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**ORIGINAL
RESEARCH**

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Clinical and Electroencephalographic Features of Carotid Sinus Syncope Induced by Internal Carotid Artery Angioplasty

BACKGROUND AND PURPOSE: Carotid sinus syncope may occur acutely during internal carotid artery angioplasty (CA). We performed this study to investigate the clinical, electroencephalographic (EEG), and hemodynamic features of carotid sinus syncope induced by CA.

MATERIALS AND METHODS: Between 1992 and 2003, clinical, EEG, and cardiovascular monitoring was performed in 359 consecutive patients undergoing CA.

RESULTS: Carotid sinus reaction (CSR) and syncope occurred in 62.7% and 18.6% of the procedures, respectively. CSR and syncopal spells were classified into cardioinhibitory, vasodepressor, and mixed type. Syncope occurred more frequently in patients with cardioinhibitory CSR ($P < .001$). The odds ratios for the risk of syncope in patients with cardioinhibitory CSR and vasodepressor/mixed CSR were 6.9 and 1.4, respectively. Sixty-one patients had cardioinhibitory syncope; 7 had the vasodepressor/mixed type. Thirteen spells were not related to cardiovascular disturbances. This last syncope subtype was significantly associated with brain hemodynamic disturbances, including a decrease in cerebral vasoreactivity ($P = .04$) and the absence of function of both communicating arteries ($P = .03$). Convulsive movements resembling supplementary sensorimotor seizures occurred in 79% of patients who experienced syncopal spells. EEG changes were more prominent in patients with cardioinhibitory syncope.

CONCLUSIONS: Syncope occurs frequently in patients undergoing CA and can be misdiagnosed as seizures. The most frequent mechanism was a cardioinhibitory response. Cerebral hemodynamic disturbances may play a crucial role in the pathophysiology of syncope with normal sinus rhythm and normotension. Moreover, direct depression of the CNS following carotid sinus distension is likely to be involved.

Carotid sinus reaction (CSR) is one of the most common complications of internal carotid artery angioplasty (CA). It may occur due to an abnormal response to a baroreflex related to an overstretch of the carotid sinus caused by the dilating balloon. Accordingly, the occurrence of CSR is usually accompanied by vasodepressor reactions, including bradycardia, asystole, and hypotension. McIntosh et al¹ previously reported abnormal cardioinhibitory responses in 80% of all CSRs and abnormal vasodepressor responses in 5%–10% of patients.

Carotid sinus hypersensitivity is most commonly found in men, at an older age,² as well as in the presence of arterial hypertension, diabetes mellitus, ischemic heart disease,³ and carotid stenosis.⁴ It follows that patients undergoing CA may have high rates of carotid hypersensitivity. Therefore, CSR may occur acutely during CA and is often accompanied by the appearance of neurally mediated reflex syncope.^{5–8}

To the best of our knowledge, no previous study has examined the prevalence of loss of consciousness during CA procedures. We performed this study to investigate the clinical, electroencephalographic (EEG), and hemodynamic features of carotid sinus syncope induced by CA.

Methods

Research Design

A CA registry was established in 1992 to provide prospective epidemiologic data on the safety of CA.

Demographic data were recorded, including age and sex. Assessment of cardiovascular risk factors included a history of any of the following: 1) hypertension (previous or current use of antihypertensive agents or self-reported), 2) dyslipidemia (previous or current use of lipid-lowering therapy or self-reported), 3) diabetes (defined as previous or current use of oral hypoglycemic agents or insulin or self-reported), 4) smoking habits, 5) a previous cardiac event (acute coronary syndrome requiring hospitalization, nonfatal myocardial infarction, coronary artery bypass graft, or percutaneous coronary intervention), and 6) peripheral vascular disease (angioplasty, bypass, or amputation).

The primary end point of the study was the occurrence of CSR and/or syncope during CA. The study protocol was approved by the institutional review board, and written informed consent was given by the participants.

Patients

We prospectively enrolled the following patient groups: 1) symptomatic patients with transient ischemic attacks (either retinal or hemispheric events) or noninvalidating stroke (modified Rankin Scale score, ≤ 2), and 2) asymptomatic patients with progression of the stenosis to 85% (duplex), positive microemboli detection (transcranial Doppler), exhausted cerebrovascular reserve (transcranial Doppler), or silent lesions on CT/MR imaging. Symptomatic patients underwent the procedure at least 4 weeks after acute stroke onset.

Before CA, all study participants underwent a comprehensive medical history, neurologic examination, and continuous-wave

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Doppler or duplex evaluation. Brain CT scans and MR angiography were also performed.

Technique

Procedures followed were in accordance with institutional guidelines. The assessment of cerebrovascular reserve before angioplasty was performed noninvasively by a breath-hold test (apnea) by using a Doppler sonographic apparatus (EME Companion; Nicolet Biomedical, Madison, Wis).^{6,7} An apnea index outside the normal range (1.30 ± 0.60) was regarded as abnormal vasoreactivity. All patients were taking aspirin, 125 mg/day, and ticlopidine, 250 mg twice daily, or clopidogrel, 75 mg/day, beginning at least 2 days before the procedure. Full-dose heparin (300 U/kg) was applied in all participants. Heparin was given as an intravenous bolus of 5000 U before angioplasty in the first 45 patients. Thereafter, heparin was titrated to maintain the activated clotting time between 250 and 300 seconds. Immediately before the procedure, 12-mg intravenous dexamethasone and 20-mg intramuscular clorazepate dipotassium were given; patients with diabetes were the only exceptions. Percutaneous femoral artery access with local anesthesia was obtained in all patients.

Angiography of the supra-aortic trunks was performed, and the percentage of artery stenosis was determined by using the North American Symptomatic Carotid Endarterectomy Trial measurement criteria.⁸ Morphologic data and plaque characteristics were recorded for analysis. We investigated the functional status of the circle of Willis by means of contralateral carotid and vertebrobasilar arteriography in all study participants. Hence, the presence of contralateral internal carotid artery (ICA) stenosis and the status of communicating arteries were investigated.

An 8F guide catheter or 6F long sheath introducer was positioned in the common carotid artery at the site of the stenosis. CA alone was performed by using a 5F balloon catheter measuring 5–6 mm in diameter and 4 cm in length. A 0.35-inch guidewire was used to cross ICA stenosis.

The balloon was inflated between 1 and 4 times for approximately 15–20 seconds. The inflation pressure was increased gradually until reaching the recommended pressure. CA was performed routinely after stents became available. In those procedures performed with 0.014-inch microwire and rapid exchange system, predilation was achieved with a 3- or 4-mm low-profile balloon. The endoprosthesis was then deployed, and final full dilation was achieved with a 5- to 6-mm balloon. The types of stent placed were Strecker (MediTech/Boston Scientific, Natick, Mass); self-expanding rolling Wallstent (Boston Scientific Target, Fremont, Calif); and Easy Wallstent, carotid Wallstent OTW, Carotid Wallstent Monorail, and Carotid Acculink (Guidant, Santa Clara, Calif). Since 2001, distal protection devices were used. The types of devices used were EPI (Boston Scientific Target), EZ (Boston Scientific Target), Spider (ev3, Plymouth, Minn), AngioGuard (Cordis; Johnson & Johnson, Warren, NJ), and Accunet filter (Guidant).

Means of Confirming Diagnosis

Neurologic status was monitored constantly throughout the procedure to detect the occurrence of loss of consciousness as well as convulsive movements.

Continuous monitoring of heart rate and blood pressure were performed every 5 minutes during the study. Measurements of blood pressure at a rate of every minute were obtained during balloon inflation and stent placement. The occurrence and duration of CSR, including bradycardia, asystole, and hypotension, were carefully recorded. Carotid sinus syncope was classified as cardioinhibitory (asystole >3 seconds), vasode-

Table 1: General characteristics of the study participants

Characteristics	Study Participants (n = 359)
Demographic data	
Age, years	63.2; 9.1
Male	281 (78.3%)
Vascular risk factors	
Hypertension	226 (63%)
Diabetes mellitus	143 (39.8%)
Dyslipidemia	158 (44%)
Smoking habits	176 (49%)
Ischemic heart disease	105 (29.3%)
Peripheral arterial disease	104 (29%)
Carotid plaque	
Grade (%) of stenosis	87.8; 8.6
Symptomatic stenosis	313 (87.2%)
Procedures	
Stent	205 (57.4%)
Distal protection device	55 (15.3%)

pressor (systolic blood pressure fall >50 mm Hg), or mixed.⁹⁻¹² If asystole occurred during the predilation or stent dilation, the balloon was deflated immediately and 1-mg atropine was administered intravenously. If hypotension persisted after the first or second balloon inflation, rapid intravenous administration of 500 mL of normal saline solution and plasma expanders was performed. When this procedure proved to be ineffective, normal saline solution, plasma expanders, and dopamine infusion were given as appropriate.

EEG monitoring was performed at a speed of 15 mm/s with a DG, 3P Examiner, Medelec digital apparatus (Nihon Kohden, Tokyo, Japan). The EEG electrodes were fitted to each participant according to the international 10–20 electrode-placement system. The sensitivity was set at 10 μ V/mm, with low-frequency 0.5-Hz filters and a high-frequency 70-Hz filter. EEG basal activity was defined as EEG activity before syncopal spells. Analysis was finished once the brain activity returned to basal 1. For the purpose of analyses, only EEG abnormalities lasting longer than 5 seconds were considered.

Syncope was diagnosed on clinical grounds (transient loss of consciousness without any neurologic sequelae) and EEG abnormalities (slowing and flattening of the EEG trace).

Statistical Methods

Continuous variables are expressed as mean; SD. Categorical variables are presented by frequency counts, and intergroup comparisons were analyzed by a χ^2 test. Fisher exact test was performed for small samples. P values lower than .05 were regarded as statistically significant. All calculations were made by using the computer software package Statistical Package for the Social Sciences 14.0 (SPSS, Chicago, Ill).

Results

General Characteristics and Syncope Occurrence

The general characteristics of the 359 patients included in the study are shown in Table 1. CSR occurred in 225 (62.7%) patients. The etiologies of CSR were as follows: cardioinhibitory (122 patients, 34.0%), vasodepressor (13 patients, 3.7%), or mixed (90 patients, 25.0%). Syncope occurred on 81 occasions in 66 patients (18.6%). In this group, 15 patients experienced 2 syncopal spells. A significant relationship between the occurrence of CSR and syncope was evident. Specifically, 54 (24%) patients with CSR experienced syncope, whereas

Table 2: Convulsive movements occurring during syncope

Convulsive Movements (n = 81)	
Absence of convulsive movements	17 (21%)
Convulsive movements*	64 (79%)
Tonic spasm	38 (46.9%)
Bilateral	37 (45.6%)
Unilateral	1 (1.2%)
Myoclonic jerks	18 (22.2%)
Bilateral	10 (12.3%)
Unilateral	8 (9.8%)
Oculocephalic conjugate deviation	14 (17.2%)
Flexion forced spasm	12 (14.8%)

* Eighteen patients showed 2 types of convulsive movements.

syncope occurred in only 10 (7.4%) patients without CSR ($P < .001$). In patients with CSR, an odds ratio for the risk of syncope during CA was 4.2 (95% confidence interval [CI], 1.9–9.1). Syncope occurred more frequently in patients with cardioinhibitory CSR (36.9%), compared with the vasodepressor/mixed type (10.0%, $P < .001$). The odds ratios for the risk of syncope in patients with cardioinhibitory CSR and vasodepressor/mixed CSR were 6.9 (95% CI, 3.2–15.0) and 1.4 (95% CI, 0.6–3.7), respectively.

Clinical Features of Syncopal Spells

Loss of consciousness was not accompanied by convulsive movements in 17 (21.0%) syncopal spells. Roaring or snoring was evident in 9% of patients. Retrograde amnesia for syncope was common, albeit a feeling of falling being reported by some patients. A total of 64 (79%) syncopal spells was accompanied by convulsive movements. The patterns of movements are presented in Table 2. A total of 18 patients showed convulsive movements of more than 1 type. Bilateral tonic spasms occurred most frequently. In 28 (35%) patients, movements were asymmetric, thereby resembling supplementary sensorimotor seizures.

EEG Changes During Syncopal Spells

The EEG changes were either focal or generalized. In 51 (63%) patients, generalized EEG changes were evident, albeit hemispheric predominance being present in the remaining 30 patients (37%). The mean duration of EEG changes during syncopal episodes was 20.4 seconds (range, 6–46 seconds).

Two types of EEG change were distinguished during syncopal episodes, namely slowing (S, theta-delta activity followed by gradual return to the basal level) and slowing-flattening-slowing (SFS, slow EEG activity followed by theta or theta-delta activity, plus sudden attenuation of cerebral activity followed by gradual return to the basal level). The 2 types of EEG changes (either S or SFS) were found at the same frequency during syncopal episodes (49.4% versus 50.6%) (Table 3). SFS EEG changes were generally associated with the presence of convulsive movements during syncope.

Subtypes of Syncope According to Hemodynamic Criteria

Syncopal spells were classified as cardioinhibitory in 61 (75.3%) patients, vasodepressor/mixed in 7 (8.7%) patients, and without hemodynamic disturbances in 13 (16%) patients. EEG patterns according to syncope subtype are presented in Table 3. The most severe EEG pattern (SFS) was more frequently observed in cardioinhibitory syncope compared with the other subtypes. In con-

Table 3: EEG changes occurring during syncope

Type of Syncope	No. (%)	EEG Changes	
		S	SFS
Cardioinhibitory	61 (75.3)	24	37
Vasodepressor/mixed	7 (8.6)	4	3
Not related to asystole/hypotension	13 (16)	12	1
Total	81 (100)	40 (49.4%)	41 (50.6%)

Note:—S indicates slowing; SFS, slowing-flattening-slowing.

Table 4: Cerebral hemodynamic differences among patients with syncope of different type

Hemodynamic Differences	Not Related to Asystole/Hypotension (n = 10)	Cardioinhibitory/Vasodepressor/Mixed (n = 56)	P
Contralateral ICA stenosis $\geq 70\%$	7 (70%)	22 (40%)	.2
Abnormal cerebral vasoreactivity	6 (60%)	9 (16%)	.04
Nonfunctioning AcomA	6 (60%)	17 (30.4%)	.07
Nonfunctioning PcomA	7 (77.8%)	31 (58.5%)	.23
Nonfunctioning AcomA plus nonfunctioning PcomA	5 (50%)	10 (18.5%)	.03

Note:—AcomA indicates anterior communicating artery; PcomA, posterior communicating artery; ICA, internal carotid artery.

trast, the less severe (S) EEG pattern was more commonly found in syncope without demonstrable hypotension or asystole. Among patients with vasodepressor/mixed syncope, the frequency of S and SFS EEG patterns was similar.

Cardioinhibitory Syncope. The duration of asystole during CA procedures ranged between 3 and 19 seconds. The mean duration of asystole was 8.8; 3.5 seconds in syncopal patients compared with 5.4; 1.8 seconds in nonsyncopal patients ($P = .05$). Among syncopal patients, the duration of asystole was significantly higher in the presence of the EEG SFS pattern (9.8; 3.9 seconds) compared with the S pattern (7.3; 2.4 seconds, $P = .008$).

Vasodepressor or Mixed Syncope. Vasodepressor syncope occurred in 6 patients, whereas the mixed type occurred in only 1 patient. Among this patient group, subjects with the EEG SFS pattern showed more severe hemodynamic disturbances (higher decrease in arterial pressure and heart rate).

Syncope without Asystole or Hypotension. Notably, this subtype invariably occurred during balloon inflation. Significant differences in cerebral hemodynamic status between subjects in this patient group compared with other types were evident (Table 4).

Discussion

During CA, 40%–100% of patients may experience CSR.^{10–13} In the present study, CSR occurred in 62.7% of patients undergoing CA. Most patients had cardioinhibitory CSR. Most interesting, patients with cardioinhibitory CSR showed a significantly higher risk of developing syncope compared with those with vasodepressor and mixed CSR. Syncope occurs frequently in patients undergoing CA. In fact, 16.5% of patients in our previously published series¹¹ and 18.6% in the current study had at least 1 syncopal episode during the procedure.

In the present study, we have demonstrated that convulsive movements accompanying loss of consciousness are a com-

mon brain response to hypoxia. Accordingly, 79% of syncope was accompanied by convulsive movements such as myoclonic jerks and/or tonic spasms. Syncope accompanied by asymmetric tonic spasms could be misdiagnosed as frontal seizures. However, the absence of epileptic discharges on EEG may be of clinical aid in distinguishing this type of syncope from epileptic seizures.

Previous studies investigating small patient series of syncope have reported the occurrence of convulsive movements during loss of consciousness. In this regard, Aminoff et al¹² observed motor activity in 10 of 15 episodes of loss of consciousness provoked by cardiac arrhythmias,¹² whereas Lempert et al¹³ reported, in a series of 56 syncopal episodes, a 90% and 79% prevalence of myoclonic activity and other abnormal involuntary movements, respectively.

Prolonged cerebral ischemia may result in loss of consciousness followed by convulsions. Accordingly, Gastaut¹⁴ studied the electroclinical features of 100 patients with attacks of unconsciousness after ocular compression. Patients in whom the cardiac arrest had lasted >14 seconds had 1 or 2 generalized myoclonic jerks. This clinical picture was followed by generalized tonic contractions resembling decerebrate rigidity. Thereafter, complete EEG flattening was evident. This entity was termed convulsive syncope.¹⁴

We did not observe cortical discharges on the scalp EEG during myoclonus. Instead, large-amplitude S waves and EEG flattening occurred during syncopal episodes. What is intriguing, the presence of convulsive movements was significantly higher in the presence of SFS changes on EEG. This most severe type of EEG anomaly was more frequently found in cardioinhibitory syncope, whereas the mildest EEG disturbances (S pattern) were most common during syncopal episodes without asystole or hypotension. In keeping with our results, Ammirati et al¹⁵ previously reported a higher prevalence of tonic-clonic jerks during loss of consciousness in patients with cardioinhibitory responses compared with those with vasodepressor syncope.

CSR is usually classified according to the accompanying cardiovascular abnormalities.^{1,4,10,12} The most common type of CSR in our study was the cardioinhibitory type, followed by the vasodepressor/mixed type. In this report, the vasodepressor and mixed types of carotid sinus syncope were grouped together due to the low number of cases.

Syncope unrelated to asystole or hypotension may occur during overstretch of the carotid sinus. Data regarding this syncope subtype, termed cerebral syncope, are scarce. Gurdjian et al¹⁶ suggested that cerebral syncopal episodes without bradycardia or hypotension may be due to cerebral ischemia caused by occlusive vascular disease. On the other hand, Weiss and Baker⁹ described 5 patients in whom sinus massage resulted in syncope without hypotension or bradycardia, whereas unilateral carotid artery occlusion did not produce the same clinical picture.

Of interest, most patients with syncope and no cardiovascular disturbances in our series had a compromise of cerebral hemodynamics. Specifically, abnormal cerebral vasoreactivity response and absence of function of both communicating arteries were significantly more frequent in this patient group compared with other subtypes. These findings support a crucial role of cerebral hemodynamic disturbance in the pathophysiology of cerebral syncope. Of interest also is the observation that cerebral syncope in our series occurred only during

overstretch of the carotid sinus due to balloon inflation. Hence, this phenomenon could not be observed during different steps of the procedure, even in the presence of ICA occlusion. It is posited that a direct depression of the central nervous system may occur following carotid sinus wall distension.

One caveat on the present study is that a beat-to-beat analysis of arterial blood pressure was not performed. It follows that an overestimation of cerebral syncope, along with underestimation of vasodepressor syncope, may have occurred. Nonetheless, blood pressure measurements were performed at 1-minute intervals during and immediately after balloon inflations. Under these circumstances, the probability of missing hypotension is deemed to be minimal. Further studies are needed to determine whether cerebral syncope may be regarded as a separate clinical entity not caused by cerebral hypoperfusion.

Conclusions

The present study was performed to investigate the clinical, EEG, and hemodynamic features of carotid sinus syncope induced by CA. Syncope occurs frequently in patients undergoing CA and can be misdiagnosed as frontal seizures. However, the absence of epileptic discharges on EEG may be of clinical aid in distinguishing this type of syncope from epileptic seizures. The most frequent mechanism was a cardioinhibitory response. Cerebral hemodynamic disturbances may play a crucial role in the pathophysiology of syncope with normal sinus rhythm and normotension. Moreover, direct depression of the central nervous system following carotid sinus distension is likely to be involved.

References

1. McIntosh SJ, Lawson J, Kenny RA. **Clinical characteristics of vasodepressor, cardioinhibitory and mixed carotid sinus syndrome in the elderly.** *Am J Med* 1993;95:203–08
2. O'Mahony D. **Pathophysiology of carotid sinus hypersensitivity in elderly patients.** *Lancet* 1995;346:950–52
3. Walter PF, Crawley IS, Dorney ER. **Carotid sinus hypersensitivity and syncope.** *Am J Cardiol* 1978;42:396–403
4. Solti F, Mogan ST, Renyi-Vamos F, et al. **The association of carotid artery stenosis with carotid sinus hypersensitivity.** *J Cardiovasc Surg* 1990;31:693–96
5. Brignole M, Alboni P, Benditt D, et al. **Guidelines on management (diagnosis and treatment) of syncope.** *Eur Heart J* 2001;22:1256–306
6. Markus M, Harrison MJG. **Estimation of cerebrovascular reactivity using transcranial Doppler including the use of breath-holding as the vasodilatory stimulus.** *Stroke* 1992;23:668–73
7. Aaslid R. **Cerebral autoregulation and vasomotor reactivity.** *Front Neurol Neurosci* 2006;21:216–28
8. Barnett HJ, Taylor DW, Eliasziw M, et al. **Benefit of carotid endarterectomy in patients with symptomatic carotid moderate or severe stenosis: North American Symptomatic Carotid Endarterectomy Trial Collaborators.** *N Engl J Med* 1998;339:1415–25
9. Weiss S, Baker JP. **The carotid sinus reflex in health and disease: its role in the causation of fainting and convulsions.** *Medicine (Baltimore)* 1933;12:297–354
10. McKeivitt FM, Sivaguru A, Venables GS, et al. **Effect of treatment of carotid stenosis on blood pressure: a comparison of hemodynamic disturbances after carotid endarterectomy and endovascular treatment.** *Stroke* 2003;34:2576–82
11. Gil-Peralta A, Mayol A, González-Marcos JR, et al. **Percutaneous transluminal angioplasty of the symptomatic atherosclerotic carotid arteries.** *Stroke* 1996;27:2271–73
12. Aminoff MJ, Scheinman MM, Griffin JC, et al. **Electrocerebral accompaniments of syncope associated with malignant ventricular arrhythmias.** *Ann Intern Med* 1988;108:791–96
13. Lempert T, Bauer M, Schmidt D. **Syncope: a videometric analysis of 56 episodes of transient cerebral hypoxia.** *Ann Neurol* 1994;36:233–37
14. Gastaut H. **Electro-encephalographic study of syncope: its differentiation from epilepsy.** *Lancet* 1957;23:1018–25
15. Ammirati F, Colivicchi F, Di Battista G, et al. **Electroencephalographic correlates of vasovagal syncope induced by head-up tilt testing.** *Stroke* 1998;29:2347–51
16. Gurdjian ES, Webster JE, Hardy WG, et al. **Non-existence of the so-called cerebral form of carotid sinus syncope.** *Neurology* 1958;8:818–26