

THE ROLE OF CLINICAL EVALUATION IN THE ERA OF CEREBRAL REPERFUSION

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ABSTRACT

The role of clinical evaluation in the diagnosis and treatment of acute ischemic stroke remains unclear in current guidelines. The manifestations of stroke are diverse, so that the approach to evaluation and treatment are not the same for each patient. In this article, we review the role of neurological examination in diagnosis and treatment of acute stroke. In particular, the important content includes identification of large vessel occlusions, posterior circulation stroke, intracranial artery stenosis and expansion of the therapeutic window time for patients who are late to hospital.

Key words: cerebral reperfusion, acute stroke

I. INTRODUCTION

Treatment of acute ischemic stroke has made great strides in recent years. Cerebrovascular revascularization with thrombolytic agents and intraarterial thrombectomy has been shown to improve the function of patients with acute stroke and has become the standard treatment [1]. The indications of tissue plasminogen activator (tPA) and mechanical thrombectomy are quite simple, mainly based on the time window, the severity of clinical symptoms relied on NIHSS, imaging studies and the exclusion of contraindications [1].

However, the manifestations of stroke are diverse and not the same for every patient. In the era of cerebral reperfusion, shortening the time to recanalization becomes the top goal. In order to do this, a quick and accurate clinical evaluation is needed to determine whether or not large vessel

occlusions, posterior circulation stroke and whether intracranial arterial stenosis is underlying cause. By answering these key questions, emergency, stroke physicians and interventionalist can provide optimal strategies to shorten the duration of treatment with final aim to improve patient outcome.

II. THE ROLE OF EARLY IDENTIFICATION STROKE TYPES TO MAKE TIMELY DECISIONS

2.1. Large vessel occlusion

What is the role of early LVOs identification?

Large vessel occlusions (LVOs), variably defined as blockages of the proximal intracranial anterior and posterior circulation. Commonly refractory to intravenous tissue plasminogen activator (tPA), LVOs place large cerebral territories at ischemic risk and cause high rates of morbidity and mortality

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without further treatment. Over the past few years, an abundance of high-quality data has demonstrated the efficacy of endovascular thrombectomy for improving clinical outcomes in patients with LVOs, transforming the treatment algorithm for affected patients [2,3].

Early identification of patients with suspected LVOs in the EDs can help to triage and provide accurate and appropriate treatment. In particular, in low-resource settings, performing brain angiography for all patients with acute stroke seems to be infeasible [4]. Therefore, screening clinically can be an economic benefit as well as reducing the workload for healthcare workers. In facilities that have not been able to implement the intervention, patients can be immediately transferred to thrombectomy-capable centers.

In the ED, under certain circumstances when identifying or suspecting LVO after a excluding brain hemorrhage by NCCT, the physician may contact the interventionalist in advance or send patients straight to the Angio suite, without providing or providing tPA in the Angio suite. This will help shorten the time to recanalization. In some places, stroke patients admitted to the hospital

with highly clinical suspicion of LVO are referred directly to the Cath lab (without NCCT to rule out hemorrhage) [5].

How to identify LVOs clinically?

The most common clinical scale for stroke is the NIHSS. A number of cut-off points has been introduced with the purpose of predicting LVOs, but its sensitivity and specificity are still low [6].

A case of small vessel occlusion in the internal capsular or basilar pons territory can result in stroke with higher than 8-point NIHSS with complete limb paralysis and severe dyspnea. Symptoms caused by cortical damage such as aphasia, neglect, gaze palsy or visual field deficit are associated with LVOs. Based on the nature of the above symptoms associated with the occurrence of conditions such as atrial fibrillation or valvular heart disease, a number of scales have been proposed by many authors to predict the possibility of LVOs with higher sensitivity and specificity (Table 1).

However, just by comprehending the vascular neuroanatomy, the clinician can quickly identify LVOs. In addition, if the symptoms are subtle and difficult to detect, it may require an experienced neurologist to identify.

Table 1: Clinical scales to detect large vessel occlusions [7 - 12]

	No. of Pts	Components	SEN %	SPEC %
3I-SS	171	Level of consciousness, gaze deviation, motor function	67	92
FAST-ED	727	Facial palsy, arm weakness, speech changes, gaze deviation, neglect	60	89
RACE	357	Facial palsy, motor function, gaze deviation, aphasia, agnosia	85	68
PASS	3127	Level of consciousness, gaze deviation, arm weakness	66	83
VAN	62	Arm weakness, visual disturbance, aphasia, neglect	100	90
GAI2AA	259	Gaze deviation, aphasia, neglect, arm weakness, atrial fibrillation	91	81

2.2. Extending therapeutic window for late presenting patient

Mechanism of reperfusion therapy is to reestablish blood flow to the ischemic penumbra where viable cells can be salvage and restore function. The selection of patients is to choose those who have large penumbra areas compared to infarction core. The volume of penumbra will gradually decrease over time. Large studies have established treatment window for intravenous tPA and mechanical thrombectomy 4.5 hours and 6 hours, respectively.

Infarct core can be identified on MRI. If the clinical symptoms of the patient are severe but the infarction core is small, then the penumbra will be large. This is the fundamental of treatment window expansion for late presenting patient. In 2018, DAWN and DEFUSE 3 are two RCTs published to expand the time window of treatment for LVO patients coming late [13,14].

DEFUSE 3 using a high-standard modern perfusion imaging is not available in many centers. Meanwhile, DAWN uses clinical and MRI mismatch as criteria which is more readily available. Therefore, for patients who are late, if NCCT is not shown hypodensity, adequate clinical examination is needed to assess whether the patient has LVO or not to order emergency MRI.

The visible infarction region on the MRI is an irreversible necrotic area. If the patient has severe clinical manifestations that cannot be explained by an MRI lesion, there could be a salvageable tissue. Therefore, the localization of lesions may be of value in selection as well as prognosis of patients for thrombectomy. According to this argument, instead of selecting patients by the volume numbers according to the MRI study, this can be based on this. The fact that there has been some analysis indicates that many patients may benefit even if the volume exceeds DAWN's selection criteria [15,16].

2.3. Posterior circulation stroke

The presentation of posterior cerebral stroke (PCS) is quite vague and varied especially at the beginning, a patient with posterior circulation stroke may still have 0-point NIHSS although the symptom can cause significant disability [17]. As a result, the rate of misdiagnosis of stroke in posterior circulation in the emergency department is double that of the anterior circulation (37% and 16%) [18]. If not diagnosed in time, PCS can lead to severe outcomes [19].

It is not easy to diagnose a case of PCS, the first is to identify the suspected symptoms, the key here is establishing an abrupt onset of symptoms, awareness of the nonspecific presentations and consideration of basilar stroke in altered patients [20]. Then evaluate more carefully and order the appropriate imaging study [21,22].

However, in terms of imaging, the MRI with DWI can miss 12% to 18% case of PCS. For those with small strokes, the false-negative rate even reaches 53%. [22]. Meanwhile, physical examination using HINTS (head impulse test, nystagmus and test of skew) was 100% sensitive and 96% specificity in differentiating neuritis from stroke [21].

Dizziness is a common reason for the ED admission and is also an independent risk factor for misdiagnosis [18]. Because these symptoms are so common, even the small fraction of misdiagnosed patients translates into a large absolute number. Recent evidence suggests that the time-honored "symptom quality" approach to dizziness (i.e., "what do you mean, dizzy?") is flawed. Despite a weak evidence base, this approach has been the predominant paradigm for decades; an approach based on "timing and triggers" is more evidence-based [23,24]. Systematically performing a neurologic examination that targets the visual fields, cranial nerves, and cerebellar function including gait is one strategy to reduce misdiagnosis in these patients.

ATTEST: Diagnostic approach to the acutely dizzy patient

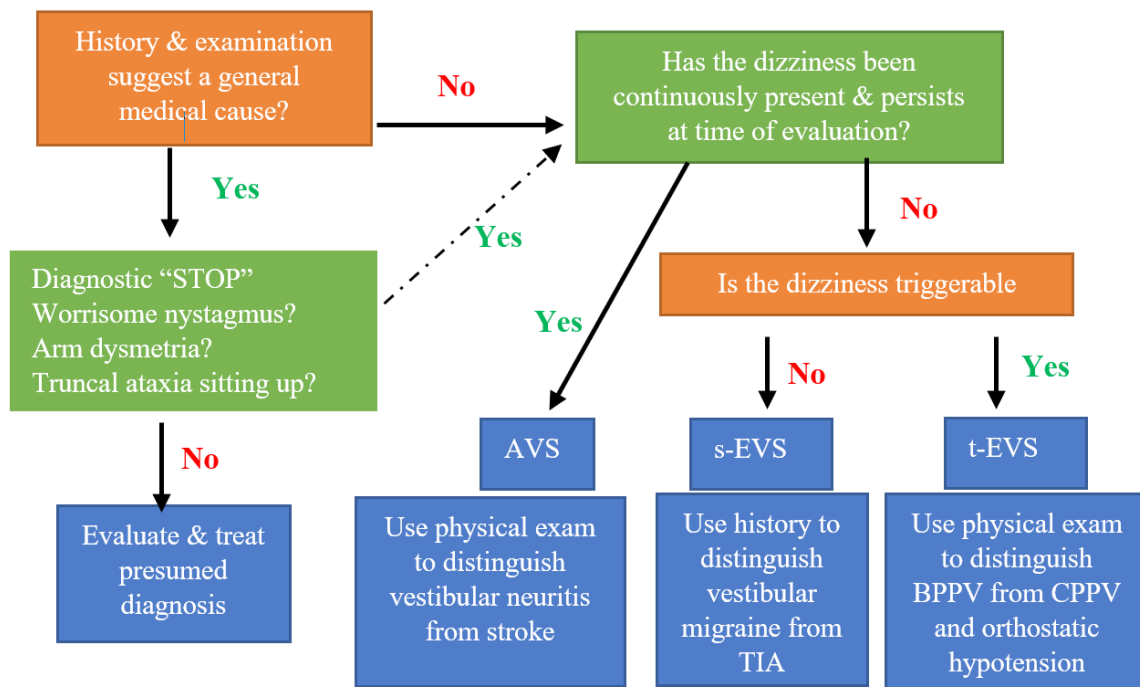


Figure 1: Diagnostic approach to the acutely dizzy patient [23]

ATTEST = A, associated symptoms; TT, timing and triggers; ES, examination signs; and T, additional testing as needed; AVS = acute vestibular syndrome; BPPV = benign paroxysmal positional vertigo; CPPV = central paroxysmal positional vertigo; s-EVS = spontaneous episodic vestibular syndrome; t-EVS = triggered episodic vestibular syndrome; TIA = transient ischemic attack.

III. INTRACRANIAL ATHEROSCLEROSIS - RELATED LARGE VESSEL OCCLUSION

The development of modern imaging has helped to identify underlying etiology of ischemic stroke. However, a complete diagnostic workup can be a waste of time. Clinical examinations offer suggestions that can help quickly identify the cause for an appropriate treatment strategy.

Acute intracranial atherosclerosis-related large vessel occlusion (ICAS - LVO) has high failure rate of mechanical thrombectomy and is often required specific rescue treatments. Thus this will prolong the procedure time leading to a poor outcome [25]. Therefore, determining whether there is intracranial atherosclerotic disease in order to offer a optimal treatment strategy is a key factor for improving treatment outcomes [26].

A typical case of ischemic stroke due to large vessel disease (including the carotid artery and the intracranial artery) typically has a stepwise clinical course, symptoms appear and recurrent on the same side. The patients usually have other risk factors for atherosclerotic disease such as diabetes, overweight, hypertension, smoking and a history of coronary artery disease and no obvious cause of embolism such as atrial fibrillation or heart valve disease.

IV. ACUTE STROKE DIFFERENTIAL DIAGNOSIS: STROKE MIMICS

The earlier the patient is treated with tPA, the more effective the patient will receive [27]. However, attempts to shorten door-to-needle time may inadvertently prescribe tPA to stroke mimics patients (4.1%) [28]. The most worrying adverse effects of

tPA are of intracerebral hemorrhage and angioedema. Intracerebral hemorrhage can still occur in stroke mimic patients receiving tPA, although this rate is not high (1.2% vs 5.1% in patients with cerebral infarction) [28,29]. Angioedema is seen in 0.5% of patients [29]. Economy is also a problem need to be mentioned if using the drug not in the indication.

The most common types were functional disorder (30.8%), migraine (17.5%) and seizure (14.2%) [28]. Depending on the cause, the clinical picture of stroke patient will vary. Experienced neurologists can quickly identify stroke mimic cases. In general, the manifestations of mimic will not follow vascular neuroanatomy. Gaze palsy, neglect, hemianopia and facial paralysis are not presented in patients with stroke mimic. On the other hand, aphasia not

accompany by weakness is more common in stroke mimic [30].

V. CONCLUSION

Imaging has flourished and has become a powerful tool for stroke physician. However, in the age of cerebral revascularization, clinical examination and neurolocalization play an important role in quickly detect cases of LVO, PCS, and ICAS-LVO as well as rule out stroke mimics.

In 2005, Shafqat stated that “the advent of modern neuroimaging has liberated neurology from the shackles of cerebral localization” [31]. This statement is true. However, until 2020, clinical value is still there and perhaps imaging will never replace the role of neurological examination and neurolocalization.

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