Neurology, Neurosurgery, Controlled Trials and Academic Accountability

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There is concern by those in both neurology and neurosurgery over how best to test the soundness of treatment procedures. Differing opinions regarding the effects of various clinical treatments recently flared with the development of microsurgical techniques. Specifically, the report of Yasargill showed that it was possible to connect the temporal artery to a branch of the middle cerebral artery (extracranial-intracranial [EC/IC] bypass), to have the anastomosis remain patent, and thus to increase circulation in patients with ischemic lesions inaccessible for carotid endarterectomy. The EC/IC bypass operation was quickly taken up by younger neurosurgeons. The techniques and instrumentation were improved, and EC/IC bypass surgery became standard for patients with transient ischemic attacks due to upper internal carotid or middle cerebral artery obstructive lesions.

There was some concern among neurologists and neurosurgeons, however, that although the operation was technically feasible, it might not necessarily benefit the patient who received it. Their attention prompted a cooperative study to evaluate the effects of EC/IC bypass surgery. Patients and controls were randomly selected, and all subjects were followed long enough to determine whether there was any difference in stroke occurrence or any decrease in the frequency of transient ischemic attacks or other manifestations of cerebral vascular disease.

The study was reported in detail in 1985 and revealed no evidence that EC/IC bypass surgery was beneficial for patients with transient cerebral ischemic symptoms. The design of the study may well have produced the best randomly controlled trial of a surgical procedure yet performed, and it has been difficult for critics to find serious flaws in its conduct or its results. Yet, some surgeons who were actively performing this operation outside the study have taken issue with the results, saying that the data were distorted by not taking into account their patients. These surgeons argued that patients outside the controlled study were different from those in the study and that they represented a group that might especially benefit from EC/IC bypass surgery. Reanalysis of the study data has failed to show that not considering these patients influenced the results.

This seemingly straightforward evaluation of a proposed treatment encountered considerable difficulty in enlisting neurosurgical departments at academic centers in the United States to join and contribute subjects to the study. Many departments were committed initially, but some later dropped out because they believed that EC/IC bypass surgery had already been proven effective and therefore should not be denied to any subject deemed suitable. As a result, subjects had to be recruited from many more centers, some outside the United States, to obtain the number of subjects needed to draw a reliable conclusion. This prolonged the study by several years and caused a curious arrangement in which some academic centers in the United States were involved in trying to settle the issue of efficacy while other equally prominent academic centers were performing many EC/IC bypasses. Several uncontrolled series showed that patency of the anastomosis was possible and that the channel did contribute to cerebral blood flow, thus suggesting that EC/IC bypass surgery was effective.

Controlled trials for neurologic science were actually introduced into the United States by a leading neurosurgeon in the United Kingdom, Dr. Wiley McKissock, best known in his time for the surgical treatment of cerebral aneurysm. In 1958, he stated that after 20 years of dealing with the problem of aneurysm and subarachnoid hemorrhage, he was convinced that all of the operations he had performed had not made any difference for his patients (personal communication). At that time, Dr. McKissock and his associates began three very important controlled studies with random allocation of patients with subarachnoid hemorrhage from anterior cerebral artery aneurysm, middle cerebral artery aneurysm, or posterior communicating artery aneurysm to either treated or control groups. His reports indicated that surgery for aneurysm had little, if anything, to offer compared with medical treatment. His work became the impetus for a similar project in...
the United States that eventually led to a national cooperative study of the complex problem of surgical versus medical management of aneurysms. The cooperative study has provided important information on the surgical care of aneurysms by gathering data on the natural history, the value and optimal timing of surgery, and the proper selection of patients.

It is now standard for neurologists or neurosurgeons to report scientific data on the treatment of subarachnoid hemorrhage and aneurysm only after carrying out a study in a carefully controlled manner. However, controlled preliminary studies have not always been the standard, and many surgical procedures designed to prevent stroke have been used without first carefully gathering data on the effectiveness of the operation. Perhaps the most notable example relates to the value of carotid endarterectomy for the prevention of stroke in patients with transient ischemic attacks or asymptomatic bruits. Many thousands of endarterectomies are carried out yearly in the United States, yet there is concern that the procedure does not produce the expected benefit and that possibly half (or more) of the operations are actually unnecessary.

A controlled study of carotid endarterectomy was completed in the mid 1960s with mixed results, and the study is now being redone to gather data to settle this question.

The difference in standards of accountability between neurosurgeons and neurologists is wide. Currently in the United States, it is virtually impossible for a clinical neuroscientist to make claims that a new drug relieves symptoms or prevents disease without very careful, long-term, controlled studies comparing the drug with a placebo. In fact, it is practically impossible for a new drug to be approved by the Food and Drug Administration without such background information. On the other hand, the attitude that a technically successful operation is a good one and therefore is of benefit to a patient is often held even though evaluation of the effect of this procedure over time may lead to abandoning it when it is no longer deemed useful. A surgical treatment for a disease with a variable and long natural history needs to be evaluated carefully to prove that the treatment results are not due to chance and that the natural history of the disease has been altered in favor of the patient. It defies imagination to think how many patients had unnecessary prefrontal lobotomies or sympathectomies that would not have been considered useful had these operations been subjected to carefully controlled trials.

Newly suggested neurosurgical techniques performed in the United States often have not been subjected to protocol evaluation since evaluations of this kind could pose problems for their development. It is difficult to develop a new surgical technique unless the condition being treated is so serious, so life-threatening, or so certain to produce major disability that there is little to lose by trying a new treatment. But once a surgical technique has been developed, a controlled trial proving its efficacy should be carried out before sides are drawn between those who are sure a procedure is effective and those who are uncertain because of lack of data. The rationale for a new surgical technique should be as sound as that required for the development of a new drug.

It is most alarming that few clinical neuroscientists in neurosurgery in the United States have voiced support for carefully controlled evaluations of treatments for their patients. There were many arguments about the inadequacy of the national cooperative study on EC/IC bypass surgery when it was being conducted, yet few leaders in neurosurgery in medical schools in the United States were willing to state publicly that they would not carry out this operation without controlled experimental protocols to determine its value. If those in academic neurosurgery are not accountable for determining that new knowledge and new procedures are truly worth the risk for a sick patient, then who will stand for establishing the efficacy of surgical procedures? It matters little whether large clinical services with no academic pretensions perform new operations once a month or 10 times a day. Those institutions that do claim academic standing and do have academic authority should be the ones to stand for the careful gathering of accurate information regarding the usefulness and benefits of any treatment program, whether surgical or pharmacological.

References
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Controlled Trials


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