IN 1967 Donaghy and Yasargil both reported a new surgical procedure designed to circumvent an occluded internal carotid artery. The introduction of extracranial/intracranial arterial bypass surgery was heralded as a significant advance in the treatment of cerebrovascular disease. Because of the inherent logic of the operation, the creation of an anastomosis between the superficial temporal artery and a branch of the middle cerebral artery quickly appealed to the neurosurgical community. For the first time a surgical procedure seemed to be available for those patients with symptomatic atherosclerotic lesions of the internal carotid or middle cerebral arteries that could not be dealt with by direct endarterectomy.

In the first decade after the introduction of intracranial/extracranial bypass procedures many reports appeared to indicate that the operation could be performed with relatively low morbidity and mortality, and the techniques could be improved to ensure a high degree of patency of the anastomoses. This was followed by anecdotal reports of improvement in patients undergoing the procedure. The indications for the operation proved a somewhat more difficult question to answer. There was widespread acceptance of the procedure as a prophylactic measure in patients with TIAs or small strokes to prevent progression to major cerebral infarction. A smaller group of neurosurgeons went so far as to claim that the operation was of benefit to patients with major completed strokes.

In an effort to avoid the problems that had evolved in the use and evaluation of carotid endarterectomy for TIAs, asymptomatic bruits and strokes, a cooperative study to test the hypothesis that intracranial/extracranial bypass procedures could reduce the incidence of stroke and death in a well-defined population was organized in 1977 under the leadership of Dr. Henry J. M. Barnett. When the study was started, neurosurgeons with demonstrated interest and established expertise in performing intracranial/extracranial bypass procedures were recruited widely in the U.S. and Canada to contribute patients. The response was disappointing as many surgical groups had concluded that the operation was both useful and effective and therefore did not need to be studied in a randomized fashion. Because of the inability to persuade enough surgeons in North America to enter the study, additional centers were sought in Europe and Asia. This created concern among both the organizers of the study as well as its critics since such an approach might be incapable of testing the hypothesis because more centers would each be contributing small numbers of patients. This development increased the need for careful selection of centers, surveillance of patient selection, surgical technique and follow-up assessment. It was essential that so diversified a study did not distort the results and render the study unreliable because of wide variation in neurosurgical and medical care.

The report of the International Cooperative Study of Intracranial/Extracranial Arterial Anastomosis (EC/IC Bypass Study) has now been published. It is a landmark study because of its size, duration, and careful attention to the details. In contrast to earlier cooperative studies on the surgical treatment of stroke, it seems to provide some definitive answers to the original question. This question, could intracranial/extracranial bypass surgery reduce the risk of subsequent stroke and stroke-related death in patients with transient ischemic attacks and mild stroke by 33%, formed the central hypothesis of the study. The patients selected for the study were those with TIAs or mild stroke who had angiographic evidence of occlusion or stenosis in the internal carotid or in the initial segment of the middle cerebral artery that were not amenable to direct approaches. To obtain a satisfactory answer, a randomized study was proposed. An estimated fourteen hundred patients were needed with 700 in both the surgically and medically treated groups to be able to achieve statistical validity. The initial report of the study outlined the methodology used and reported on the success of the random allocation of patients to each group. The two groups were almost identical for age, sex, race, occurrence of TIAs, severity of stroke, and other medical problems.

By September 1982 the required number of patients had been entered and the follow-up assessments were well underway. To the great credit of the principal investigator and his colleagues no patient who entered the study was lost to follow-up. Follow-up was equally good from centers that contributed large numbers of patients and those that contributed smaller numbers. Ninety-eight percent of those allocated to surgical treatment had the bypass performed. The overall bypass patency rate was 96% and did not differ significantly between centers or by location in North America, Asia or Europe.

The data obtained from follow-up has been analyzed, and it is clear that extracranial/intracranial arterial bypass surgery utilizing an anastomosis of the su-
perforated temporal artery to the middle cerebral artery
does not provide protection in preventing subsequent
stroke or stroke-related death. This result has been
carefully analyzed and does not appear to be influ-
enced by a number of factors including the type of
arterial lesion found on cerebral angiography whether
occlusion or stenosis, the presence of complicating
medical diseases, the side of the ischemic event, the
age or sex of the patient, or the size or location of the
participating center. The number of single strokes that
occurred during follow-up was almost identical in the
two groups, 18% of the medically treated and 20% of
the surgically treated patients; more than one stroke
occurred in 10% of the medical group and in 11% of
those assigned to surgery.

Analysis of several subgroups of patients in whom a
benefit might have been anticipated also failed to re-
veal any significant benefit of extracranial/intracranial
arterial bypass surgery. Those situations in which by-
pass surgery was most likely to provide benefit such as
internal carotid artery occlusion, severe distal (siphon)
stenosis, and recent onset of TIA's were analyzed sepa-
ately. No evidence of benefit from surgery was found.
The concept that improving cerebral blood flow to an
area which has become ischemic or has marginal flow
might improve the outcome was investigated. The
functional status of both groups of patients during fol-
low-up was compared; there was no difference in the
number of medically or surgically treated patients who
improved, remained the same or died. The effect of
surgery on recurrence of TIA's in those patients who
originally presented with these events was evaluated,
and no difference was observed in the frequency of
TIA's between the two treatment groups. Identical per-
centages of patients in each group experienced a mini-
num of a 50% reduction of TIA's.

In patients with middle cerebral artery stenosis or
in those with internal carotid artery occlusion and
continuing TIA's, extracranial/intracranial arterial by-
pass surgery was found to have a higher incidence of
stroke and stroke-related deaths than nonsurgical
 treatment. Of even greater interest was the finding that
those patients who developed a stroke after a patent
EC/IC bypass had been established did not fare better
than the group of medically treated patients who sus-
tained cerebral infarctions during the course of the
study. Benefit from surgery in these two categories of
patients might have been expected by even the most
skeptic physician.

Another strikingly negative outcome was the com-
parison of those patients with poor angiographic ap-
pearance of the bypass with those with excellent by-
passes on the post-operative studies. Outcome was no
better in those patients with the best angiographic flow
through the bypass than in those with the poorest flow.

An important part of the study was the meticulous
follow-up. Not a single patient was lost to follow-up
and patient assessment was excellent. Fortunately the
results leave little doubt about the value of extra-
 cranial/intracranial arterial bypass surgery. Too often
studies of this sort leave the medical community uncer-
tain as to whether surgical procedures are useful or not
because of poor study design, inadequate follow-up or
indefinite results. This often leads to misuse of the
procedure usually in the form of too frequent use. The
conclusion that fatal and non-fatal stroke are not pre-
vented by extracranial/intracranial arterial bypass sur-
gery in the overall study or in the subgroups examined
is strengthened by the size and care of the study, the
evenness of the randomization and the uniformity of
the population studied. The high percentage of patency
and the low surgical morbidity and mortality, as good
as reported in any of the non-controlled studies in the
literature, leave no room to fault the design of the
study. Many centers were involved, but all measured
up to the high standards set by the investigators.

Several "internal controls" add strength to the lack
of support for the central hypothesis. There was no
benefit seen in those patients with excellent bypasses
when compared with the poor anastomoses as analyzed
by post operative angiography. There was no differ-
ence in the degree of reduction of TIA's in the medical-
ly or surgically treated patients. Finally the outcome of
those patients who sustained a stroke after randomiza-
tion was no different in the medical or surgical group.

Is this a "negative" study? The answer to this ques-
tion is emphatically "no". For the first time a rigorous
study with "state of the art" methods for clinical trials
has looked at a widely accepted surgical procedure.
The first reaction of neurosurgeons and neurologists
must be one of disappointment since a logical oper-
ation way for future investigation. Why is increased CBF
ineffective in preventing stroke or mitigating the extent
of the infarct once the bypass is established? Perhaps
the approach to stroke has been too simplistic. In re-
cent years most attention has been focused on large
vessel disease as the primary etiologic factor. Platelets
and the larger vessels supplying the brain may not be
the only cause of stroke. It may lie at the microvascular
level in the endothelium or systemically in the blood
perfusing the brain. Undoubtedly some will try to res-
cue the procedure. It may still have applications but
not for the prevention of stroke due to atherosclerosis.

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References
Georg Thieme Verlag, St. Louis
2. The EC/IC Bypass Study Group. Failure of Extracranial/Intracranial
Arterial Bypass to Reduce the Risk of Ischemic Stroke. Results of an
1985
3. The EC/IC Bypass Study Group: The International Cooperative
Study of Extracranial/Intracranial Arterial Anastomosis (EC/IC By-
pass Study): Methodology and Entry Characteristics. Stroke 16:
397-415, 1985
EC/IC Bypass Study.
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