Despite the advances in surgical techniques, cardiopulmonary bypass circuits and the medical treatment of patients subjected to cardiac surgery, perioperative complications involving the nervous system continue to develop and the underlying mechanisms are sometimes poorly understood. Neurological complications (NC) in these patients can affect the brain, spinal cord and peripheral nerves. However, the involvement of the central nervous system, and cerebrovascular involvement in particular, is the most common adverse event. It is associated with high rates of morbidity and mortality, longer hospital stays and greater utilization of health care resources, in addition to the severe financial and social distress that these complications bring upon the patients and their families.

The incidence of NC following cardiac surgery depends on the methodology employed for its diagnosis, on the terminology utilized and on the application of a prospective or retrospective approach in its evaluation. In a recent report assessing the type of surgery performed, NC (transient ischemic attack or stroke) presented in 1.7% of the patients undergoing coronary revascularization, in 3.6% of those having single valve replacement, in 3.3% of those subjected to both procedures and in 6.7% of those undergoing multiple valve replacement. These values agree with those reported for previous series, which indicated a greater number of NC after valve replacement than after coronary revascularization. In fact, in some series of patients subjected to valve replacement, an incidence of stroke of up to 16% has been observed.

The pathogenesis of these complications remains uncertain. The pathogenic mechanisms traditionally proposed are systemic hypoperfusion and embolic events (clearly documented by transcranial Doppler ultrasound) involving macroemboli and microemboli originating in the aorta, the cardiac chambers or in the cardiopulmonary bypass circuit itself; NC is less common in patients undergoing coronary revascularization without an extracorporeal pump. Pathological studies show diluted arterioles and capillaries that suggest the presence of microemboli in the distal bed as the cause of these complications. The presentation of NC later on in the postoperative period appears to be related to other causes; among the factors associated with the development of stroke several days after the surgical procedure are anemia, reactive thrombocytosis, a procoagulant state and the presence of certain arrhythmias, mainly atrial fibrillation.

A number of single-center and multicenter studies, both prospective and retrospective, have attempted to identify the preoperative, intraoperative and postoperative variables associated with the development of NC following cardiac surgery. Unfortunately, the terms utilized to define these complications are often imprecise and the neurological symptomatology associated with each is overly heterogeneous. The multicenter study, McSPL, which assessed the neurological events following coronary revascularization, perhaps assuming a focal cause or diffuse brain injury, classified NC into two groups: type I, comprising focal lesions or those causing a state of unconsciousness or coma at the time of discharge, and type II, which includes intellectual deterioration, memory deficits and convulsive seizures. In the latter group, the variables associated with poor prognosis are older age, chronic lung disease, hypertension, alcohol abuse, peripheral arterial disease or previous coronary revascularization, postoperative arrhythmia (mainly atrial fibrillation) and antihypertensive therapy. However, although advanced age and bronchial disease are also associated with the incidence of NC in patients in the first group, we find other risk factors, such as the presence of...
Zabala JA. Neurological Complications of Cardiac Surgery

proximal aortic atherosclerosis, previous cerebrovascular disorders, diabetes mellitus and the use of intraaortic balloon counterpulsation, all of which show highly significant correlations. According to other studies, the variables associated with the presence of stroke after cardiac surgery are chronic renal failure, recent myocardial infarction, carotid artery stenosis, moderate-to-severe left ventricular dysfunction, low cardiac output and the presence of atrial fibrillation. Intraoperative variables, such as the duration of aortic cross-clamp time, hemodynamic changes and cardiopulmonary bypass time, are also associated with NC. Although the influence of sex as a predictor of poor prognosis has been widely discussed, women present a greater number of perioperative neurological events following any type of cardiac surgery, and the 30-day mortality is greater when they occur.4

In most of the published series, cerebral infarction is considered as a single variable, independently of the time of presentation and the infarct subtype; however, these 2 variables may be correlated with the etiology of this condition. If we classify the strokes as early (those occurring intraoperatively and detected at the time of emergence from anesthesia) and late (those that present after emergence involving no abnormal neurological signs), we observe that 65% of infarctions occur late and that, of the variables studied, the presence of atrial fibrillation with a low cardiac output is associated in a fundamental way with late stroke; this circumstance obliges us to be aggressive in the therapeutic management of these 2 complications. It has been suggested that the etiological and pathogenic mechanisms, in this case, could be related to intracardiac thrombus formation. In other series studied, a high rate of cerebrovascular events is observed even several days after the surgical procedure. In fact, nearly 40% of infarctions are produced from the third postoperative day.

From the strictly neurological point of view, it is important to stress the few references made to the different subtypes of stroke and the various cerebrovascular syndromes presented by these patients. These subclassifications can and should be relevant when it comes to raising the question of possible etiological and pathogenic correlations. In the analysis of a series of 2211 patients who had undergone cardiac surgery, 44 (2%) presented perioperative cerebral infarction; 70% of them presented a hemispheric syndrome, 14%, a vertebrobasilar syndrome and 16%, a lacunar syndrome. In 29 of these patients, computed tomography revealed the presence of new infarctions, 20 of which were territorial, 5 lacunar and 4 corresponded to a watershed territory. It should be pointed out that all the patients who presented infarction in a watershed territory had been subjected to cardiopulmonary bypass for more than 120 minutes; this may be related to the concept that watershed infarctions basically reflect low distal flow, although we can not rule out the possibility of the presence of distal microemboli. Territorial infarctions are not as closely related to the cardiopulmonary bypass time; their presence has been more widely associated with emboli originating in the ascending aorta or the cardiac chambers. Since they were first described, lacunar infarctions have been associated with arterial lipohyalinosis related to chronic hypertension. The presence of lacunar infarctions following cardiac surgery may appear to be somewhat surprising; however, recently, the role of emboli in lacunar infarctions in general is increasingly being reported, and it is calculated that they may be the cause of up to 20% of these infarctions.

Patients subjected to cardiac surgery frequently report symptoms that they had initially considered to be of little importance. “I’m unable to concentrate on things,” “I can’t perform well at work,” “I have trouble thinking” are some of the complaints repeated to neurologists by patients that have undergone heart surgery. Likewise, signs of psychiatric disorders (depressive or psychotic), sleep-wake cycle disturbances or evident cognitive deterioration are commonly detected and lead us to suspect that the stroke and other clearly visible complications (epileptic seizures, stupor, coma, etc) are a part, and probably the minor part, of the overall NC of these patients. The incidence of cognitive deterioration is directly related to the number and complexity of neuropsychological tests performed. The comparison of the studies on the incidence of cognitive changes is complicated by the different methodologies utilized. In the immediate postoperative period, intellectual deterioration is observed in over 80% of the patients. These sequelae may disappear over time, but frequently persist for months or even years. The etiology and pathogenesis of these processes is more complex since, in addition to the possible participation of embolic phenomena, undoubtedly, overall hypoperfusion, metabolic changes, hypothermia, the drugs administered, prior neuropsychological status, etc, influence the course.

In addition to the clinical evaluation, a number of techniques have been employed to assess and quantify perioperative NC. Neuropsychological tests such as electroencephalography and evoked potential measurement provide little information on the etiology of these processes. Doppler ultrasound of the brachiocephalic trunk is a highly sensitive, noninvasive test performed preoperatively in candidates for surgery, and it should be carried out systematically in those patients with clinical signs of or in whom there is reason to suspect coronary or systemic atherosclerosis. In addition to revealing the presence of microemboli during cardiopulmonary bypass, transcranial Doppler could be useful for monitoring cerebral perfusion during cardiac surgery. Serum biochemical markers, both glial and neuron-specific, have been used to confirm brain da-
mage, mainly in patients with postoperative cognitive deterioration. High levels of both the protein S100β and neuron-specific enolase are observed in these pa-
tients. However, these determinations present many limitations: a number of conditions, such as hemo-
sis, renal failure, etc, can interfere with their quantifi-
cation; the results vary enormously depending on the sampling time; they are not specific markers, since their levels can be elevated in other neurological disor-
ders and there is a direct relationship between them and the volume of brain damaged. This means that, on occasion, patients with strategic infarcts associated with marked neurological changes (paralysis due to in-
ternal capsule involvement, frank dementia due to a strategic basal ganglia infarct) may present lower le-
vels than patients with subtle neurological damage.

Imaging techniques have proved to be useful in the diagnosis and clinical management of a considerable number of patients with NC following cardiac surgery, but the results raise more questions, and the findings shed no light on the etiological and pathogenic doubts arising in many cases. Cranial CT is useful for ruling out hemorrhagic lesions and, in ischemic diseases in-
volving large vessels, for detecting parenchymal changes in a very high percentage of cases. In patients with cognitive complications or decreased level of consciousness, cranial CT is frequently normal.

Conventional magnetic resonance (MR) offers greater sensitivity for the visualization of small is-
chemic lesions in the vertebrobasilar territory, in very distal branches and in deep territories. With this im-
aging method, some authors detect new ischemic lesions in more than a third of cardiac surgery patients, but in other studies, the results are negative. In this issue of REVISTA ESPAÑOLA DE CARDIOLOGÍA, a group of authors describes the contribution of cranial MR in a series of patients with perioperative NC. Of 668 pa-
tients subjected to surgery for different heart diseases, 8.28% developed NC, which were divided nearly equally between stroke and encephalopathy, which was predominantly mild. Brain CT performed within the first 24 hours was normal, a finding that is not sur-
prising since it is a well-known fact that a high per-
centage of CT scans are normal during the early postinfarction hours, or revealed only indirectly rela-
ted anomalies (loss of the gray matter-white matter in-
terface, cortical sulcal effacement, etc). In 18 patients, in whom the clinical neurological signs persisted and in whom a second CT scan continued to be normal, conventional MR was carried out with T1-weighted, T2-weighted and fluid-attenuated inversion recovery (FLAIR) sequences. In 10 of the 11 patients presen-
ting the clinical signs of stroke, areas of acute or sub-
acute infarction were observed and, in 6 of the 7 cases of encephalopathy, ischemic lesions similar to those encountered in stroke were visualized. (In the patient in whom MR was normal, the symptoms were mild.)

In those cases in which follow-up CT reveals no changes, conventional MR may be of value in detect-
ting parenchymatous lesions that substantiate the clinical findings. The presence of new ischemic le-
sions on MR does not guarantee a correlation with the clinical condition of the patient; in fact, ischemic lesions are observed in a high percentage of cases (21%) in which no clinical signs are observed, a cir-
cumstance that some have referred to as subclinical.

Given the clinical features of coronary patients, it is common to find ischemic changes in preoperative conventional MR. Diffusion-weighted MR enables us to differentiate acute ischemia from chronic ischemia, as well as to visualize it earlier and detect very small lesions. This technique has been used to study patients who had undergone coronary revascu-
larization, and the attempt has been made to correlate the findings with the neurological and neuropsycho-
logical complications. In 26% of the patients stud-
died, very slight signal changes which, in somewhat more than half of the cases, are bilateral. It is inter-
esting to note that these patients do not present focal clinical neurological or significant anomalies in neuropsychological tests. In patients subjected to aortic valve replacement, the results are very simi-
lar. In diffusion-weighted MR, 38% of the surgical patients presented new ischemic lesions. Of these, 21% presented focal clinical signs and the imaging study revealed both territorial infarcts and small, nonspecific lesions. In the remainder of the patients, the presence of lesions was not associated with apparent clinical changes.

The temporary postoperative neuropsychological deterioration is associated with a transient disorder of neuronal metabolism. MR spectroscopy reveals a de-
crease in the N-acetylaspartate/creatine ratio due to the lower level of the first metabolite, and this is accompa-
nied by the presence of changes in the neuropsycho-
logical tests. Ten to 14 days later, both the ratio and the neuropsychological features are restored to nor-
mal.

With the advances in imaging techniques, our knowledge of perioperative NC increases in terms of both practical and theoretical aspects. However, the findings raise new questions: how can we explain the presence of relevant clinical changes if imaging stud-
ies are normal? Are the subclinical lesions observed really subclinical? Should the image be the indispen-
able requirement for possible clinical trials? Which imaging technique should be employed? Which is more valuable: the clinical signs or the image? Etc.

Neuropsychological complications continue to be a com-
mon cause of morbidity and mortality during the post-
operative period following cardiac surgery. Although a great deal of progress has been made, many questions still remain to be resolved. The research in this respect is complex, given the numerous variables to be consi-
dered. Although it appears to be a contradiction in terms, the first concerns the multitude of specialists involved in the management of these patients and their excessively partial and limited vision of the course of the latter. Who hasn’t heard, “my actions had nothing to do with it” or “did my part go okay”? Cardiac surgeons, cardiologists, anesthetists, neurologists, psychiatrists, neuropsychologists, neuroradiologists, neuropathologists, biochemists, pathologists, etc, should cooperate in a joint effort in the study of these patients. Another major problem to be considered is the imprecise terminology that has been utilized on occasion, with different clinical conditions grouped under the same term or similar clinical entities classified separately. From the etiological and pathological points of view, is dementia due to strategic infarcts in the basal ganglia different from a capsular infarct that provokes a hemiparesis? The third important inconvenience is related to the large number of risk factors that must be assessed. The basal condition of the patient and the perioperative and postoperative variables should be systematized. The preoperative neurological evaluation of the patient should be exhaustive, with clinical assessment, brain MR, Doppler ultrasound of the brachiocephalic trunks, transcranial Doppler, neuropsychological tests, etc.

These studies, their follow-up and the number of parameters to be evaluated result in yet another considerable problem: the cost entailed in carrying out these tasks both in terms of personnel (time) and funding. Despite the inconveniences summarized here, the performance of multidisciplinary and multicenter studies would be worthwhile. They would enable the identification of the patients at high risk of cerebrovascular complications, who would be the major beneficiaries in the near future of neuroprotective therapies presently under development, and would also be the target group for the reduction of modifiable risk factors (endarterectomy, adjustment of the intraoperative arterial blood pressure, etc).

REFERENCES