Editorial
Finding a compromise between the heart and the brain: strategies for stroke risk reduction in coronary artery surgery

Gianfederico Possati, Mario Gaudino

Department of Cardiac Surgery, Catholic University of the Sacred Heart, Rome, Italy

(Ital Heart J 2002; 3 (3): 146-150)

Received March 19, 2001; revision received February 27, 2002; accepted February 28, 2002.

Address:

Prof. Gianfederico Possati

Divisione di Cardiochirurgia Università Cattolica del Sacro Cuore Policlinico A. Gemelli Largo A. Gemelli, 8 00168 Roma E-mail: possati@tiscalinet.it

Perioperative stroke is probably the most devastating complication of coronary artery surgery with major clinical, social and economic implications.

The current incidence of perioperative stroke is 0.3-3.2% in retrospective series and 1.5-5.2% in prospective studies[1-3]. Of note, despite the progressive reduction in the operative risk for coronary artery bypass graft (CABG) patients, the incidence of perioperative stroke has remained fairly constant (or even increased) in the last decade[3].

The occurrence of perioperative stroke worsens dramatically the in-hospital and mid-term prognosis[4,5]. Even more devastating are the consequences on the postoperative quality of life: only a small minority of patients regain full autonomy, whereas the great majority are condemned to a life-long stay in a rehabilitation facility[6].

The social and economical costs of perioperative stroke are enormous: it is estimated that currently 2-4 billion US dollars are spent every year due to this complication[7].

Etiology and risk factors

Although the pathophysiological determinants of perioperative stroke can be heterogeneous and the impairment of cerebral blood flow autoregulation can play some role, there is now substantial evidence that the great majority of episodes during and after CABG surgery are embolic in nature and that the emboli usually originate from the heart or, more frequently, from atherosclerotic plaques of the ascending aorta and arch and the carotid arteries.

In fact, in all the studies which were aimed at the identification of the risk factors for perioperative stroke in coronary surgery it was found that atherosclerotic disease of the aorta and the carotid arteries (and their surrogate markers such as advanced age, peripheral vasculopathy, diabetes, hypertension, and previous stroke), together with recent myocardial infarction and postoperative atrial fibrillation, are the most powerful determinants of perioperative stroke, strongly supporting the hypothesis of an embolic etiology[8-10].

In case of patients with some of these risk factors the surgeon has the possibility of adopting specific surgical strategies aimed at reducing the neurological risk by acting on the only two variables amenable to surgical modulation: ascending aortic and carotid artery disease.

The role of the referring cardiologist

For this reason, the preoperative identification of an atherosclerotic pathology of the ascending aorta or internal carotid arteries is of paramount importance for the reduction of the neurological risk.

Even in the absence of rigorous data derived from prospective randomized series on the cost-effectiveness of systematic preoperative carotid screening, it is our opinion that all patients referred for coronary operations (independently of their age, previous neurological history or any other clinical characteristics) should be

submitted to a preoperative echo-Doppler evaluation of the carotid vessels as a part of the routine preparation for surgery. In fact, although some authors have advocated the performance of this investigation only in cases with clinical features predictive of disease, the neurological risk associated with carotid lesions largely outweighs any economical or logistic consideration.

The preoperative identification of ascending aortic pathology is by far more complex: actually less than one third of patients with circumferential disease of the ascending aorta (the unclampable ascending aorta) are identified preoperatively, while the remaining two thirds constitute an unexpected intraoperative discovery (with obvious disadvantages for the surgeon who looses the possibility of an accurate preoperative planning of an alternative surgical strategy).

Although neither the chest X-ray nor the transthoracic echocardiogram or the coronary angiogram have an absolute sensitivity in detecting aortic disease, and in spite of the fact that the routine application of more sophisticated diagnostic modalities such as transesophageal echocardiography or computed tomography is limited by economic and practical considerations, the maintenance of a high index of suspicion by the referring cardiologist is probably the key factor for the improvement of the preoperative diagnosis. Particular attention must be paid in those patients who have one or more clinical features known to be associated with an unclampable ascending aorta (Table I)[11]. If correctly performed and carefully evaluated, even the routine preoperative exams can be of great value in suggesting the presence of a diseased ascending aorta. We have described how at retrospective review the diagnosis of atherosclerotic involvement of the ascending aorta could have been made in a substantial proportion of patients simply on the basis of the routine preoperative echocardiogram, although in the majority of cases the performing echocardiographist did not elicit this doubt[11]. This finding reflects the limited knowledge of cardiologists regarding the importance of the status of the ascending aorta in CABG patients and it is likely that a more accurate preoperative aortic evaluation would translate in a significant diagnostic improvement.

Table I. Preoperative predictors of an unclampable ascending aorta.

Age > 70 years
Diabetes
Hypertension
Smoking
Unstable angina
Three-vessel disease
Left main disease
Peripheral vasculopathy

From Gaudino et al.[11], modified.

The surgeon's resources

Once the presence of an atherosclerotic involvement of the ascending aorta or internal carotid arteries has been diagnosed preoperatively, the surgeon has the possibility of modifying the operative strategy, tailoring it to the anatomic and functional characteristics of the individual patient.

Combined carotid and coronary operations. The efficacy of prophylactic carotid endarterectomy for the reduction of the neurological risk has been proven only for those patients with concomitant symptomatic disease of the carotid arteries[12,13]. In these cases carotid surgery can be performed either a few days prior to or in concomitance with the CABG procedure ("staged" and "simultaneous" approach respectively) depending on the severity of the anginal symptoms and of the angiographic lesions. In case of bilateral carotid disease the most severe lesion is usually treated first.

Instead, for asymptomatic carotid stenosis the controversy on the role of prophylactic endarterectomy is still open.

The scant available data seem to suggest that in asymptomatic cases the treatment of the carotid lesion before or concomitantly with coronary surgery confers only slight (if any) benefit in terms of a reduced neurological risk in the perioperative period[14,15].

However, no comparison between the results of the surgical vs nonoperative approach to the carotid lesion in the mid-term period has been carried out.

In a recent study, we have compared the early and mid-term clinical results of a cohort of 139 consecutive CABG patients with severe (< 70%) monolateral asymptomatic carotid stenosis operated upon at our Institution[16]. In the first 73 patients the carotid lesion was left untouched at the time of coronary surgery, whereas in the remaining 66 the lesion was treated either immediately before or concomitantly with the CABG procedure.

The in-hospital incidence of perioperative stroke was similar between the two groups (1/73 vs 1/66, p = NS); however, at mid-term follow-up 17 out of the 70 patients in whom the carotid lesion was not treated suffered cerebral events ipsilateral to the carotid pathology or necessitated surgical intervention on the lesion, in contrast to only 1 of the 64 patients who had their carotid pathology addressed at the time of CABG (p < 0.001). The protective effect of prophylactic carotid surgery was particularly evident among dyslipemic and hypertensive patients.

Although these data suffer the obvious methodological limitations of retrospective non-randomized series, they suggest that in asymptomatic patients the treatment of the carotid stenosis at the time of CABG, although not influencing the in-hospital results, confers significant neurological protection in the years after surgery. Hypertensive and dyslipemic cases probably

represent a further subset of patients at very high cerebrovascular risk in whom prophylactic carotid endarterectomy seems even mandatory.

Hopefully, in the future further data, ideally derived from prospective randomized investigations, will definitely clarify the benefits of prophylactic carotid endarterectomy in CABG patients with reference to both the early and late neurological outcomes.

The challenge of the unclampable ascending aorta. Several technical alternatives have been described to deal with the unclampable ascending aorta: ascending aorta graft replacement, aortic endarterectomy, use of fibrillatory arrest and hypothermic cardiopulmonary bypass (CPB) combined with maximal utilization of pedicled arterial grafts (no-touch technique) and beating heart revascularization (no-pump technique) have all been used for this purpose.

Aortic endarterectomy or graft replacement (both performed during a period of hypothermic circulatory arrest) have been proposed as the only radical treatment for patients with an unclampable ascending aorta as they simultaneously permit the performance of the revascularization procedure and eliminate a possibly dangerous font of systemic emboli[17,18]. However, these procedures are highly complex and invasive and carry a considerable operative risk.

The no-pump and no-touch techniques are clearly less aggressive and hazardous and are the strategies most widely adopted to revascularize patients with an unclampable ascending aorta.

Undoubtedly, the beating-heart technique offers an inferior possibility of complete revascularization; in fact, although in selected instances it is possible to perform a complete revascularization on the beating heart by constructing the proximal anastomosis of venous grafts on the proximal part of a mammary conduit, the no-pump grafting of the postero-lateral branches of the circumflex artery is not always feasible. On the other hand, the no-touch technique involves the insertion of the arterial cannula in a diseased aorta or the retrograde flow via the femoral artery, both conditions that can predispose to systemic and cerebral emboli and can increase the operative risk. As an unclampable ascending aorta is a marker of diffuse vasculopathy and is usually found in patients with systemic vascular involvement, the advantage of avoiding CPB (thus minimizing the risk of cerebral, renal and mesenteric embolization) must then be weighed against that of a complete surgical revascularization.

In a recent study, we have found that the adoption of the no-pump or no-touch technique in cases with severe pathology of the ascending aorta is able to reduce the incidence of perioperative stroke to the same level as that of patients at low neurological risk[11]. However, the global number of neurological complications (transient ischemic attack + stroke) is significantly superior in the no-touch group (11/129 vs 1/82 in our series, $p = 0.01$), testifying the risk of cerebral embolization associated with even minimal aortic manipulation. Even though the two surgical strategies are comparable in terms of overall mortality and morbidity, the no-touch revascularization technique is associated with a superior incidence of renal failure and with a longer stay in the intensive care unit and in the hospital (36.2 ± 12.1 vs 20.9 ± 7.8 hours and 8.7 ± 4.6 vs 5.2 ± 2.4 days respectively in our series, $p < 0.001$), whereas the no-pump technique offers an inferior possibility of revascularization. However, the combination of the beating heart revascularization technique with percutaneous cardiological interventions (the so-called "hybrid approach") allows the surgeon to overcome this last limitation. In fact, in our series patients operated without CPB had a superior incidence of recurrent ischemia (12.6 vs 1.6% at 3 years of follow-up), but this finding did not apply to cases treated with the integrated strategy in which angina did not recur at all. In addition, it must be noted that in the great majority of our cases postoperative myocardial ischemia was detected only instrumentally and only marginally affected the quality of life of the patients who, in most instances, were old, polyatherosclerotic, affected by associated systemic pathologies and with limited functional capacities.

On the basis of these data it seems that when complete revascularization can be achieved by no-pump grafting (alone or in combination with percutaneous interventions) the beating heart technique should be regarded as the first choice strategy for unclampable ascending aorta patients, whereas in the other cases the choice between the two techniques must take into account the relative merits and limits of each strategy and, most of all, be tailored to the clinical and angiographic characteristics of the individual patient.

Cardiopulmonary bypass temperature and extension of intraoperative stroke. The possibility of a negative effect of normothermia on the neurological outcome of CABG patients has been hypothesized since the early days of normothermic CPB. The well-known neuroprotective effect of hypothermia (indeed pioneered by cardiac surgeons) and the intuitive relation between the body temperature and the extent of the ischemic damage led several authors to question the neurological safety of a normothermic extracorporeal circulation and to hypothesize a worse neurological outcome for patients operated upon in normothermia. Moreover, two of the first series which compared hypo- vs normothermic CPB found a superior incidence of perioperative stroke among normothermic patients[19,20], fueling considerable debate in the surgical community. However, later investigations did not reproduce the results of these two studies[21] which were therefore attributed mainly to methodological flaws or to factors other than the CPB temperature.

Of note, all the studies which investigated the possible relations between the CPB temperature and the

neurological outcome focused on the incidence of perioperative stroke; however, it is conceptually difficult to hypothesize that the CPB temperature *per se* can determine the occurrence of a cerebral insult, whereas it is far more likely than the temperature of the extracorporeal circulation can influence the severity and extent of a cerebral ischemic event, once it has already been precipitated by other factors.

We have recently described how the clinical severity (measured using the Glasgow outcome scale) and the computed tomographic extension of the lesion in case of intraoperative stroke is significantly superior among cases operated in normo- vs hypothermia[22].

This finding has an obvious theoretical explanation in the well described neuroprotective effect of even moderate degrees of hypothermia[23] and is concordant with anecdotal observations reported by others[24]. For these reasons it seems that, as long as further data on this subject remain unavailable, the widespread adoption of normothermic CPB for myocardial revascularization procedures should not be recommended; on the other hand, moderately hypothermic CPB is a far more safe option.

The concept of the individualization of the surgical strategy. On the basis of these considerations, in October 1993 we prospectively started a study aimed at reducing the stroke risk in CABG patients by the adoption of an integrated protocol of screening of the ascending aorta and internal carotid arteries and by tailoring the surgical strategy to the status of these two vascular districts[25].

The protocol of pre- and intraoperative screening is summarized in table II and included the systematic performance of an echo-Doppler evaluation of the carotid arteries, the radiological, echographic and intraoperative evaluation of the ascending aorta, and a detailed neurological history.

On the basis of this assessment, patients were divided into three categories of neurological risk: 1) low in case of the absence of disease of both the aorta and carotid vessels, 2) moderate in case of moderate disease of one or both vascular districts, and 3) high when severe aortic and/or carotid disease was present[25]. Patients of the low risk group were treated using the conventional operative technique (median sternotomy, CPB, cardioplegic arrest, and complete myocardial revascularization), whereas in the moderate and high risk groups we adopted different surgical strategies depending on the status of the ascending aorta and carotid vessels. In these groups the reduction of the neurological risk was always considered to be more important than the completeness of the revascularization (once that the protection of the left anterior descending artery by a mammary graft had been achieved).

On the basis of the current literature, the adoption of the standard CABG operation in the moderate and high risk groups would have resulted in a stroke incidence estimable at around 10-15%[1-5,7], and in any case significantly superior to that of low risk cases. In our series, the adoption of specific surgical strategies led to a very low incidence of perioperative stroke in all three groups (around 1%) without significant differences between patients at low, moderate and high neurological risk. The price paid for the reduced neurological risk was a higher rate of incomplete revascularization and a superior incidence of scintigraphic evidence of residual ischemia at mid-term follow-up in the high risk group, with a rate of freedom from clinical or instrumental evidence of ischemia recurrence and/or cardiac death of 98% in the low and moderate risk groups and of 85.3% in the high risk series ($p < 0.01$). However, this price seemed worthwhile in view of the impressive perioperative neurological benefits achieved.

It should be noted that the technical solutions that we adopted have all been extensively described and are known to all cardiac surgeons. Our efforts have fundamentally been directed to the systematic careful characterization of each case and to the tailoring of the surgical approach to the physio-anatomical characteristics of the individual patient.

Table II. Screening protocol for the reduction of the risk of stroke in coronary artery bypass patients.

Preoperatively
Echo-Doppler evaluation of the internal carotid arteries
Careful evaluation of chest X-ray and coronary angiography
Transthoracic echocardiography
Intraoperatively
Digital palpation of the ascending aorta and arch
If deemed necessary, transesophageal evaluation of the ascending aorta

Practical implications: towards a deeper collaboration between cardiologists and surgeons

Although several factors can determine the occurrence of a perioperative stroke, it seems highly likely that the adoption of specific technical strategies can have a significant impact on the reduction of the incidence of this devastating complication. The careful pre- and intraoperative characterization of the anatomic and physiological features of every single patient (with particular attention to the status of the ascending aorta and internal carotid arteries) and the adoption of individualized surgical strategies has been demonstrated to be able to achieve excellent results in terms of a reduction in the incidence of postoperative neurological events even in cases considered at very high cerebrovascular risk.

For this purpose the role of the referring cardiologist is of paramount importance, as the maintenance of a high index of suspicion during the preparation of the patient for surgery is the key factor for the improve-

ment of the preoperative diagnosis of associated aortic and carotid pathologies. Once the surgeon has been timely informed on the possible presence of these conditions, he can plan the adaptation of his surgical strategy to the individual characteristics of the single patient.

The concept of a single type of surgical myocardial revascularization procedure, equal for all patients, is outdated and potentially dangerous. After a careful balance of the cardiac and systemic status of the patients, the surgeon must choose, for every single case, the technical solution which is most likely to fulfill the needs of the patient at the lowest operative risk. In this context, even the completeness of revascularization can probably be sacrificed in order to reduce the perioperative neurological risk (as everyone would agree that a minor degree of residual ischemia in an old polyvasculopathic patient with limited functional capabilities is by far preferable to a perfectly revascularized but decerebrated individual).

References

1. Mc Khann GM, Goldsborough MA, Borowicz LM, et al. Predictors of stroke risk in coronary artery bypass patients. Ann Thorac Surg 1997; 63: 516-22.
2. Reed GL III, Dinger DE, Picard EH, DeSanctis RW. Stroke following coronary-artery bypass surgery. N Engl J Med 1988; 319: 1246-50.
3. Gardner TJ, Horneffer PJ, Manolio TA, et al. Stroke following coronary artery bypass surgery: a ten-year study. Ann Thorac Surg 1985; 6: 574-81.
4. Rao V, Christakis GT, Weisel RD, et al. Risk factors for stroke following coronary bypass surgery. J Card Surg 1995; 10: 468-74.
5. Mickleborough LL, Walker PM, Takagi Y, Ohashi M, Ivanov J, Tamariz M. Risk factors for stroke in patients undergoing coronary artery bypass grafting. J Thorac Cardiovasc Surg 1996; 112: 1250-9.
6. Blossom GB, Fietsam R, Bassett JS, Glover JL, Bendick PJ. Characteristics of cerebrovascular accidents after coronary artery bypass grafting. Am Surg 1992; 58: 584-9.
7. Hogue CW, Murphy SF, Schechtman KB, Davila-Roman VG. Risk factors for early or delayed stroke after cardiac surgery. Circulation 1999; 100: 642-7.
8. Lynn GM, Stefanko K, Reed JF III, Gee W, Nicholas G. Risk factors for stroke after coronary artery bypass. J Thorac Cardiovasc Surg 1992; 104: 1518-23.
9. Roach GW, Kanchuger M, Mangano CM, et al. Adverse cerebral outcome after coronary bypass surgery. N Engl J Med 1996; 335: 1857-63.
10. Ricotta JJ, Faggioli GL, Castilone A, Hassett JM, for the Buffalo Cardiac Cerebral Study Group. Risk factors for stroke after cardiac surgery. J Vasc Surg 1995; 21: 359-64.
11. Gaudino M, Glieca F, Alessandrini F, et al. The unclampable ascending aorta in coronary bypass patients. A surgical challenge of increasing frequency. Circulation 2000; 102: 1497-502.
12. Khaitan L, Sutter FP, Goldman SM, et al. Simultaneous carotid endarterectomy and coronary revascularization. Ann Thorac Surg 2000; 69: 421-4.
13. Plestis KA, Ke S, Jiang ZD, Howell JF. Combined carotid endarterectomy and coronary artery bypass: immediate and long-term results. Ann Vasc Surg 1999; 13: 84-92.
14. Brener BJ, Brief DK, Alpert J, Goldenkranz RJ, Parsonnet V. The risk of stroke in patients with asymptomatic carotid stenosis undergoing cardiac surgery. J Vasc Surg 1987; 5: 269-79.
15. Furlan AJ, Craciun AR. Risk of stroke during coronary artery bypass graft surgery in patients with internal carotid artery disease documented by angiography. Stroke 1985; 16: 797-9.
16. Gaudino M, Glieca F, Luciani N, et al. Should severe monolateral asymptomatic carotid stenosis be treated at the time of coronary artery bypass operation? Eur J Cardiothorac Surg 2001; 19: 619-26.
17. Kouchoukos NT, Wareing TH, Daily BB, Murphy SF. Management of the severely atherosclerotic aorta during cardiac operations. J Card Surg 1994; 9: 490-4.
18. Vogt PR, Hauser M, Schwarz U, et al. Complete thromboendarterectomy of the calcified ascending aorta and aortic arch. Ann Thorac Surg 1999; 67: 457-61.
19. Martin TD, Craver JM, Gott JP, et al. A prospective, randomized trial of retrograde warm blood cardioplegia: myocardial benefit and neurologic threat. Ann Thorac Surg 1994; 57: 298-304.
20. Singh AK, Bert AA, Feng WC, Rotemberg FA. Stroke during coronary artery bypass grafting using hypothermic versus normothermic perfusion. Ann Thorac Surg 1995; 59: 84-9.
21. The Warm Heart Investigators. Randomised trial of normothermic versus hypothermic coronary bypass surgery. Lancet 1994; 343: 559-63.
22. Gaudino M, Martinelli L, Di Lella G, et al. Superior extension of intraoperative brain damage in case of normothermic versus hypothermic systemic perfusion. J Thorac Cardiovasc Surg 1999; 118: 432-7.
23. Busto R, Dietrich WD, Globus MY, Valdes I, Scheinberg P, Ginsberg MD. Small differences in intra-ischemic brain temperature critically determine the extent of ischemic neuronal injury. J Cerebr Blood Flow Metab 1987; 7: 729-38.
24. Craver JM, Bufkin BL, Weintraub WS, Guyton RA. Neurologic events after coronary bypass grafting: further observations with warm cardioplegia. Ann Thorac Surg 1995; 59: 1429-34.
25. Gaudino M, Glieca F, Alessandrini F, et al. Individualised surgical strategy for the reduction of stroke risk in coronary artery bypass patients. Ann Thorac Surg 1999; 67: 1246-53.