

## Long-term follow-up of acute functional stroke mimic in comparison to mild acute ischaemic stroke

### INTRODUCTION

Each year many patients are admitted to the emergency department with a suspicion of acute ischaemic stroke (AIS). There are several conditions that can present with acute stroke-like symptoms, of which the most common are seizures, migraine and functional disorder. The latter are called functional stroke mimics (FSM). While the outcome of patients with AIS has extensively been studied, little is known about the outcome of FSM. Short-term follow-up studies in acute FSM have shown that about 80% of patients with FSM still reported symptoms after 2 months,<sup>1</sup> but long-term follow-up studies are lacking. We therefore compared the long-term outcome in patients with FSM with patients diagnosed with mild AIS.

### METHODS

#### Patient selection

This single centre retrospective cohort study was performed in the University Medical Centre Groningen. Patients with FSM and AIS who presented between January 2016 and December 2018 were identified from a local patient registry. Inclusion criteria were: (1) suspicion of AIS by the ambulance; (2) age between 18 and 80 years; (3) mild–moderate symptoms (National Institutes of Health Stroke Scale (NIHSS) ≤10); (4) patients with AIS treated with intravenous thrombolysis; and (5) functionally independent at 3 months after admission (Modified Ranking Scale [mRS] 0–2). Final diagnosis was made by a vascular neurologist based on clinical information and imaging.

Participants were approached 13–42 months after admission by mail to complete the questionnaires. Patients were also given the option to only rate their change in symptoms and severity of symptoms by telephone.

#### Outcomes measures

Participants rated their change in symptoms compared with admission and severity of symptoms at the time of follow-up using the Clinical Global Impression-Improvement (CGI-I) scale and the CGI-Severity (CGI-S) scale. The

RAND 36-item Health Survey (RAND-36) was used to measure general health.

### Statistical analyses

Groups of patients with FSM and AIS were compared using the Pearson  $\chi^2$  test for dichotomous data and the Mann-Whitney U test for continuous data. A two-sided p value of 0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics (V.23).

### RESULTS

#### Baseline characteristics

Of the total of 326 patients that we approached, 116 patients agreed to participate, of whom 38 had been diagnosed with FSM and 78 with mild AIS. Four patients in the FSM group and three in the AIS group only answered CGI-I and CGS-S questions by telephone.

Follow-up time was longer in patients with FSM (median months 28 (IQR 24–35) vs 25 (IQR 21–29);  $p=0.002$ ). Patients with FSM were younger (median years 53 (IQR 45–66) vs 66 (IQR 55–72);  $p=0.001$ ) and more often women (25 (66%) vs 26 (33%);  $p=0.001$ ). The

baseline median NIHSS at admission was lower in patients with FSM (1 (IQR 0–3) vs 4 (IQR 3–5);  $p<0.001$ ).

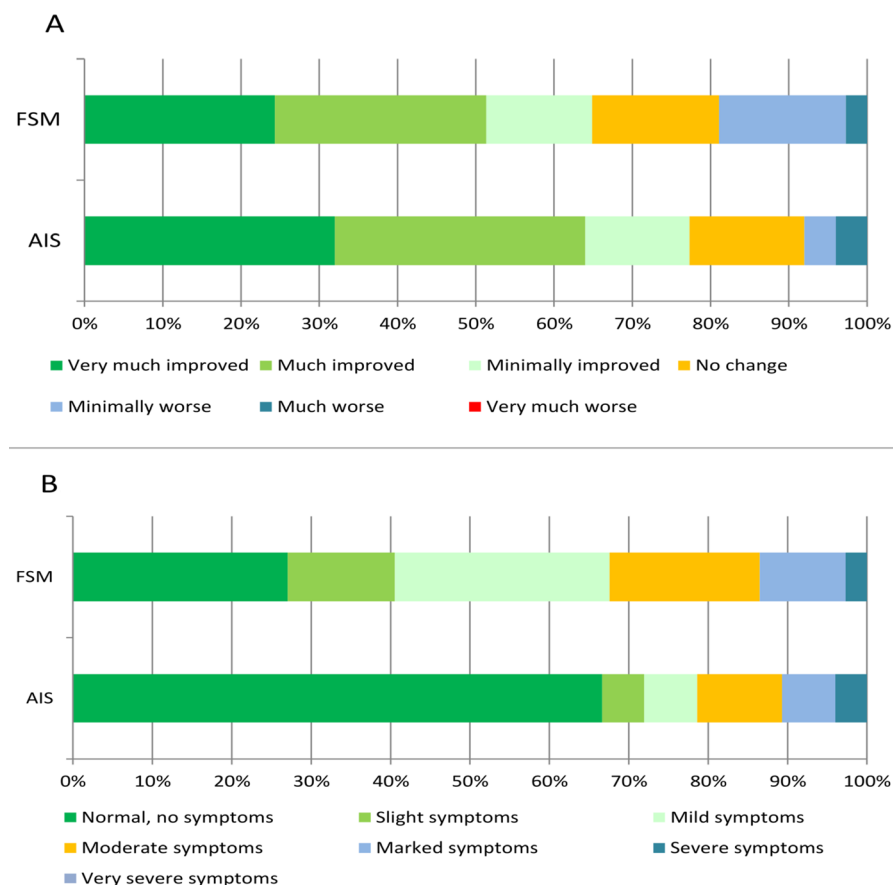
#### Symptom severity and change

The degree of improvement was similar in both patients groups (median 2 (IQR 2–4) vs 2 (IQR 1–3);  $p=0.155$ ): 65% of patients with FSM and 77% of patients with AIS reported some improvement. In contrast, 19% of patients with FSM and 8% of patients with AIS reported worsening of symptoms (figure 1A).

Patients with FSM had more severe symptoms at follow-up than patients with AIS (median 3 (IQR 1–4) vs 1 (IQR 1–3);  $p=0.001$ ). In total, 27% of patients with FSM and 67% of patients with AIS reported no symptoms at follow-up (figure 1B).

#### Health-related quality of Life

Patients with FSM scored significantly lower on several subdomains of the RAND-36 at follow-up: social functioning (median 56 (IQR 50–75) vs 75 (IQR 63–88);  $p=0.016$ ), mental health (median 66 (IQR 57–80) vs 76 (IQR 68–88);  $p=0.027$ ), vitality (median 45 (IQR



**Figure 1** (A) Clinical global impression—improvement scale (% within group). (B) Clinical global impression—severity scale. AIS, acute ischaemic stroke; FSM, functional stroke mimics.

35–55) vs 60 (IQR 41–69);  $p=0.003$ ), bodily pain (median 45 (IQR 45–67) vs 78 (IQR 55–100);  $p=0.002$ ) and general health perceptions (median 40 (IQR 25–59) vs 55 (IQR 35–65);  $p=0.008$ ). There were no significant differences on other subdomains (physical functioning, physical and emotional role limitations).

## DISCUSSION

The self-rated long-term outcome of patients with FSM was worse compared with patients with mild AIS. Although in both groups the symptom improvement was comparable, patients with FSM reported more severe symptoms. Importantly, the burden of FSM was higher compared with mild AIS at long-term follow-up.

The outcome in patients with AIS is comparable to previous studies.<sup>2</sup> In our study, the outcome in patients with FSM is similar to short-term<sup>1</sup> and long-term follow-up in chronic functional weakness.<sup>3</sup>

FSM has a great negative impact in several domains of quality of life, which is significantly worse compared with mild AIS. The reductions in quality of life domains in patients with AIS and in patients with FSM found in our study were comparable to those found in earlier studies.<sup>1,4</sup> Therefore, FSM has an impact on quality of life in patients that is similar to or worse than that of mild AIS.

The prognosis of FSM can be considered poor, given the 80% with persistent symptoms and its major impact on quality of life.<sup>3</sup> This highlights the importance of follow-up care in this patient group. Currently, the pathways of care are limited to physiotherapy and psychological interventions. Stepped care with rehabilitation services as next step is limited,<sup>5</sup> while prevention of long-term chronic functional neurological symptoms is important given the burden it places on the individual and society.<sup>3</sup> Long-term prospective studies are required to gain more insight

into factors influencing the outcomes of FSM and effects of current treatments for FSM.

To our knowledge this is the first study that compared long-term follow-up of patients with FSM and AIS. All measures were self-reported, which adequately reflects the actual patient experiences. On the other hand, self-reported questionnaires are limited by subjectivity. Limitations to the study were the retrospective approach and the absence of questionnaire data at presentation. This might lead to recall bias, since change of symptoms is rated based on memory.

## CONCLUSION

Patients with FSM have more persistent symptoms after 2 years compared with patients with mild AIS. They also have a worse quality of life. Our findings suggest a debilitating long-term disorder in these patients that requires more attention.

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