

## Prevalência e Caracterização de *Stroke Mimics* numa Unidade de Acidentes Vasculares Cerebrais

### *Prevalence and Characterization of Stroke Mimics in a Stroke Unit*

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#### Resumo

**Introdução:** *Stroke mimics* são doenças não vasculares que simulam o acidente vascular cerebral (AVC). A sua prevalência varia com a diferenciação dos clínicos, critérios de admissão e recurso a meios complementares de diagnóstico. Os autores pretendem caracterizar os *stroke mimics* numa Unidade de AVC (UAVC), integrada num departamento de medicina dum hospital universitário.

**Material e Métodos:** Estudo observacional, descritivo e retrospectivo dos doentes admitidos numa UAVC durante 26 meses. Considerou-se *mimic* quando os dados clínicos/imagiológicos sustentavam uma causa não vascular para o défice neurológico.

**Resultados:** Coorte 367 doentes, idade mediana 76 anos, 12% *mimics*. Os diagnósticos principais foram: doenças somatoformes, vertigem periférica, doenças metabólicas, síncope, Munchausen, tumores intracranianos, epilepsia e malformação de Chiari. Os *mimics* eram mais novos, mais mulheres, tinham menor défice neurológico à admissão, menos fibrilhação auricular e doença cerebrovascular ( $p < 0,05$ ). Fatores de risco vascular não foram critério de distinção entre *mimics* e AVC.

**Conclusão:** Contrariamente ao que se poderia pensar o internamento de *stroke mimics* numa UAVC não é residual (12%). Alguns destes casos corresponderam a patologia grave, necessitando de intervenção urgente.

**Palavras-chave:** Acidente Vascular Cerebral; Doenças Somatoformes; Doenças Vestibulares; Serviço de Urgência Hospitalar

#### Introduction

The diagnosis of stroke sometimes presents a challenge for emergency clinicians because non-vascular clinical syndromes can also present with focal neurological deficits.<sup>1</sup> An estimated 3–30% of patients with suspected stroke in a hospital emergency room acquire a diagnosis of stroke mimic. The prevalence of a mimic is disparate and depends on whether patients are seen in an emergency context, in a hospital

#### Abstract

**Introduction:** *Stroke mimics* are non-vascular disorders that simulate the presence of stroke. Its reported prevalence varies according to clinical differentiation, admission criteria and resource to complementary means of diagnosis. The authors pretend to characterize stroke mimic admitted to a stroke unit, integrated in an internal medicine department of a university hospital.

**Material and Methods:** An observational, descriptive and retrospective study of patients over a 26-month period. *Stroke mimics* were considered whenever clinical and/or radiological data supported a non-vascular cause of the neurological deficit.

**Results:** From a cohort of 367 patients, with a median age of 76 years old, 12% were classified as *stroke mimics*. The main diagnoses were: somatoform disorder, peripheral vertigo, metabolic diseases, syncope, Munchausen syndrome, intracranial tumors, epilepsy and Chiari malformations. *Mimics* were generally younger, more often women, had a lower neurologic deficit on admission, as well as lower rates of previous known atrial fibrillation and cerebrovascular disease ( $p < 0.05$ ). Vascular risk factors were not a criterion of distinction between *mimics* and stroke.

**Conclusion:** Contrary to what we might expect, there is a substantial prevalence of *stroke mimics* within a stroke unit (12%). The nature of these *mimics*, some of which require urgent intervention, can be used to better inform emergency clinicians and plan for alternative interventional pathways.

**Keywords:** Emergency Medical Services; Somatoform Disorders; Stroke; Vestibular Diseases

ward or during fibrinolysis.<sup>1–3</sup> Epilepsy, migraine, psychogenic disorders, peripheral neuropathies and toxic/metabolic causes are among the most frequent stroke mimics.<sup>2–6</sup>

Early distinction between acute stroke and a mimic avoids inappropriate fibrinolysis and subsequent treatment risks, despite their infrequent occurrence.<sup>3,7</sup> Even amongst those patients unsuitable for fibrinolysis, considerable clinical time needs to be invested determining whether the patient merits admitting or discharging. Emergency department examinations and associated investigations are often initiated by non-neurologists such as general physicians or internists. Additionally, these emergency clinicians may encounter serious

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**Table 1:** Comparative characteristics between mimics (n = 42) and non-mimics (n = 310)

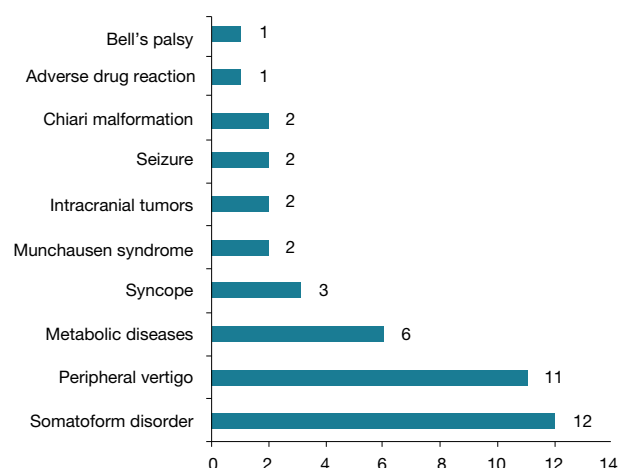
	Mimics	Non-mimics	p value (df)
Length of stay (days) median [Q1-Q3]	5.0 [3.0-8.0]	7.0 [5.0-10.0]	0.001 <sup>†</sup> (78.2)
Age median [Q1-Q3]	66.5 [56.5-75.0]	77.0 [68.0-83.0]	0.000 <sup>†</sup> (47.7)
NIHSS at admission	1.36 ± 1.2	5.71 ± 5.64	0.000 <sup>‡</sup> (40.5)
Female / Male gender	71.4% / 28.6%	51.9% / 48.1	0.017* (1)
Atrial fibrillation	2.4%	21.4%	0.003* (1)
Cerebrovascular disease	19%	37.7%	0.017* (1)
Vascular risk factors	90.5%	92.6%	NS
Normal 24h-Holter	60.5%	39.9%	0.027* (2)
Normal cCT	19%	9.1%	0.000* (4)
Normal cMRI	53%	6.9%	0.000* (1)

Q1: Quartil 1; Q3: Quartil 3; cCT: Cranial CT; cMRI: Cranial MRI; CVD: Cerebrovascular disease; <sup>†</sup>Mann-Whitney U test; <sup>\*</sup>Chi-square test; <sup>‡</sup>Student t-test; NS: Not significant; df: Degree of freedom

**Table 2:** Comparison of investigation requests between mimics (n = 42) and non-mimics (n = 310)

Investigation	% mimics	% non-mimics	p value* (df)
2nd cCT	7.1	24.3	0.012 (1)
cMRI	38.1	9.0	0.000 (1)
CVD	54.8	64.8	NS
TCD	52.4	64.2	NS
TTE	38.1	68.4	0.000 (1)
TEE	0	3.5	NS
24h-Holter	21.5	24.5	NS
Prothrombotic study	2.4	4.0	NS

Legend: cCT: Cranial CT; cMRI: Cranial MRI; CVD: Carotid and vertebral Doppler; NS: Not significant; TCD: Transcranial Doppler; TEE: Transesophageal echocardiography; TTE: Transthoracic echocardiography; df: Degree of freedom. <sup>\*</sup>Chi-square test

**Figure 1:** The number of diagnosed mimics by etiology

neurological diseases requiring urgent attention and will therefore need to have a high level of clinical suspicion for or against a stroke mimic before engaging specialist input.<sup>8</sup> Finally, investigations into the suspected cerebrovascular etiology may involve unnecessary costs.

In Portugal, little is known about the etiologies and prevalence of mimics. In 1998, Ferro *et al* detected 9% mimics from 237 patients with neurological deficits in an emergency department. In that study, etiologies comprised acute neurological, psychiatric or medical diseases.<sup>8</sup> Hemmen *et al* found that amongst stroke team activations, 26% were for mimics, which nevertheless required urgent intervention.<sup>9</sup> Given the wide prevalence rates of mimics we aimed to study the prevalence and characterization of stroke mimics within a stroke unit of a medical department at a university public hospital.

## Material and methods

Study design consisted on an observational, descriptive and retrospective study of all patients consecutively admitted to a stroke unit of an internal medicine department at a university public hospital. The study was conducted between January 2011 and January 2013. Emergency department (ED) clinicians were responsible for admission of patients to the stroke unit. In the ED, patients were seen by a medical specialist and general specialty internists and, occasionally, by neurologists when the "Via verde AVC" was activated (a national program for the prevention and control of stroke) or during the daytime, if requested. The final diagnosis was defined as that most likely at discharge. The final diagnosis was agreed by both the internist and the vascular neurologist, based on the results of neuroimaging and other additional diagnostic tests. Each patient was classified as stroke or mimic. A diagnosis of mimic was made when the clinical and laboratory data, and/or imaging data supported a non-vascular cause for the symptoms presented.

Measured variables included demographic characteristics

**Table 3:** Comparative analysis of stroke mimics across multiple studies<sup>1-4,9</sup>

Study % Mimics (Mean age)	Main etiologies	Characteristics
Hemmen <i>et al</i> , USA, 2008 n = 411 19% (65.0 ± 17.6)	1. Prior deficit 2. Hypotension 3. Seizures 4. Poisoning	Nil defined
Vroomen <i>et al</i> , The Netherlands, 2008 n = 637 5%	1. Migraine with prolonged aura 2. Conversion disorder 3. Partial epilepsy 4. Hypoglycemia	Nil defined
Tobin <i>et al</i> , Ireland, 2009 n = 206 22%	1. Encephalopathy 2. Seizures 3. Syncope 4. Migraine	DBP < 55 mmHg lack of CVD
Guillan <i>et al</i> , Spain, 2012 n = 621a 2.4% (53.7 ± 16.0)	1. Somatoform disease 2. HaNDL syndrome 3. Glial tumor 4. Encephalitis	Younger lower NIHSS lack of T2DM
Alves <i>et al</i> , Portugal 2013 n = 367 12% (64.8 ± 14.6)	1. Somatoform disease 2. Peripheral vertigo 3. Metabolic disease	Decreased LOS younger female Nil AF or CVD
Merino <i>et al</i> , USA, 2013 n = 8194 30%	Nil defined	Younger female African American lack of vascular risk factors

aUnderwent thrombolysis. Legend: AF: Atrial fibrillation; CVD: Cardiovascular disease; DBP: Diastolic blood pressure; HaNDL: Headache and neurologic deficits with cerebrospinal fluid lymphocytosis; LOS: Length of stay; NIHSS: NIH stroke scale; T2DM: Type II diabetes mellitus

(age, gender), the severity of neurological deficit (NIH stroke scale (NIHSS)), length of stay and the presence of comorbidities including vascular risk factors (hypertension, obesity, smoking, dyslipidemia, and type II diabetes mellitus), known history of atrial fibrillation (AF) and cerebrovascular disease (CVD). Further analysis of the data set included comparison of the use of complementary diagnostic investigations (CDE). These included cranial computed tomography (cCT), cranial magnetic resonance imaging (cMRI), transcranial and carotid-vertebral Doppler ultrasound, transthoracic (TTE) and transesophageal echocardiography (EET), 24h-Holter electrocardiography and measurement of prothrombotic factors.

Data analysis was performed using SPSS version 21.0 (IBM Corp., Armonk, NY). A statistical analysis was made using the Mann-Whitney and student T-test for continuous variables, and the chi-square test for categorical variables. Statistical significance was set at  $p < 0.05$ .

## Results

A total of 367 patients were admitted to the stroke unit through the ED. Their median age was 76 years [66–83] and 46% were male. At admission to the ED, 96% were diagnosed as having ischemic stroke (n = 352) and 4% as having hemorrhagic stroke (n = 15). The proportion of mimics of amongst ischemic stroke was 12%. Of the 67 patients admitted to the ED for probable posterior circulation infarct, 15% turned out to be mimics (peripheral vertigo). None of the patients diagnosed with mimic

underwent fibrinolysis.

The most common diagnoses in the group of mimics were somatoform disorders (also known as somatic symptom disorders, 29%), peripheral vertigo syndrome (26%) and metabolic disorders (14%). Amongst all patients with suspected ischemic stroke, the metabolic disorders of hyponatremia, hypo/hyperglycemia, hepatic encephalopathy and post-infection deterioration accounted for 3.4%, 3.1% and 1.7%, respectively (Fig. 1).

Analysis of mimic versus non-mimic patients showed that the former were, on average, 10 years younger, more often female, had a milder neurological deficit at admission (NIHSS 1.36 vs 5.71), had a shorter hospitalization period (median 5.0 [3.0–8.0] vs 7.0 [5.0–10.0] days), had less atrial fibrillation (2.4% vs 21.4%) and fewer previously known cerebrovascular diseases (19% vs 37.7%) (Table 1). The presence of at least one vascular risk factor was not a criterion for distinguishing between mimic and stroke patients. In terms of investigations, 24h-Holter, cCT, and cMRI were more frequently normal in patients with a final diagnosis of mimic (Table 1).

Amongst CDEs, TTE requests and repeat cCTs were requested less frequently in mimics than stroke patients. Cranial MRI was more frequently performed in patients with a final diagnosis of mimic (Table 2).

## Discussion

The prevalence of stroke mimics varies widely in the literature. The variability comes principally from the differences in

**Table 4:** Comparative analysis mimics versus cerebrovascular disease. Adapted from<sup>5,7,11</sup>

	TIA	Migraine	Seizure	Syncope	Somatoform disease	Peripheral vertigo
Demographic	<ul style="list-style-type: none"> <li>• Old age</li> <li>• Vascular risk factor</li> <li>• Males &gt; females</li> </ul>	<ul style="list-style-type: none"> <li>• Young age</li> <li>• Females (70%)</li> </ul>	<ul style="list-style-type: none"> <li>• Any age</li> </ul>	<ul style="list-style-type: none"> <li>• Any age (young &gt; old)</li> <li>• Females &gt; males</li> </ul>	<ul style="list-style-type: none"> <li>• Young age</li> <li>• Females &gt; males</li> </ul>	<ul style="list-style-type: none"> <li>• Young age</li> </ul>
Neurological symptoms	<ul style="list-style-type: none"> <li>• Negative symptoms, initial maximum intensity</li> <li>• LOC is unusual</li> </ul>	<ul style="list-style-type: none"> <li>• Positive symptoms</li> <li>• Visual symptoms are common</li> <li>• Symptoms can evolve</li> <li>• LOC very rare</li> </ul>	<ul style="list-style-type: none"> <li>• Positive symptoms</li> <li>• LOC and amnesia can occur</li> <li>• Negative symptoms (Todd's palsy) may persist for days</li> </ul>	<ul style="list-style-type: none"> <li>• Sensation of fainting</li> <li>• Vision changes</li> <li>• Hearing changes</li> <li>• LOC</li> </ul>	<ul style="list-style-type: none"> <li>• Isolated sensory symptoms</li> <li>• Symptoms are inconsistent</li> </ul>	<ul style="list-style-type: none"> <li>• Nystagmus: combined, horizontal and torsional</li> <li>• Inhibited by fixing the gaze; unchanged on contralateral side</li> </ul>
Time	<ul style="list-style-type: none"> <li>• Abrupt onset</li> <li>• Duration: mins</li> <li>• Can last for days/weeks</li> </ul>	<ul style="list-style-type: none"> <li>• Duration 20–30 min (or longer)</li> <li>• Can last for years (frequency decreases with age)</li> </ul>	-	<ul style="list-style-type: none"> <li>• Seconds</li> </ul>	<ul style="list-style-type: none"> <li>• Tendency to be recurrent and stereotyped</li> </ul>	<ul style="list-style-type: none"> <li>• Sec/min to hours/days</li> <li>• Disappears in days</li> </ul>
Associated symptoms	<ul style="list-style-type: none"> <li>• Headache in 27% of cases</li> </ul>	<ul style="list-style-type: none"> <li>• Nausea, vomiting, photophobia, phonophobia</li> </ul>	<ul style="list-style-type: none"> <li>• Tongue bite</li> <li>• Sphincter incontinence</li> <li>• Muscle pain</li> <li>• Headache</li> </ul>	<ul style="list-style-type: none"> <li>• Sweating</li> <li>• Pale</li> <li>• Nausea</li> <li>• Quick recovery</li> </ul>	<ul style="list-style-type: none"> <li>• Emotional or psychosocial stress</li> <li>• Anxiety - Hoover sign (principle of synergistic contraction)</li> </ul>	<ul style="list-style-type: none"> <li>• Loss of hearing</li> <li>• Headache</li> <li>• Tinnitus</li> <li>• Severe imbalance</li> <li>• Prior viral infection</li> <li>• Precipitated by sudden head movements</li> </ul>

LOC: Loss of consciousness

study settings, expertise of medical staff and the availability of additional diagnostic tests (Table 3).<sup>1–3</sup> In the present study, the prevalence of mimic patients hospitalized at a stroke unit over a period of 26 months was 12%. While this prevalence was higher than that found in a previous study using similar methodologies,<sup>2</sup> it was still lower than that described elsewhere.<sup>1,4,9</sup>

Patients analyzed in the present study were about one decade older than those patients included in previous studies.<sup>1,3,9</sup> This difference may be related to the fact that the stroke unit participating in the present study is a part of an Internal Medicine Service, which is without exclusion criteria for admission, and that doctors external to the stroke unit admitted patients from the ED. Given that all patients with acute stroke benefit from treatment within a specialized care unit, age should not be a criterion for exclusion.<sup>10</sup>

Amongst the mimics, some were serious diseases that benefited from hospitalization and quick medical intervention. However, as with previous studies,<sup>2,3</sup> functional disorders, including somatoform disorders, factitious disorders and feigning accounted for most mimic diagnoses. To expedite diagnosis and avoid inadequate therapy, doctors should be aware of some of the specific characteristics of these mi-

mics and some of the maneuvers used to detect them (e.g. altered sensation in the prone position and the Hoover test).

In previous studies, benign paroxysmal positional vertigo (BPPV) has only comprised a small fraction of mimics (4–7%),<sup>5,7</sup> including a Portuguese study by Ferro *et al* in which there was only one diagnosis of BPPV.<sup>8</sup> In the present study there was a high prevalence of acute vestibular disorders that were initially interpreted in the ED as posterior circulation stroke, highlighting the inherent diagnostic difficulties distinguishing peripheral from central vertigo. Table 4 provides a list of features that may help distinguish the most common mimics from stroke.<sup>5,7,11</sup>

The demographic and clinical characteristics associated with mimics described in the current study are consistent with those previously reported (Table 3). While analysis did not reveal the presence of one particular vascular risk factor that could distinguish between stroke and mimic groups, the absence of atrial fibrillation or previously known cerebrovascular disease was positively associated with mimics. Furthermore, 91% of mimics in the study had at least one known vascular risk factor upon admission, which may be related to the age of these patients. Similarly, only 19% of the cCTs in the mimic group were normal, with most displaying sequelae alterations.

Stroke mimics are associated with episodes of non-vascular neurological deficit, whose targeted diagnosis and treatment are important. In our study, stroke mimics were more often found in younger patients, of female gender, with no prior atrial fibrillation or cerebrovascular disease. Somatoform disorder and acute vestibular disorders comprised most mimics, pointing towards a difficulty differentiating peripheral vertigo versus central vertigo. Ultimately, the results highlight a cluster of neurological conditions that can be targeted for future ED training and diagnostic awareness, leading to less futile intervention and better patient outcomes. ■

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