Cerebrovascular disease is the most common life-threatening neurological event in the US. Intracranial atherosclerosis is responsible for approximately 40,000 of these events per year, representing 10% of all ischemic strokes. In general, intracranial atherosclerosis is associated with several risk factors, many of which are the same as those for coronary artery disease. These include non-caucasian race, diabetes, hypertension, hypercholesterolemia, and cigarette smoking. Unfortunately, there are currently few treatment options for intracranial atherosclerosis, and despite maximal medical therapy, the prognosis for patients with this condition remains poor.

Endovascular procedures, which have recently gained popularity in the treatment of intracranial atherosclerosis, have tremendous potential to alter the current standard of care for cerebrovascular disease. These techniques, however, carry substantial risks, and their benefit must be weighed against the prognosis for conservative management in this patient population. In this paper we critically review relevant studies of medically managed intracranial CA atherosclerosis in an attempt to understand better the pathophysiological features and natural history of this condition.

Pathophysiological Features of Intracranial Atherosclerosis

The CA is the most frequent site of intracranial stenosis, accounting for approximately 50% of cases. The overwhelming majority of these are diagnosed when the patient presents with an acute ischemic event, either stroke or a TIA. Published data in studies in which transcranial Doppler ultrasonography and/or cerebral angiography were used have shown intracranial stenoses to be dynamic lesions that may undergo progression, regression, or remain stable during the follow-up period with medical treatment alone. The factors associated with atherosclerotic progression, however, have yet to be elucidated. In addition, current imaging modalities do not accurately predict the natural history of these lesions, leaving clinicians with difficult management decisions.

Our understanding of the pathological features of atherosclerotic plaque is based largely on autopsy studies. In comparison with white plaques, yellow plaques are more commonly found in the setting of acute coronary syndromes, indicating that yellow plaques have a higher level of mechanical vulnerability. Yellow plaques, however, become white plaques over time, potentially representing a healing process. Unfortunately, in vivo morphological data are still lacking because of limitations in angiographic and ultrasonic technology.

Intracranial atherosclerosis may lead to stroke by three mechanisms: 1) perfusion failure; 2) local thrombosis with arterioarterial thromboembolism; and 3) occlusion of penetrating arteries. Each of these mechanisms results in different pathophysiological features with relevance to endovascular treatment. Perfusion failure occurs when the
Addressing the issue of proper medical management of symptomatic intracranial atherosclerosis, the Aspirin Versus Anticoagulants in Symptomatic Intracranial Stenosis trial, is underway. We hope that the results of this study will clarify this topic and delineate the most efficacious management of the disease in this patient population.

**Prognosis of Patients With Intracranial CA**

**Atherosclerosis**

In the largest retrospective series, Borozan, et al., reviewed the outcomes in 93 patients with angiographically documented intracranial stenosis of at least 20%. Seventy-one patients had unilateral and 22 had bilateral disease; 24% were symptomatic. Over a mean follow-up period of 22.5 months, 23% of patients died; cardiac disease was the cause of death in six individuals (6.5%). The annual ipsilateral stroke and mortality rates were 5.1 and 10.3%, respectively. These individuals were identified among 885 consecutive patients in whom cerebral angiograms were obtained.

Marzewski, et al., published the first detailed review regarding the outcomes in 66 patients with angiographically documented intracranial ICA stenosis of at least 50%; 41% of these patients were symptomatic. Over a mean follow-up duration of 3.9 years, 12.1% of patients experienced an isolated TIA in the ICA territory and 15% suffered a stroke. In this study, 50% of patients died during the follow-up period; cardiac disease was the cause of death in 18 individuals (27.2%). The ipsilateral stroke rate was 3.1% annually.

Another retrospective series was published by Craig, et al. These authors reviewed the outcomes in patients with angiographically documented intracranial stenosis of at least 30%. Of these 58 patients, 81% were symptomatic. After a mean follow-up duration of 30 months, the authors found that 43% of patients experienced an isolated TIA or stroke in the ICA territory. In addition, 43% of patients died during the follow-up period; cardiac disease was the cause of death in 11 individuals (19%). The annual ipsilateral stroke and mortality rates were 7.6 and 17.2%, respectively. Of interest, there were no differences between the death rates in symptomatic (42%) and asymptomatic (45%) patients.

Bogousslavsky reviewed the outcomes in 22 patients with angiographically documented intracranial stenosis of at least 30%. Over a mean follow-up period of 40.4 months, 32% of patients died; cardiac disease was the cause of death in six individuals (27.3%). The annual ipsilateral stroke and mortality rates were 8.1 and 9.5%, respectively.

Wechsler, et al., reviewed the outcomes in 15 patients with angiographically documented intracranial stenosis of at least 50%; 80% of these patients were symptomatic. Over a mean follow-up period of 51 months, 20% of patients suffered a stroke in the ICA territory. In this study, 20% of patients died during the follow-up period; cardiac disease was the cause of death in two individuals (13.3%). The annual ipsilateral stroke and mortality rates were 3.1 and 4.7%, respectively. An important finding in this study was that the initial clinical presentation correlated with the presence of hemodynamically significant stenosis; 71% of symptomatic patients had evidence of impaired flow on
angiography. In comparison, only 20% of asymptomatic patients had similar findings. The authors hypothesized that the strokes were the result of embolism distal to the stenosis and that TIAs were the result of slow flow.

The aforementioned studies reveal annual mortality and ipsilateral stroke rates ranging from 4.7 to 17.2% and 3.1 to 7.6%, respectively. Nevertheless, these investigations have limitations that must be taken into account when interpreting their results. First, each is subject to retrospective bias due to the study design. Second, the patient populations are highly selective and variable, with availability of cerebral angiography studies as an entry criterion and degrees of stenosis ranging from 20 to 70%. Third, the cohorts are small and heterogeneous, and the severity of ipsilateral stroke is not clearly defined. Regardless of their limitations, however, these studies indicate that patients with intracranial CA atherosclerosis are at high risk for recurrent stroke or death and that medical management frequently fails in their treatment. Future prospective investigations are needed to clarify the prognosis for these patients.

CONCLUSIONS

Despite maximal medical management, intracranial CA atherosclerosis continues to portend a poor prognosis. Conservative management frequently fails in this disease, leaving patients at high risk for cerebral infarction and death. Given the natural history of this condition, advancements in its treatment, particularly those related to endovascular methods, are of the utmost importance.

References


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