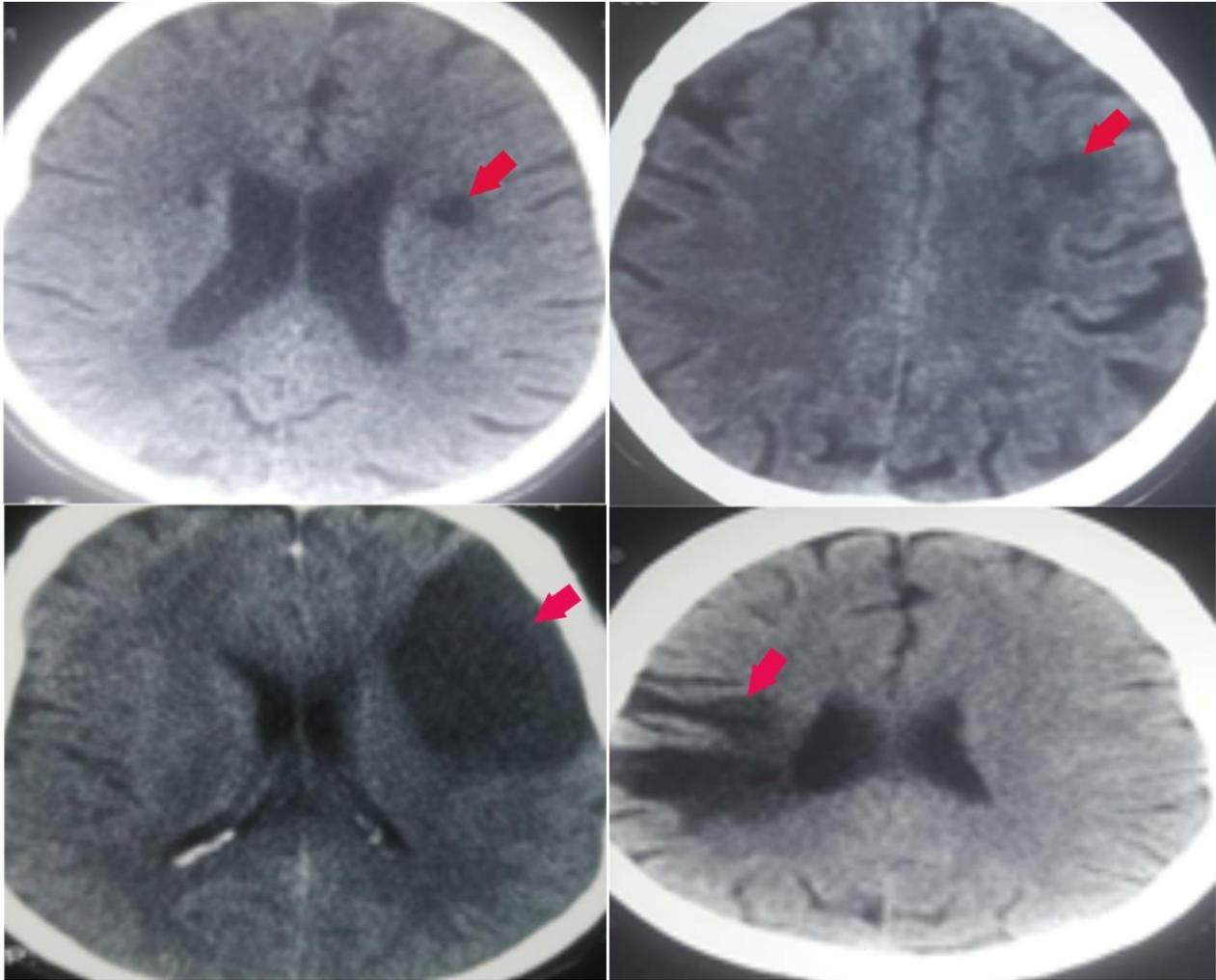


Figure 4. Focal non-M1 occlusions of the middle cerebral artery.

a patient. All patients with occlusions of M1 segment, developed severe hemiplegia in less than ten-minutes after the onset of symptoms. NIHSS of > 6 was found in 76 patients. Average NIHSS of these patients was 13.85 ± 3.2 . The mean NIHSS of the forty patients with M1 segment's occlusions was 15.6 ± 2.4 . The LAMS score of the true positive cases was 5. The positive predictive values of the H3H scale, VAN scale and the LAMS were slightly better than the NIHSS [H3H: 70%, VAN: 62%, LAMS: 57%, NIHSS: 52%]. The negative predictive value was 100% for all. The true negative predictions i.e. the specificity of each of the H3H scale, VAN scale and the LAMS for the occlusion of M1 segment of MCA were relatively similar and better than NIHSS [H3H: 86%, VAN: 81%, LAMS: 77%, NIHSS: 72%]. The details of the performance

of each scale are given in Table 2 and 3. We observed that the muscle strength, speech, vision and sensations were commonly affected by infarctions of small and moderate sizes of the middle cerebral artery. Therefore, the scales with less number of clinical parameters for stroke i.e. the H3H scale, LAMS and the VAN scale, showed better reliability for occlusion of M1 segment than NIHSS.

DISCUSSION AND CONCLUSION

This prospective cross-sectional study has determined the performance of the simple H3H scale in predicting occlusions of larger M1 segment and focal branches of MCA in comparison to the NIHSS, LAMS and the VAN scale. The territory of MCA is larger than all other vessels of the brain. It

Table 1. Definitions of statistical terms.

$$\text{Sensitivity} = \frac{\text{True positive detections}}{\text{True positive detections} + \text{False negative detections}}$$

$$\text{Specificity} = \frac{\text{True negative detections}}{\text{True negative detections} + \text{False negative detections}}$$

$$\text{Positive predictive value} = \frac{\text{True positive detections}}{\text{No of positive detections}}$$

$$\text{Negative predictive value} = \frac{\text{Negative detections}}{\text{No of negative detections}}$$

$$\text{Accuracy} = \frac{\text{True positive detections} + \text{True negative detections}}{\text{Total number of tested patients}}$$

True Positive detection: Patient with definite M1 segment's occlusion
 True Negative detection: Patient with no M1 segment's occlusion and has only focal infarction
 False Positive detection: Patient declared positive by the scale but has no M1 segment's occlusion
 False Negative detection: Patient declared negative by the scale but has M1 segment's occlusion

is a common site of ischemic infarction. It nourishes the most important motor structures in each hemisphere as shown in Figure 5 (13). These include primary motor cortex, corona radiata, internal capsule and the basal ganglia. The axonal fibers of speech and optic radiations also traverse through the territory of the MCA. In our study, small to moderate size of infarctions of the MCA produced a considerable decline in muscle strength, impaired the quality of speech and some were associated with the contralateral sensory and or visual hemineglect. The speech is usually determined by the left dominant hemisphere in most individuals, whereas the hemineglect of the body and vision is a common finding with infarctions of the right MCA (14, 15). Therefore, many cases of focal infarctions of the MCA of either of the hemispheres presented with a combination of contralateral weakness, facial palsy of the upper motor neuron type, slurred speech and sometimes hemineglect. Each of these clinical parameters are covered and scored by the NIHSS. A severe weakness on the contralateral side of the face and

Table 2. M1 and non-M1 occlusions of the middle cerebral artery determined by the clinical scales and the brain CT.

	M1 occlusion	Non-M1 occlusion	Total cases	M1 occlusion on brain CT	Non-M1 occlusion on brain CT
H3H scale+	40	17	57		
H3H scale-	0	113	113		
VAN+	40	24	64		
VAN-	0	106	106		
LAMS+	40	29	69		
LAMS-	0	101	101		
NIHSS > 6	40	36	76		
NIHSS < 6	0	94	94	40	130

*H3H; Hemiplegia in the first three hours Scale, *NIHSS; National Institute of Health Stroke Scale, *LAMS; Los Angeles Motor Scale, *VAN; Vision, Aphasia, Neglect Scale.

Table 3. Positive predictive values, negative predictive values, sensitivity, specificity, and accuracy of each clinical scale.

	Positive predictive value	Negative predictive value	Sensitivity	Specificity	Accuracy
1. H3H scale	40/57=70%	113/113=100%	40/40=100%	113/130=86%	153/170=90%
2. VAN	40/64=62%	106/106=100%	40/40=100%	106/130=81%	146/170=85%
3. LAMS	40/69=57%	101/101=100%	40/40=100%	101/130=77%	141/170= 82%
4. NIHSS	40/76=52%	94/94=100%	40/40=100%	94/130= 72%	134/170= 78%

*H3H; Hemiplegia in the first three hours, *NIHSS; National Institute of Health Stroke Scale, *LAMS; Los Angeles Motor Scale, *VAN; Vision, Aphasia, Neglect Scale.

body within an hour of focal infarction accomplish a score of 11 on the NIHSS. For this reason many cases of focal infarctions of the MCA obtained a score of > 6. We found the NIHSS more sensitive and less specific for the territory of the MCA as compared to other scales. The anterior cerebral

artery (ACA) supplies only a limited area on the medial aspect of the frontal lobe. Of all the cases of anterior circulation's ischemic stroke that we had screened for our study, we received only two cases of infarction of ACA. Its presentation is rare. We could not separate distal focal occlusion of ACA

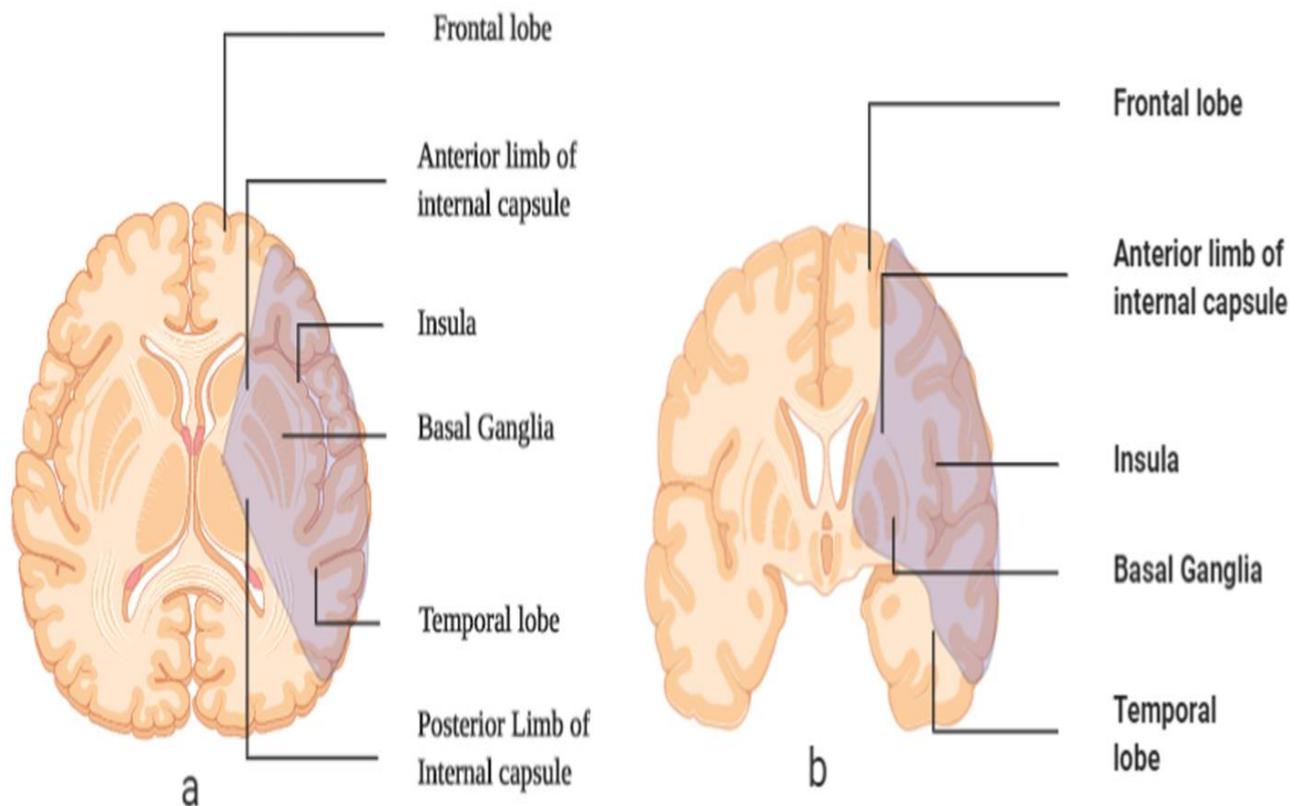


Figure 5. Anatomical structures of the brain in the territory of the middle cerebral artery in axial (a) and coronal (b) view.

precisely from its proximal large segment on plain images of the brain CT due to its limited territory and partial resolution of the infarct at presentation. For this reason, we could not include the neurovascular territory of ACA in our study. Both cases had severe hemiplegia at presentation. Focal infarctions of ACA may only produce contralateral hemiplegia (16). It will not affect the contralateral vision and sensations of the body and may not affect the speech if the right hemisphere is involved. Because ACA's infarctions produce motor predominant weakness, therefore, H3H scale will give better predictions of its focal and large segments' occlusions. The posterior occipital lobe is a pure visual area and is mainly supplied by the PCA. Focal and large segments' infarctions of PCA are usually not associated with severe hemiplegia (17). As mentioned earlier, the H3H scale depends on motor predominant weakness for its sensitivity, and hence, its implementation for the territory of

PCA will not be appropriate. We excluded clinical cases of homonymous hemianopia from our study as involvement of the PCA was very likely in those cases. Based on these anatomical limitations, we recommend that the quick and brief scales like H3H, VAN and the LAMS should all be tested separately for the territories of major vessels of the brain and their limitations highlighted to the clinicians. In our study, the values of true negative predictions of the VAN scale, LAMS and the NIHSS for focal infarctions of the MCA were 81%, 77% and 72% respectively. The H3H scale, VAN scale and the LAMS, all have competitive sensitivities and specificities for occlusion of M1 segment of the MCA. The severe weakness of hemiplegia of all the forty cases of M1 segment's occlusions developed within ten-minutes after the onset of symptoms. The average NIHSS of the 40 patients with M1 segments' occlusions was 15.6 and the mean of the 76 patients with NIHSS of > 6 was 13.8. The true

negative predictions of the H3H scale for occlusion of M1 segment was 14% better than the NIHSS and only 5% better than the VAN scale. The patients with focal infarctions of MCA who retained some movement in the first hour after the onset of symptoms were usually negative by the H3H scale but at the time of presentation, the contralateral weakness was more pronounced and proved positive on the NIHSS and LAMS but remained negative on the VAN scale. For this reason both H3H and the VAN scale showed competitive results. The severe weakness of hemiplegia is a common incidence of M1 segment's occlusion as it dysfunctions the internal capsule and the motor area of the frontal lobe. Therefore, the sensitivity of the H3H scale remained 100% and equal to the

VAN scale, NIHSS and the LAMS. The true negative predictions of the H3H scale, VAN scale, LAMS and the NIHSS depend upon the location and volume of the focal infarction of the MCA as illustrated in Figure 6. The H3H scale is simple and easy to use. It does not need calculation of a score. It can also be used in the unconscious patients. The muscle strength of the affected side of an unconscious patient is usually determined by applying a painful stimulus and the duration of symptoms can be enquired from a close relative. We may not be able to attain a specificity of 100% for any scale due to variability of functions of the two hemispheres, onset of severe symptoms with small volume of infarction and lack of adequate correspondence in some patients.

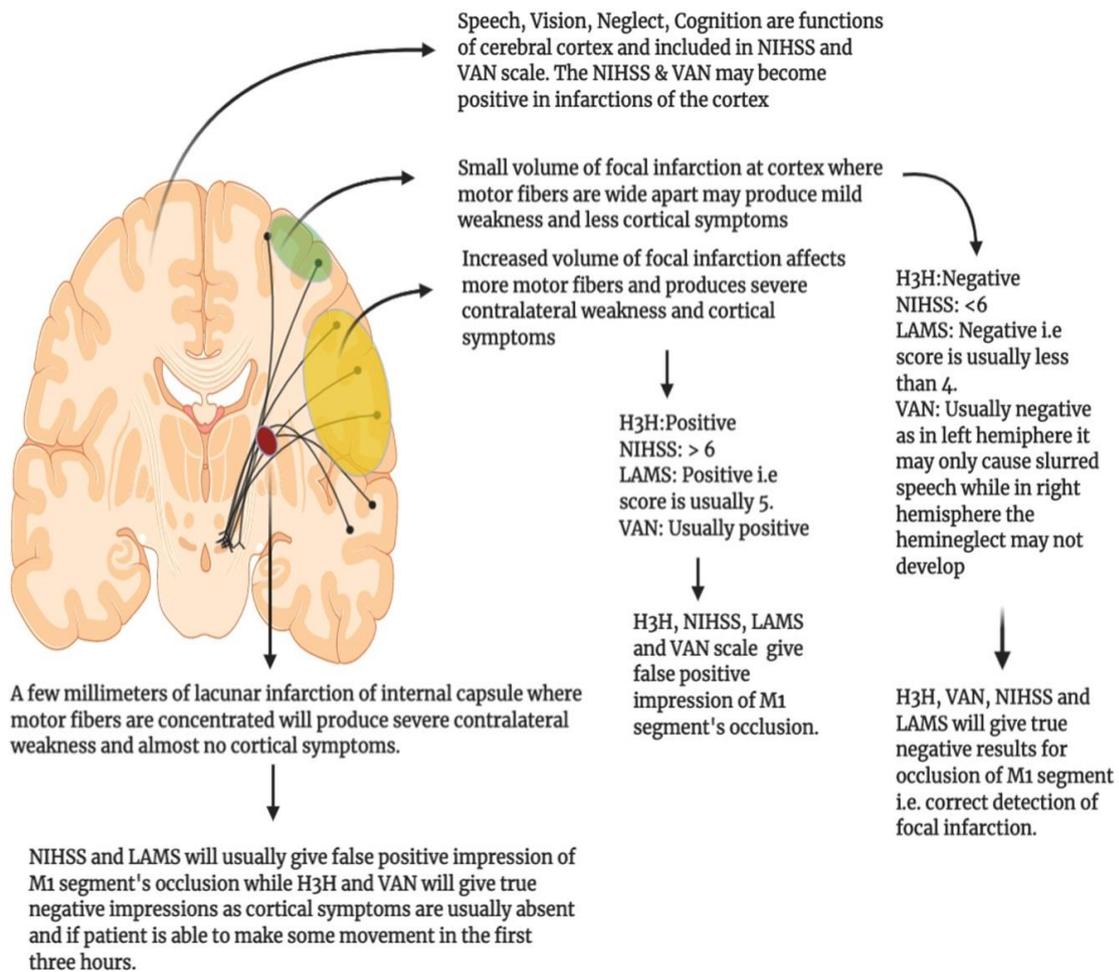


Figure 6. Effects of volume and location of focal infarction on the specificities of H3H, NIHSS, LAMS and VAN scale (*H3H; Hemiplegia in the first three hours; *NIHSS; National Institute of Health Stroke Scale; *LAMS; Los Angeles Motor Scale; *VAN; Vision, Aphasia, Neglect Scale).

In a future study, we would like to determine the performance of H3H scale on CT perfusion imaging of the brain for the distal segments of MCA aka the distal M1 and M2 segments, in patients which undergo prehospital triage for a suspected anterior circulation's ischemic stroke in the first three hours of symptoms.

As a conclusion, the territory of the MCA is the most common site of ischemic infarctions. The H3H scale i.e. hemiplegia in the first three hours of symptoms is a novel time-dependent clinimetric tool. It's quick, accurate and reliable than other scales like NIHSS, LAMS and VAN in predicting occlusion of M1 segment of the MCA. The scale reduces the time to diagnose the large vessel occlusion and it's also convenient for the technical staff in the prehospital triage of patients.

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Ethics

Ethics Committee Approval: The study was approved by Ethical Committee of DHQ, Teaching Hospital KDA Kohat (Number: 116/K-17, Date: 11.01.2019).

Informed Consent: The authors declared that informed consent was signed by the patients.

Copyright Transfer Form: Copyright Transfer Form was signed by all authors.

Peer-review: Internally peer-reviewed.

Authorship Contributions: Surgical and Medical Practices: SA, Concept: SA, Design: SA, Data Collection or Processing: SA, MS, SFS, AA, FN, MH. Analysis or Interpretation: SA, MS, SFS, AA, FN, Literature Search: SA, MH, Writing: SA, MS, SFS, MH.

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