Surgical and Anticoagulant Therapy of Occlusive Cerebrovascular Disease

ROBERT G. SIEKERT, M.D., F.A.C.P., JACK P. WHISNANT, M.D., and
CLARK H. MILLIKAN, M.D., F.A.C.P
Rochester, Minnesota

THE THERAPY of patients with focal ischemic cerebrovascular disease continues to be a challenge. Each regimen must be considered carefully in regard to its immediate therapeutic effect, its long-term prophylactic effect, and any risks attendant on its use. Meaningful comparisons between treated and untreated patients are extremely difficult to make. It is essential in any study that the investigator defines carefully the patients analyzed and the larger group from which they were selected, and takes into account variations in the natural course of the disease. The present report concerns our experience to date with anticoagulant and surgical therapy.

DEFINITIONS

The simple, dynamic classification that has been used refers to the clinical status of the patient when he is seen by the physician. The course of the disease is divided into three stages or categories.

Stage 1, or incipient stroke, refers to attacks of focal ischemia, sometimes called "intermittent insufficiency," that last 15 to 30 minutes. Between attacks, the patients are normal.

Stage 2, or progressing stroke, refers to a neurologic deficit that increases while the physician is observing the patient. The period of evolution rarely exceeds 24 hours.

Stage 3, or completed stroke, refers to the deficit that did not increase in amount and the cerebral infarct that remained relatively stable. Patients with a completed stroke may have had intermittent insufficiency, progressing stroke, or both, in the past, but at the time of the current examination the ischemic process had been completed.

These categories depend on the temporal relationship of the clinical neurologic deficit rather than on the degree or type of deficit or on the exact pathophysiologic mechanism involved.

Atherosclerosis is a factor in most patients with ischemic cerebrovascular disease. Delineation of its degree, namely, stenosis or occlusion, and of its location or locations, namely, intracranial or extracranial, is important, particularly when surgical therapy is contemplated. Since atherosclerosis, both extracranial and intracranial, is common, and may be asymptomatic, the clinical symptoms presented by the patient must be interpreted carefully.

SELECTION OF CASES

The primary goals of therapy for patients with these diseases, stated briefly, are to prevent cerebral infarction and to prevent extension of an evolving cerebral infarct. With these goals in mind we advised, from 1954 to 1958, the use of anticoagulants in

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the treatment of all patients, except when contraindicated, with incipient stroke and with progressing stroke (stages 1 and 2), but not for patients with a stable infarct. During the last 4 years, surgical management has been advised for patients with certain varieties of occlusive cerebrovascular disease, and anticoagulant therapy has continued to be used in the other patients.

Because anticoagulant therapy has been relatively successful, the surgical treatment of these patients has been approached rather cautiously. Other investigators (1) have reported an operative mortality, in all categories, of about 6 per cent, and we have had similar experience.

The diagnosis of ischemic disease was based on clinical examination; contrast arteriographic studies, generally of 4 major cerebral vessels, were performed, not as a primary diagnostic procedure, but to identify the site or sites and the completeness of the occlusive process. Since some risk has been associated with arteriography in patients with symptoms of ischemia, we selected for this procedure principally those patients who had some clinical evidence to suggest extracranial occlusive phenomena, such as alteration in the pulses in the carotid or subclavian arteries, the presence of bruits over these arteries, and differences between the blood pressures recorded in the 2 brachial and the 2 retinal arteries. Evidence for the presence of intracranial occlusive phenomena is commonly noted on arteriography and at present appears to be a contraindication for surgical procedures on the extracranial arteries. Furthermore, the patient's general health should be such that, if an operable lesion is demonstrated, the necessary operation can be performed with reasonable safety.

Comments concerning the actual surgical technique are beyond the scope of this report. However, it is important to note that in completely occluded arteries, normal circulation can be restored by a surgical procedure directed to that artery (endarterectomy) in less than 20 per cent of these patients. Even this is accomplished with some risk of cerebral embolization, since thrombotic material commonly extends distally beyond the occluded segment of the cervical vessel, and often it is not possible to control all of this clotted material at the time of operation. Because of the low incidence of restored circulation and the risk of embolization, we no longer recommend exploration of the cervical portion of the cerebral arteries that are judged to be occluded, except when the occlusion is near the aortic arch. In these special instances, a synthetic graft can be placed that bypasses the occluded segment, or when thrombo-endarterectomy is performed, control of the thrombotic material can be complete. Occasionally, a patient with occlusion of one internal carotid artery and stenosis of the other will have transient ischemic symptoms from the cerebral hemisphere or the eye ipsilateral to the occluded artery. In these instances, surgery may be directed at the stenotic artery to increase the total amount of blood supplying the brain.

Results of Therapy

For each clinical category comments will be made concerning the anticoagulant and the surgical treatment.

Patients with completed strokes, stage 3, were not treated by us with anticoagulant drugs. If new ischemic trouble occurs, and the condition of the patient falls into the categories of incipient or progressing stroke, then anticoagulation therapy can be used. Groch (2) presented evidence that the progress of carefully selected patients with completed strokes was better when anticoagulant therapy was started several days after the stroke than the progress of a similar group not given the therapy, particularly as to the occurrence of other disease. Similar experience was reported by Thomes (3) who found, over

several years, the incidence of new or additional strokes was lower in patients who received anticoagulant therapy than in those not so treated.

Our results in the 8 patients with stable infarcts, in whom we were able to restore the circulation by endarterectomy, are not different from those that might be expected from patients not given any specific therapy. As a consequence, no surgery is currently performed on patients in this category. Evidence to indicate that surgery on patients in this category is of long-term prophylactic value for preventing additional cerebral infarcts has not been accumulated as yet.

Progressing stroke, stage 2, seems to us to be of such a critical nature that we have continued to administer anticoagulants to the patients with this type of stroke, and surgical procedures have not been used. Our results with anticoagulant therapy continue to be good; on a statistical basis, mortality and morbidity rates have been lower in patients treated with anticoagulants than in similar patients not so treated. Heparin may be given as emergency treatment and its use continued until effective anticoagulation has been achieved with a coumarin derivative. In patients with actively advancing or progressive stroke in the carotid system, the proportion of those with hemiplegia or those who do not survive has been reduced from 35 per cent to 6 per cent by this therapy. In actively advancing stroke in the vertebral-basilar system, the mortality has been reduced from 58 per cent to 8 per cent (4).

Carter (5) studied 76 patients with progressive strokes and treated half of them with anticoagulants, the selection having been made by random sampling. The mortality among the treated patients was 8 per cent and that among the untreated patients was 18 per cent.

There has been considerable speculation about the results of immediate operation soon after a stroke occurs or as it is occurring. Data on this point have not been gathered, but an interesting case was reported recently (6). The patient had had transient ischemic attacks, each lasting for a few minutes, and arteriography had shown evidence of carotid stenosis. As the skin incision was being made, one of the characteristic attacks of hemiparesis occurred. Within minutes an endarterectomy was performed and normal blood flow was restored. The patient's hemiplegia persisted until his death a week after operation.

Patients with intermittent insufficiency, stage 1, are the ideal candidates for anticoagulant and surgical treatment.

From 1954 to 1958, we observed 335 patients with transient ischemic attacks for whom anticoagulant therapy was advised, unless specifically contraindicated. One hundred seventy-five patients received long-term anticoagulant therapy, and 160 did not receive it or received it only briefly. The follow-up period ranged from 3 to 8 years (7). The results are shown in Table 1. At the end of the period, 74.9 per cent of the treated and 51.9 per cent of the untreated patients were normal. The incidence of nonfatal cerebral infarction was 2.3 per cent in the treated groups and 20.6 per cent in the untreated group. The incidence of fatal cerebral infarction was 1.7 per cent in the treated group and 11.2 per cent in the group not treated. The incidence of fatal cerebral hemorrhage was higher in the group treated with anticoagulants (7.4 per cent *versus* 4.4 per cent) but this increase is minimal compared with the incidence of fatal thrombotic infarcts. No explanation is offered for the slightly higher incidence of unrelated (cancer, myocardial infarction, and trauma) fatalities in the treated group.

Thirty-two patients with transient ischemic attacks, selected as previously described, and each with a well-defined and appropriate occlusive lesion in an extracranial artery, have been treated surgically

TABLE 1. Anticoagulant Therapy for Cerebrovascular Intermittent Insufficiency: 3- to 8-year Follow-up in Stage 1, or Impending Stroke

Result	Treated		Untreated*	
	Number	Per cent	Number	Per cent
Normal	131	74.9	83	51.9
Cerebral infarct	4	2.3	33	20.6
Dead:	40	22.8	44	27.5
Cerebral infarct	3	1.7	18	11.2
Cerebral hemorrhage	13	7.4	7	4.4
Other unrelated causes	24	13.7	19	11.9
Total	175	100.0	160	100.0

* Or treated only for several months.

(8). Endarterectomy was performed in 30 of these patients and synthetic bypass grafts were placed in 2 patients.

Shortly after surgery, 25 patients (78.1 per cent) were normal on neurologic examination. However, several patients continued to have episodes of intermittent insufficiency, and a clinical diagnosis of recurrent thrombosis at the site of surgery was made in one patient.

Five patients (15.6 per cent) had a cerebral infarct at surgery or immediately thereafter; one of these patients died, and 4 had persistent neurologic deficits. Two other patients died postoperatively: one from a cerebral hemorrhage on the side operated on and one from myocardial infarction. The total operative mortality was 9.4 per cent.

The 32 patients who had surgery have been studied for 1 to 3 years. The follow-up results are shown in Table 2 and are contrasted with those of 48 patients who had intermittent insufficiency of the carotid system, received no treatment, and had clinical evidence of extracranial carotid atherosclerosis in the form of bruits or reduced retinal arterial pressures. Their follow-up period is longer. The group that had surgery includes the 3 patients who died in the immediate postoperative period. Seventy-five per cent of the treated group were normal, while 52.1 per cent of the untreated group were normal. The follow-up data show that the incidence of nonfatal cerebral infarction was 9.4 per cent in the treated group and 27.1 per cent in the group not treated; the incidence of fatal cerebral infarction was 6.2 per cent in the treated group and

TABLE 2. Intermittent Insufficiency: Results of 1- to 3-year Follow-up after Surgical Therapy with Circulation Restored Contrasted with Results in a Group Not Treated

Result	Treated		Untreated	
	Number	Per cent	Number	Per cent
Normal	24	75.0	25	52.1
Cerebral infarct	3	9.4	13	27.1
Dead:*	5	15.6	10	20.8
Cerebral infarct	2	6.2	6	12.5
Cerebral hemorrhage	1	3.1	1	2.1
Other causes	2	6.2	3	6.2
Total	32	100.0	48	100.0

* Includes 3 patients who died in the immediate postoperative period.

12.5 per cent in the untreated group. Thus, aside from the surgical risk, highly selected patients did well in the long run.

Conclusions

Examination of the data presented leads to the following conclusions and current opinions about the treatment used.

1. Patients with stable infarcts are not candidates for anticoagulant or surgical therapy in so far as the existing deficit is concerned. If new ischemic phenomena occur, specific treatment can be given depending on the manifestation of the ischemia. The data suggest that these therapies have a long-term prophylactic value against further cerebral infarcts, but this conclusion is not completely documented.

2. Patients with evolving stroke respond well to anticoagulant therapy. We do not believe surgical therapy has been shown to improve the statistical results in these patients.

3. Patients with intermittent insufficiency can be benefited either by anticoagulant therapy or by surgical therapy as measured by long-term prevention of cerebral infarction.

a. With only rare exceptions anticoagulant therapy may be given to all of these patients for long periods, but with some risk of unwanted hemorrhage.

b. At present, surgical therapy can be applied principally to those patients whose arterial lesion is extracranial and stenotic in type. Arteriography should be performed although it carries some risk. Although the operation itself is associated with some morbidity and mortality, it provides long-term prophylactic value against cerebral infarcts.

Summario in Interlingua

Es discutite le tractamento a anticoagulante e le therapia chirurgic pro patientes con (1) transiente attaccos ischemic, (2) progressive accidente cerebro-vascular, e (3) infarcimento complete.

Patientes con transiente attaccos ischemic (insufficientia intermittente) pare beneficiar del un e del altere therapia, a judicar per le criterio del prevention a longe vista de infarcimentos cerebral.

Patientes con progressive (o evolutive) accidente cerebro-vascular responde a therapia a anticoagulante, e le methodo del intervention chirurgic ha non producite clarmente meliorate resultatos statistic in iste gruppo.

Patientes con infarcimento completate (i.e. stabile) non es candidatos pro le un e non pro le altere typo de therapia, in tanto que le existente deficit es concernite. Datos pro le effecto de un prophylaxia a longe vista ha non essite determinate.

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