Acta neurol. belg., 2008, **108**, 135-138

Original articles

Stroke-related seizures in patients with a partial anterior circulation syndrome

J. De Reuck[1,3], G. Van Maele[2], C. Cordonnier[3] and D. Leys[3]

Departments of [1]Neurology and [2]Medical Statistics, University Hospital, Ghent, Belgium ; Department of [3]Neurovascular Neurology, University Hospital, Lille, France

Abstract

Background : Partial anterior circulation syndrome (PACS), due to cerebral infarction, is the most common stroke presentation of patients with seizures. This study investigates the characteristics of such patients according to their seizure onset time.

Patients and methods : The characteristics of 151 patients with a PACS and seizures were compared to 310 without seizures. The seizure groups were classified as those of early- (EO), of late- (LO) and of very late-onset (VLO) and those due to recurrent infarcts (RI).

Results : Temporal lobe infarction is the main risk factor for developing seizures ($P < 0.02$). Seizures are responsible for increased dependency except in patients with those of VLO ($P < 0.03$). Patients with EO seizures have the worse outcome ($P = 0.0111$) with a trend of more status epilepticus ($P = 0.066$) but less recurrence ($P = 0.003$). A cardiac-embolic source is more common in patients with seizures due to RI ($P = 0.015$). Post-ictal EEG patterns are significantly different from those in the patients without seizures ($P < 0.001$) except for seizures of VLO.

Conclusions : There are significant differences in the seizure characteristics according to their time of onset.

Key words : Stroke-related seizures ; cerebral infarct ; partial anterior circulation syndrome ; seizure onset ; infarct location ; seizure recurrence ; EEG ; outcome.

Introduction

In the only performed prospective study an overall incidence of stroke-related seizures of 8.9% was found (Bladin *et al.* 2000). This correlates more or less with the 9.8%, observed in the Stroke Unit of the Ghent University Hospital (De Reuck 2007). Although the relative risk is higher in patients with an intracerebral hemorrhage (10.6%), seizures are commonly related to the more frequently occurring ischemic strokes (Bladin *et al.* 2000 ; De Reuck 2007).

Seizures are mainly observed in patients with large cortical infarcts and a severe neurological deficit (Giroud *et al.* 1994 ; Reith *et al.* 1997 ; Bladin *et al.* 2000 ; Arboix *et al.* 2003 ; De Reuck *et al.* 2006a). The infarcts predominate in the temporal and parietal regions (Heuts-van Raak *et al.* 1996 ; De Reuck *et al.* 2008a). Overall, there is no evidence that cardiac-embolic infarcts are more prone to give rise to seizures than thrombo-embolic ones. Only, in patients with seizures due to recurrent strokes a cardiac-embolic source is more frequent (De Reuck *et al.* 2007a). Chronic obstructive pulmonary disease is the only significant "vascular" risk factor for stroke-related seizures (De Reuck *et al.* 2007b).

When using the Oxfordshire Community Stroke Project classification (Bamford *et al.* 1991) the partial anterior circulation syndrome (PACS) appears to be by far the most common stroke presentation (De Reuck *et al.* 2005).

In a paradigm comparable to posttraumatic epilepsy an arbitrary cut point of 2 weeks after stroke onset is considered to distinguish between early- and late-onset seizures (Jennett 1974). Most late-onset seizures occur between 6 and 24 months after stroke, but still some of them appear more lately (De Reuck *et al.* 2008b). Also, some late-onset seizures are the clinical expression of a new stroke (De Reuck *et al.* 2007a).

The present study compares in patients with a PACS the characteristics of those with seizures, according to their onset time and aetiology, to those who remain seizure-free.

Patients and methods

This open observational retrospective study with matched cohort design concerns 151 consecutive patients admitted between 2000 and 2007 to the Department of Neurology of the Ghent University Hospital for seizures related to a PACS.

According to their onset in relation to the stroke, the seizures were subdivided into those of early-onset (EO), of late-onset (LO) (average : 11.5 months), of very late-onset (VLO) (average : 73.0 months) and those due to recurrent infarction (RI).

According to the description of the family or the caregivers the seizures were classified as simple or complex partial, with or without secondary generalization and as primary generalized tonic-clonic,

being aware that most probably the latter were of focal onset with rapid generalization.

For comparison 310 consecutive patients, admitted between 2001 and 2004, with a PACS but without seizures on a follow-up until August 2007, were selected out of a series of 1,444 stroke patients.

All patients were admitted for their ischemic stroke. Patients who developed seizures were readmitted after the single or the last epileptic spell. All patients had a complete cardiovascular work-up, a computed tomography (CT) scan and/or a magnetic resonance imaging (MRI) scan of the brain and other neuroradiological investigations, when necessary. On admission for the stroke, CT scan of the brain was performed in all patients and MRI in 42% of them. In patients with seizures a CT scan was repeated in 89.4% and an MRI in 51.0% of the patients.

In all patients an electroencephalogram (EEG) was performed on a 14-channel Nihon-Koden EEG machine with a 21-electrode combination. The electrodes were placed over the frontal, central and occipital regions in accordance with the international 10-20 system of electrode placement. The EEG was performed within 48 hours after seizure onset in the first group and during the first week after stroke onset in those without seizures.

Age, gender, vascular risk factors, stroke etiology, degree of neurological impairment on admission, assessed with the National Institute of Health Stroke (NIHS) scale (Goldstein *et al.* 1989), and the degree of disability, assessed with modified Rankin scale (mR) (Uyttenbogaart *et al.* 2007) on discharge from the hospital, were compared between the patients with and without seizures. Patients with a mR score of 0 up to 2 were considered as independent, while those with a higher score as dependent ones.

Statistical analysis was performed with the SPSS statistical package (SPSS Inc., version 14.0, Chicago, Ill., USA) (R Development Core Team 2007). Univariate comparisons of unpaired groups were done with Fisher's exact test for categorical data. The non-parametric Mann-Whitney U test was used to compare continuous variables. The significance level was set at $\alpha = 0.05$, two-tailed.

Results

Mean age and gender distribution of the four seizure groups are not significantly different, compared to the non-seizure group. Arterial hypertension is less frequent in the EO ($P = 0.036$) and more in the RI group ($P = 0.026$). There is a trend of a higher incidence of isolated atrial fibrillation in the RI group ($P = 0.076$). Cardiac valve disorders are more observed in the VLO group ($P = 0.034$). Diabetes is significantly more present in the patients with VLO ($P = 0.001$) (Table 1).

Cardiac-embolic strokes are statistically only more common in patients with RI ($P = 0.015$). Although the median NIHS scores on admission for the stroke are not significantly different between the seizure groups and the non-seizure population the median mR score on hospital discharge is worse in the EO group ($P = 0.0111$). After the seizures significantly fewer patients remain independent in the EO, LO and RI groups ($P < 0.03$) (Table 2).

On neuroimaging, frontal lobe involvement is less frequent in the LO group compared to the non-seizure patients ($P = 0.018$). Temporal lobe infarction is more common in the seizure groups ($P < 0.02$), except for the VLO group. Parietal and occipital lobe involvement are significantly more present in the LO group ($P < 0.03$) (Table 3).

On post-ictal EEG, diffuse slowing, intermittent rhythmic delta activities (IRDAs) and periodic lateralized epileptic discharges (PLEDs) are significantly more present in the seizure groups ($P < 0.001$), except for the VLO one (Table 4).

The seizure types do not differ significantly between the four groups ($P = 0.670$). There is a trend that status epilepticus occurs more frequently in the EO and RI groups ($P = 0.066$). Seizure recur-

Table 1

Percentage comparison of the demographic features of the patients who remain seizure-free (SF) and those with seizures of early- (EO), late- (LO) and very late-onset (VLO), and those due to recurrent infarctions (RI)

Item	SF (n = 310)	EO (n = 21)	LO (n = 81)	VLO (n = 24)	RI (n = 25)	Fisher's Exact test
Age (years) : mean	69.9	67.0	68.8	70.1	72.0	NS*
SD	13.5	17.7	15.1	11.4	15.3	
Gender : female	40.3	38.1	49.4	37.5	44.0	NS
Arterial hypertension	66.1	42.9**	72.8	70.8	88.0**	< 0.05**
Coronary artery disease	35.8	28.6	32.1	50.0	32.0	NS
Isolated atrial fibrillation	30.3	14.3	39.5	33.3	48.0	NS
Cardiac valve disease	7.1	0.0	9.9	20.8**	8.0	0.034**
Hypercholesterolemia	30.0	14.3	22.2	25.0	28.0	NS
Diabetes	20.6	23.8	16.0	54.2**	24.0	0.001**
Smoking	14.8	4.8	13.6	8.3	12.0	NS
COPD	7.7	14.3	13.6	8.3	16.0	NS

* = Mann-Whitney U-test ; ** = items that are statistically different.

Table 2

Comparison of stroke etiology, National Institute of Heath Stroke (NIHS) score, median Rankin, after stroke (mR) and percentage independent patients who remain seizure-free (SF) and those with seizures of early- (EO), late- (LO) and very late-onset (VLO), and those due to recurrent infarctions (RI)

Item	SF (n = 310)	EO (n = 21)	LO (n = 81)	VLO (n = 24)	RI (n = 25)	Fisher's Exact test
Cardiac-embolic stroke	33.9%	23.8%	38.3%	41.7%	60.0%*	
Thrombo-embolic stroke	66.1%	76.2%	61.7%	58.3%	40.0%*	0.015*
NIHS score : median	9.0	8.0	10.0	6.0	9.0	NS
IQR	5-13	7-12	6-14.	4.8-10.5	6-16	
mR after stroke : median	2.0	4.0*	2.0	1.5	2.0	0.0111*
IQR	1-4	2.5-5	2-3	0.3-3	1.5-3	
% Independent	53.2%	23.8%*	27.2%*	50.0%	28.0%*	< 0.03*

* = items that are statistically different ; IQR = Interquartile Range.

Table 3

Comparison of the percentage topographic distribution of the cerebral infarcts between the seizure-free (SF) group and the seizure groups of early- (EO), late- (LO) and very late-onset (VLO), and those due to recurrent infarctions (RI)

Item	SF (n = 310)	EO (n = 21)	LO (n = 81)	VLO (n = 24)	RI (n = 25)	Fisher's Exact test
Frontal	55.8	38.1	40.7*	58.3	40.0	0.018*
Temporal	25.2	52.4*	48.1*	37.5	48.0*	< 0.02*
Parietal	25.5	38.1	54.3*	33.3	32.0	< 0.001*
Occipital	5.5	4.8	13.6*	0.0	4.0	0.026*
Subcortical	25.5	23.8	16.0	20.8	20.0	NS

* = items that are statistically different.

Table 4

Percentage comparison of the EEG findings between the seizure-free (SF) group and the seizure groups of early- (EO), late- (LO) and very late-onset (VLO), and those due to recurrent infarctions (RI)

Item	SF (n = 310)	EO (n = 21)	LO (n = 81)	VLO (n = 24)	RI (n = 25)
Normal	42.0	19.0	21.3	36.8	8.0
Focal slowing	44.7	19.0	24.6	31.6	40.0
Diffuse slowing	8.0	33.3	31.1	21.1	32.0
IRDAs	4.7	14.3	16.4	5.3	16.0
PLEDs	0.7	14.3	6.6	5.3	4.0
Fisher's exact test		< 0.001	< 0.001	NS	< 0.001

rence is low in the EO group compared to the other groups (P = 0.003) (Table 5).

Discussion

The main risk factor for developing seizures in patients with a PACS is the location of the infarct in the temporal lobe (De Reuck *et al.* 2008a).

The present study confirms that a cardiac embolic source has to be suspected in patients in which the "late-onset" seizure is the only clinical expression of a new infarct (De Reuck *et al.* 2007a).

The differences in some vascular risk factors, according to the onset time of the seizures, are only observed in the small-sized subgroups. When comparing the largest subgroup of LO seizures to the non-seizure group no statistical differences are observed, even for COPD (De Reuck *et al.* 2007b).

The present study also confirms that IRDAs and PLEDs are more frequent on post-ictal EEG (De Reuck *et al.* 2006b) and can help to differentiate inhibitory seizures from recurrent ischemic events (De Reuck *et al.* 2006c).

Seizures in patients with a PACS have different characteristics, according to their onset time. Patients with EO have a bad outcome with a somewhat higher risk of status epilepticus, but less risk of recurrence in case of survival. VLO have less disadvantageous effects. VLO are more observed in patients with lacunar strokes in which their mutual relation is questionable (De Reuck *et al.* 2007c). As presently the follow-up time after stroke varies from 30 to 66 months in our control group, we cannot exclude that still some patients can develop seizures of VLO. This possibility is reinforced by the finding of IRDAs and PLEDs on post-stroke EEG in a few

Table 5

Percentage comparison of the seizure characteristics between the groups of early- (EO), late- (LO) and very late-onset (VLO), and those due to recurrent infarctions (RI)

Item	EO (n = 21)	LO (n = 81)	VLO (n = 24)	RI (n = 25)	Fisher's Exact test
Seizure type : complex partial	9.5	13.6	25.0	20.0	
simple partial	66.7	64.2	62.5	68.0	
tonic-clonic	23.8	22.2	12.5	12.0	NS
Single seizure	85.7	43.2	58.3	44.0	
Recurrent seizures	14.3	56.8	41.7	56.0	0.003
Status epilepticus	28.6	12.3	4.2	24.0	0.066

cases. However, patients with seizures of VLO represent only a minority (< 16%). Most probably the few possible cases of VLO seizures, missed and included in the control group, will not influence significantly the final results of this study.

The time of onset of seizures in relation to the occurrence of the PACS must be taken in to account whether sustained antiepileptic drug treatment should be started after the first epileptic spell : it should mainly be started in the late-onset group (De Reuck *et al.* 2008c).

REFERENCES

ARBOIX A., COMES E., MASSONS J., GARCIA-EROLES L., MASSONS J. B. *et al.* Prognostic value of very early seizures for in-hospital mortality in atherothrombotic infarction. *Eur. Neurol.*, 2003, **50** : 78-84.

BAMFORD J., SANDERCOCK P., DENNIS M., BURN J., WARLOW Ch. Classification and natural history of clinically identifiable subtypes of cerebral infarction. *Lancet*, 1991, **337** : 1521-1526.

BLADIN C., ALEXANDROV A., BELLAVANCE A., BORNSTEIN N., CHAMBERS B. *et al.* Seizures after stroke : a prospective multicenter study. *Arch. Neurol.*, 2000, **57** : 1617-1622.

DE REUCK J. Stroke-related seizures and epilepsy. *Neurol. Neurochir. Pol.*, 2007, **41** : 1-6.

DE REUCK J., GOETHALS M., VONCK K., VAN MAELE G. Clinical predictors of late-onset seizures and epilepsy in patients with cerebrovascular disease. *Eur. Neurol.*, 2005, **54** : 68-72.

DE REUCK J., CLAEYS I., MARTENS S., VANWALLEGHEM PH., VAN MAELE G. *et al.* Computed tomographic changes of the brain and clinical outcome of patients with seizures and epilepsy after an ischaemic hemispheric stroke. *Eur. J. Neurol.*, 2006a, **13** : 402-407.

DE REUCK J., GOETHALS M., CLAEYS I., VAN MAELE G., DE CLERCK M. EEG findings after a territorial infarct in patients who develop early- and late-onset seizures. *Eur. Neurol.*, 2006b, **55** : 209-213.

DE REUCK J., DE GROOTE L., VAN MAELE G. Delayed transient worsening of neurological deficits after ischaemic stroke. *Cerebrovasc. Dis.*, 2006c, **22** : 22-27.

DE REUCK J., VANHEE F., VAN MAELE G., CLAEYS I. Magnetic resonance imaging in patients with an ischemic stroke. *Cerebrovasc. Dis.*, 2007a, **23** : 339-343.

DE REUCK J., PROOT P., VAN MAELE G. Chronic obstructive pulmonary disease as a risk factor for stroke-related seizures. *Eur. J. Neurol.*, 2007b, **14** : 989-992.

DE REUCK J., NAGY E., VAN MAELE G. Seizures and epilepsy in patients with lacunar strokes. *J. Neurol. Sci.*, 2007c, **263** : 75-78.

DE REUCK J., DE GROOTE L., VAN MAELE G., PROOT P. The cortical involvement of territorial infarcts as a risk factor for stroke-related seizures. *Cerebrovasc. Dis.*, 2008a, **25** : 100-106.

DE REUCK J., SIEBEN A., VAN MAELE G. Characteristics and outcome of patients with seizures according to the time of onset in relation to stroke. *Eur. Neurol.*, 2008b, **59** : 225-228

DE REUCK J., DE GROOTE L., VAN MAELE G. Single seizure and epilepsy in patients with a cerebral territorial infarct. *J. Neurol. Sci.*, 2008c, **271** : 127-130.

GIROUD M., GRAS P., FAYOLLE H., ANDRE N., SOICHOT P. *et al.* Early seizures after acute stroke : a study of 1640 cases. *Epilepsia*, 1994, **35** : 959-964.

GOLDSTEIN L. B., BERTELS C., DAVIS J. N. Interrater reliability of the NIH Stroke Scale. *Arch. Neurol.*, 1989, **46** : 660-662.

HEUTS-VAN RAAK L., LODDER J., KESSELS G. Late seizures following a first symptomatic brain infarct are related to large infarcts involving the posterior area around the lateral sulcus. *Seizure*, 1996, **5** : 185-195.

JENNETT B. Early traumatic epilepsy. Incidence and significance after nonmissile injuries. *Arch. Neurol.*, 1974, **30** : 394-398.

R DEVELOPMENT CORE TEAM. A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna. ISBN 3-900051-07-0, 2007.

REITH J., JORGENSEN H. S., NAKAYAMA H., RAASHOU H. O., OLSEN T. S. Seizures in acute stroke : predictors and prognostic significance. The Copenhagen Stroke Study. *Stroke*, 1997, **28** : 1585-1589.

UYTTENBOGAART M., LUIJCKX G. J., VROOMEN P. C., STEWART R. E., DE KEYSER J. Measuring disability in stroke : relationship between the modified Rankin scale and the Barthel index. *J. Neurol.*, 2007, **254** : 1113-1117.

Jacques L. DE REUCK, M.D., Ph.D.,
Leopold II laan 96,
B-9000 Ghent (Belgium).
E-mail : dereuck.j@gmail.com