

Postinfarction Seizures

A Clinical Study

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We retrospectively studied 90 patients with postinfarction seizures to determine the clinical features (onset, number, type), prognosis, and electroencephalographic and computed tomographic findings; we included infarctions of all etiologies. Thirty-three percent of the 90 seizures appeared early (within 2 weeks after the infarction), and 90% of the 30 early seizures appeared within 24 hours after the infarction. Seventy-three percent of the 90 seizures occurred within the first year, and only 2% occurred >2 years after the infarction. Fifty-six percent of the 90 seizures were single, and status epilepticus was seen in only 8%. Early-onset seizures were more likely to be partial (57% of 30); late-onset seizures were more likely to be generalized (65% of 60). Thirty-nine percent of the 90 initial seizures recurred, and there was no significant difference in recurrence rate between early- or late-onset initial seizures. Twenty-two percent of the 90 initial seizures became multiple recurrent seizures, and we could identify a precipitating factor in 86% of the 35 recurrent seizures. The most common electroencephalographic abnormality in the 61 patients so examined was focal slowing (61%), but recurrent seizures occurred in 100% of the four patients with periodic lateralized epileptiform discharges and in 75% of the eight patients with diffuse slowing. Computed tomography in 61 patients showed that large infarctions were associated with early ($p < 0.021$) and multiple ($p < 0.05$) seizures. Deep infarctions on computed tomograms (cortical infarctions extending to subcortical structures) tended to cause recurrent seizures ($p < 0.057$). Seizures in 88% of the 90 patients could be managed with monotherapy. (*Stroke* 1988;19:1477-1481)

The relation between seizures and cerebrovascular diseases has been recognized since 1864¹; however, there has been little agreement as to the incidence of poststroke (cerebral infarction [CI] and hemorrhage) seizures. Incidence has been reported to vary from 7.7% to 42.8%,²⁻⁷ partly due to different study designs. Louis and McDowell² studied nonembolic CI and noted an incidence of 7.7%. Dodge et al³ and Black et al⁴ included CIs and hemorrhages, and their incidences were 12.5% and 10%, respectively. Holmes⁵ and de Reuck et al⁶ studied embolic and nonembolic CIs and noted incidences of 13.8% and 7.9%, respectively. Holmes⁵ noted a higher incidence with embolic (23%) than with nonembolic (12.4%) CIs. The highest incidence of seizures, 42.8%, was reported by Meyer et al⁷ in embolic CI. Although it appears from the studies of Holmes⁵ and Meyer et al⁷ that

the incidence of postinfarction seizures is higher in embolic CI, the data of Black et al⁴ do not support this view. Whereas there have been various studies regarding the incidence of poststroke seizures, there have been fewer studies^{2,3} of the clinical features and prognosis of these seizures. We report the clinical features (onset, number, type), prognosis, and electroencephalographic (EEG) and computed tomographic (CT) findings of postinfarction seizures.

Subjects and Methods

We retrospectively studied 90 consecutive patients with the diagnosis of postinfarction seizures seen on the neurology in- and out-patient services at the Veterans Administration Hospital, Hines, Illinois, between April 1985 and March 1987. Postinfarction seizures were defined as those either at the beginning of or after CI in a patient without a history of seizure disorder. We excluded patients with previous brain surgery, intracerebral hemorrhage, or significant head trauma (contusion, subarachnoid hemorrhage, or subdural hemorrhage). Sex, age, date of the CI, symptoms and signs of CI, and duration of follow-up after the CI were recorded.

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An attempt was made to determine the etiology (embolic versus nonembolic) of the CI.

We defined initial seizure as the first seizure after CI. Onset of the initial seizure in relation to CI was recorded as early (≤ 2 weeks after CI) or late (> 2 weeks after CI). We further classified early-onset seizures; immediate seizures occurred ≤ 24 hours after the CI. We considered one or two seizures to be single and more than two to be multiple. The presence of focal or generalized status epilepticus was determined. We classified seizures by type as partial (simple partial, complex partial) or generalized (primarily generalized, secondarily generalized) on clinical grounds according to the International Classification of Epilepsy.⁸ The presence of any seizure-precipitating factor (e.g., noncompliance, electrolyte imbalance, systemic infection, anoxia, alcohol or drug intoxication, etc.) was identified.

We defined recurrent seizures as those occurring at least 2 weeks after the onset of the initial seizure. The presence, number, and type of as well as precipitating factors for recurrent seizure were noted as in initial seizure.

We studied the EEGs done during the first or subsequent hospital admission after the CI and categorized the findings as Type I, normal; Type II, diffuse slow; Type III, focal slow with or without diffuse slowing; Type IV, focal spike; or Type V, periodic lateralized epileptiform discharges (PLEDS).

We determined the type (ischemic, hemorrhagic, mixed), side, and location (frontal including frontal, frontoparietal, frontotemporal, and frontoparietotemporal; parietal including parietal, parietotemporal, parieto-occipital, and temporal; occipital including occipital, occipitotemporal, and occipitoparietal) of the CI on axial CT scans performed ≥ 2 weeks after infarction. The greatest diameter on that CT slice showing the largest area involved was used to determine the size of the CI as small (< 5 cm) or large (> 5 cm). We defined the CI depth as cortical or cortical-subcortical.

Monotherapy versus polypharmacy for the treatment of seizures was noted.

We determined the percentages of the findings, and we used χ^2 analysis to determine statistical significance when appropriate.

Results

The patients comprised 89 men and one woman ranging in age from 31 to 92 (mean 61.6) years. Fifty-one patients (57%) had a left CI with right hemiparesis, and the remaining 39 patients (43%) had a right CI with left hemiparesis. Follow-up duration ranged from 1 month to 13 years, with a mean of 29.8 months. A cardiac source of emboli (atrial fibrillation, valvular heart disease, mural thrombus with or without ventricular aneurysm) could be identified in 18 of the 90 patients. It is possible that the cardiac source of emboli was not the cause of CI in some of these 18 patients due to

the presence of associated diffuse atherosclerosis. Moreover, a potential embolic source was present in the proximal carotid arteries in some other patients. We could not retrospectively determine a clear etiology of CI in many patients; therefore, etiology was not used for any correlation or statistical purposes.

There were 30 (33%) early-onset and 60 (67%) late-onset initial seizures. Of the 30 early-onset seizures, 27 (90%) were immediate; 30 (50%) of the 60 late-onset seizures occurred 6–15 months after the CI. Of the 90 initial seizures, 30% occurred ≤ 24 hours, 33% ≤ 2 weeks, 43% ≤ 3 months, 73% ≤ 12 months, 88% ≤ 15 months, and 98% ≤ 2 years after the CI (Table 1). Fifty initial seizures (56%) were single and 33 (36%) were multiple. Eight percent of all initial seizures presented as status epilepticus; 6% were focal and 2% were generalized. Of all 90 initial seizures, 38 (42%) were partial (32% were simple partial, 8% were complex partial) and 52 (58%) were generalized (42% were primarily generalized, 18% were secondarily generalized). We identified precipitating factors for initial seizures in only four patients; one had hypoglycemia with a single simple partial seizure, one had hyponatremia with generalized status epilepticus, and two had fever due to pneumonia presenting as a single simple partial seizure and as a single secondarily generalized seizure.

Of the 90 patients, 35 (39%) had recurrent seizures; 15 of the 35 (43%) had single recurrent seizures, and the remaining 20 (57%) had multiple recurrent seizures. Therefore, only 20 of the 90 initial seizures (22%) became multiple recurrent seizures, and of these 20 the initial seizures were of early onset in 55% and of late onset in 45%. No status epilepticus occurred during recurrent seizures. Fourteen of the 35 recurrent seizures (40%) were partial and the other 21 (60%) were generalized. Of the 35 patients with recurrent seizures, 30 (86%) had an identifiable precipitating factor; 26 had the precipitating factor of noncompliance and subtherapeutic anticonvulsant levels, three had urinary tract infections, and one had nasogastric tube suction.

TABLE 1. Onset of Seizures After Cerebral Infarction in 90 Patients

Onset	Time after infarction	Number of seizures	Cumulative percent
Early	0–24 hr	27	30
	24 hr to 2 wk	3	33
All early		30	33
Late	2 wk to 3 mo	9	43
	3–6 mo	10	54
	6 mo to 1 yr	17	73
≤ 1 yr		66	73
	1–2 yr	22	98
	> 2 yr	2	100
Total		90	100

TABLE 2. Number, Type, and Recurrence of Early- vs. Late-Onset Initial Seizures After Cerebral Infarction in 90 Patients

	Onset			
	Early (n=30)		Late (n=60)	
Initial seizure	No.	%	No.	%
Number				
Single	13	43	37	62
Multiple	13	43	20	33
Status epilepticus				
Focal status	2	7	3	5
Generalized status	2	7	0	0
Type				
Partial	17	57	21	35
Generalized	13	43	39	65
Recurrent	12	40	23	38

We compared the number, type, and recurrence of early- and late-onset initial seizures (Table 2); 43% of the early-onset and 62% of the late-onset seizures were single. Status epilepticus was more common in early-onset (14%) than in late-onset (5%) seizures. Early-onset seizures were more likely to be partial (57%), whereas late-onset seizures were more likely to be generalized (65%). Overall, we noted no difference in the recurrence rate of early- compared with late-onset initial seizures (40% vs. 38%, respectively).

Of the 90 patients, 61 had EEG; of the 61, 20 had early- and 41 had late-onset initial seizures (Table 3). Of all 61 EEGs, nine (15%) were categorized as Type I, eight (13%) as Type II, 37 (61%) as Type III, three (5%) as Type IV, and four (6%) as Type V. When we compared EEG abnormalities of the patients with early- and late-onset seizures, Type III abnormalities were most common in both groups, but Type II abnormalities were more common in early- than in late-onset seizures. Seizures recurred in 75% of the eight patients with Type II abnormalities and in 100% of the four patients with Type V abnormalities. We noted no difference in the incidence of recurrent seizures between the early- and late-onset groups for the 37 patients with Type III or for the three patients with Type IV abnormalities (Table 3).

CT scans were available in 61 of the 90 patients. All CIs in the 61 patients were ischemic; 24 (39%) were on the right and the remaining 37 (61%) were on the left side. Thirty-five of the 61 CIs (57%) were frontal, 18 (30%) were parietal, and the remaining eight (13%) were occipital. Of the 61 CIs visualized by CT, 24 (39%) were small and the other 37 (61%) were large. Fifteen of the 61 CIs (25%) were cortical, whereas the remaining 46 (75%) were cortical-subcortical. There was no significant correlation of location or depth of CI on CT with onset, number, or type of initial seizures. However, there were significant correlations of size of the CI on CT to onset (early onset, $p < 0.021$) and number (multiple seizures, $p < 0.05$), and side of the CI was associated with number (left-sided CIs correlated with multiple seizures, $p < 0.018$). There was no correlation of any CT criteria except depth to recurrent seizure (cortical-subcortical CI caused recurrent seizures in 75% of the 61 patients opposed to cortical infarctions causing recurrence in only 25%, $p < 0.057$).

Eleven of the 90 patients (12%) were on more than one antiepileptic medication. Ten patients received a combination of phenytoin and phenobarbital, whereas one received phenytoin and primidone. One patient in the phenytoin and phenobarbital group was also treated with diazepam initially. Monotherapy in the remaining 79 patients included phenytoin in 76 (84%) and carbamazepine in one (1%); two patients received either carbamazepine or divalproex sodium. (These last two patients were enrolled in Veterans Administration Cooperative Study Number 264 testing the efficacy and toxicity of carbamazepine versus divalproex sodium in controlling partial seizures.) Standard dosages of these anticonvulsants were used in most patients and were altered, if needed, in some patients.

Discussion

Various mechanisms have been proposed for the pathogenesis of epilepsy after cerebral ischemia.^{6,9-11} These mechanisms include anoxia, a hemodynamic factor such as impaired cardiac output with or without extracranial or intracranial vascular disease, and scar formation. It has been

TABLE 3. Electroencephalographic Findings in 61 Patients With Early- vs. Late-Onset Seizures After Cerebral Infarction

Finding	Initial seizures (N=61)	Early (n=20)		Late (n=41)		Recurrent seizures	
		No.	%	No.	%	No.	%*
Type I	9	2	10	7	17	2	22
Type II	8	6	30	2	5	6	75
Type III	37	10	50	27	66	16	43
Type IV	3	1	5	2	5	1	33
Type V	4	1	5	3	7	4	100

Type I, normal; Type II, diffuse slow; Type III, focal slow with or without diffuse slowing; Type IV, focal spike; Type V, periodic lateralized epileptiform discharges.

*% of initial seizures for electroencephalographic finding.

suggested that scar tissue produces its effect through anoxia or dendritic deformation and hypersensitivity or denervation supersensitivity. Even using pathologic studies, it was difficult to separate apoplectic seizures from those occurring due to scar formation after CI since postapoplectic epilepsy was induced by either occurrence of a new stroke or by hemodynamic disturbance. The importance of involvement of the cerebral cortex was also emphasized in the pathogenesis.³

The time of onset of seizures after CI is variable. A higher incidence of early-onset seizures has been reported by Louis and McDowell² (55% in 2 weeks), Holmes⁵ (62% in 1 month), and Black et al⁴ (57% in 1 week). In our study, the incidence of early-onset seizures (≤ 2 weeks after CI) was only 33%. There are some differences between these cited studies and ours. Thirty-nine percent of the early-onset seizures in the study of Louis and McDowell² preceded the CI; the time between the onset of seizures and the CI was not given, but we did not encounter any patient with seizures preceding CI. The earliest seizures we saw occurred at the beginning of the CI. Holmes⁵ included as early-onset seizures those occurring up to 1 month after CI, and Black et al⁴ included hemorrhages.

Early-onset seizures were more likely than late-onset seizures to be partial in our study, as in that of Louis and McDowell,² but we found proportionally more generalized seizures in our 60 patients with late-onset seizures; 62% of the seizures in this group were single. Although multiple seizures were present in 36% of our 90 patients, status epilepticus was seen in only 8%. This number (36% multiple seizures) is slightly higher than the 26% in the study by Louis and McDowell.²

There is no general agreement as to the incidence of recurrent seizures after the initial postinfarction seizures. It has been a general contention that recurrent seizures are less frequent if the initial seizure occurs early after CI than if it occurs late. The literature, however, does not support this very well. Louis and McDowell² reported that 6% of early- and 81% of late-onset seizures recurred, with an overall incidence of 40% for recurrent seizures. In the group studied by Dodge et al,³ 46% of all initial seizures recurred, and of these recurrent seizures, the initial seizures were of early onset in 50%, of late onset in 33%, and in 17% the exact time of onset in relation to CI could not be determined. In our study, 39% of the 90 initial seizures recurred and we noted no difference in the incidence of recurrence with regard to the onset of the initial seizures. We identified a precipitating factor for 86% of our recurrent seizures. Moreover, only 22% of all 90 initial seizures became multiple recurrent, and there was no difference in the incidence of multiple recurrent seizures with regard to the onset of the initial seizures. We conclude that the incidence of recurrent seizures will be much lower than

the 39% we observed if precipitating factors are avoided.

Holmes⁵ studied the EEG abnormalities with CI and correlated them with the onset of epilepsy. He suggested that 98% of patients with EEG findings of sharp waves, spikes, and PLEDS developed seizures after CI; he did not correlate the EEG findings with recurrent seizures. The most common abnormality we found in patients undergoing EEG was focal slowing (Type III, 61%). The abnormalities were equally distributed among early- and late-onset seizures except for a higher incidence of Type II diffuse slowing among patients with early-onset seizures (Table 3); 75% of our eight patients with Type II diffuse slowing abnormalities and 100% of our four patients with Type V PLEDS had recurrent seizures (Table 3). These higher incidences of recurrence can be explained by the fact that these two types of EEG abnormalities indicate a larger area of brain involvement than Types I, III, and IV.

Size of the infarction was the only CT factor related to early and multiple initial seizures. Recurrent seizures were associated with deep CIs involving cortical-subcortical structures. Multiple initial seizures were seen more frequently with CIs on the left side, which may be due to the fact that 62% of large CIs were in the left hemisphere.

These postinfarction seizures were not difficult to control as seizures in 88% of the 90 patients were managed with monotherapy. Some patients on polypharmacy had been somehow started on more than one anticonvulsant agent and had been continued on the same. Some of these patients may not have required polypharmacy if an attempt had been made for monotherapy.

Recently, Shinton et al¹² studied the frequency, characteristics, and prognosis of epileptic seizures at the beginning of stroke. Their overall incidence of seizures was 5.7%, but only 3% of their patients had new-onset seizures. This incidence is lower than those in earlier reports, but they included only early-onset seizures. Shinton et al¹² suggested that seizures at the beginning of stroke indicate poorer prognosis. The prognosis appeared good with new-onset seizures as all five survivors remained seizure-free for 30 months. However, this number is too small to make any comparison with our study.

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