The asymptomatic severe carotid artery stenosis must be always treated before the cardiac surgery

Agonist

OSCAR A. MÉNDIZ[MTSAC, 1]

IMPORTANCE OF THE PROBLEM

Carotid artery stenosis (CAS) ranges from 7% to 9% in patients over the age of 65; (1) the presence of asymptomatic stenosis varies according to age (0.5% at the age of 60, and about 10% over 80). Its incidence may increase up to 62% in patients undergoing coronary surgery (CRS), and severe unilateral CAS occurs in about 10% (13-14% with 3-vessel or left main coronary artery disease), and bilateral in 2%. (2) These stenosis are associated with increased risk of stroke and of death due to vascular causes. (3)

The risk of stroke is estimated at 2-3% per year for stenosis > 50%, and increases according to stenosis degree. The severity of the blockage should not be taken only as a binary concept, since the incidence of homolateral stroke in 5 years is related to the blockage degree (14.8% for blockages of 60-74%, 18.5% for blockages of 75-94%, 14.7% for those of 95-99%, and 9,4% for occlusions), and also to the characteristics of the plaque, although these findings were more evident in symptomatic patients. (4-6)

On the other hand, a greater incidence of vascular events –mainly cardiac events– has been found in patients who had irregular or ulcerated carotid plaques. (7)

It is important to remember that out of 18% risk of stroke in 5 years, only 9.9% is usually related to a large vessel, 6.0% is a lacunar defect, and 2.1% is a cardioembolic stroke (8), and that stroke incidence caused by large vessels disease is also influenced by other conditions that increase the risk, such as silent infarctions, diabetes, and stenosis degree.

It is known that while the infarction and other causes not related to stroke are the main causes of death in CAS patients, strokes are the second major adverse event, although only 30-50% of them can be attributed to homolateral carotid artery disease. (8)

The presence of stenosis or contralateral occlusion not only influences on the prognosis but also on the surgery outcomes. The risk of death and post-surgical stroke reported by the ACE Study was 3.7% in cases of contralateral CAS, and 12.3% in asymptomatic patients with occlusion. (9)

We also know that stroke is still a potential serious complication of cardiovascular surgery (CVS). Its reported incidence ranges from 0.2% to 5.2%, with a series that revealed an incidence of 9% in patients > 75 of age, and 16% if it was a valve replacement surgery.

Many studies connect CAS with perioperative stroke; (10, 11) in a meta-analysis, the stroke incidence in patients who did not have CAS was 1.9% (a figure similar to the one recently reported by the Syntax Study) versus 3% in patients who had unilateral CAS of 50-99% (predominantly asymptomatic), while its incidence was 5% when it was bilateral and 7-11% in cases of occlusion. (12)

Treating CAS before CVS decreases the risk but does not eliminate it, and this group has more events than those who do not have significant CAS requiring surgery. (13)

Bucerius et al. (14) reported on 16,184 patients who underwent CVS. Their global incidence of stroke was 4.6%; it was 3.8% in cases of CRS and decreased to 1.9% when CRS was performed with no extracorporeal circulation.

Therefore, we can say that connecting carotid artery disease with heart disease –especially coronary disease– is frequent and important for the patient's general prognosis and the CVS, when required.

SHOULD WE TREAT THEM ALL?

Even though the evidence that sustains the indication of surgery in patients with asymptomatic severe CAS is grounded on five randomized studies –including ACAS and ACST studies– and on some meta-analyses that showed an absolute reduction of 5-6% of risk of stroke or death in five years, these studies –carried out some years ago– are still controversial. Moreover, if we consider that there are no studies specifically designed to prove the hypothesis that to operate an asymptomatic CAS before a CVS prevents events like stroke or death, this fact explains the relevance of this discussion.

The controversy about whether surgery is more helpful than medical treatment has been grounded on the fact that this benefit is clearly influenced by two elements: periprocedural rate of complications and patient's life expectancy. However, in the circumstances of this discussion, the first element will be relevant in terms of morbimortality related to neuro-

[MTSAC] Full Member of the Argentine Society of Cardiology
[1] Chief of the Department of Interventional Cardiology at the Hospital Universitario. Fundación Favaloro. Buenos Aires, Argentina

logical complications, even accepting that the rate of cardiac events may be slightly higher. However, life expectancy should not be included in our discussion, because the patient's condition has justified a major CVS, always bearing in mind that having heart disease increases at least twice the mortality of asymptomatic CAS patients, compared to those who do not have it.

The rationale for treatment is based on the possibility of reducing the potential causes of a serious and frequent complication of CVS. However, in a study that compared patients who had severe unilateral asymptomatic CAS and were not operated before the coronary surgery (n = 73) with a group (n = 66) that received prior or concomitant endarterectomy (according to the severity of angina), a mid-term higher incidence of transitory or permanent homolateral neurologic events and higher need for surgery were observed, although there were no differences in hospital evolution.

Faggioli et al. (15) also reported an increase of the risk of stroke (OR 9.9) in patients with CAS > 75% who underwent CRS without prior endarterectomy. This risk decreased when the carotid was previously operated.

Therefore, and in line with most of the experts' consensus, we can say that every asymptomatic CAS > 80% should be operated in order to decrease the chance for perioperative complications in cardiac surgery and decrease the incidence of stroke events in the mid-term follow-up, provided it is expected to have a rate of events related to carotid surgery of around 3%.

This assertion is even more significant in patients with more critical blockages, ulcerated plaques, contralateral occlusions or blockages, severe intra-cerebral or intra-thoracic disease, older adults, lacunar defects, or previous silent ischemia. Little is known about the benefit carotid surgery prior to a CVS may have on the neurocognitive function.

In conclusion, based on experience and available evidence, I am convinced that we need to treat them, if not all, at least nearly all of them.

HOW AND WHEN?

The sequence to be performed with both procedures has been studied quite a lot. Although many of those studies have not been properly designed, today there seems to be an agreement that an early carotid surgery decreases the incidence of stroke –but may slightly increase the rate of myocardial infarction–, that endarterectomy following CABG increases the risk of stroke and death during the perioperative period, and that combined surgery may increase the risk of global morbimortality. As a result, it is generally accepted that, depending on the degree of severity of the coronary condition and the possibility to carry out a strategy in stages, performing endarterectomy and then the CABG is a better option. In cases of emerging CABG, both procedures can be performed at the same time. (16)

We must remember that the rate of complications for endarterectomy has to be around 3% in order to achieve the patient's desired benefit. It may be threatened by the experience of the group and the complexity of this particular population, which does not closely match the asymptomatic CAS patient with no other comorbidity and that has been studied in some of the controlled trials. For this reason, the emergence of stent-assisted carotid angioplasty with cerebral protection offers an alternative for this high-risk group.

As pointed out in the SAC consensus managed by Dr. Fustinoni, the endarterectomy without prior angiography (only with echo-Doppler, without angioresonance or complementary multislice CT) should not be performed, since the narrow margin for benefit may be lost if plaques were unnecessarily operated (Doppler overestimation); also, if intrathoracic plaques, or intracerebral plaques or associated pathologies passed unnoticed, or if some patients were not operated although they required surgery (Doppler underestimation).

Today, chances of complications related to prior angiography observed in some of the most important randomized studies are minimized by the experience and do not seem to tarnish angioplasty with stent-graft outcomes, which requires angiographic confirmation of prior Doppler findings, and whose complications have always been expressed globally. However, in experienced groups like ours, the 30-days incidence of any stroke and death for asymptomatic patients is 2.1% (288 asymptomatic patients out of 602 procedures), even if it is a population with higher risk than that of the mentioned randomized studies.

Performing these procedures in stages (more than 30 days between both of them) will decrease the risk in both surgeries, especially because, in patients who have a stent, it will enable the correct dual antiplatelet therapy (ASA + clopidogrel) for at least 30 days prior to CVS, and then stop it for 7 days. But for the few cases in which it cannot be performed, a combined procedure has proved to be safe.

For the combined procedure, the patient continues receiving antiaggregate therapy with aspirin. He/she undergoes angioplasty with stent-graft under heparin anticoagulation, and once the procedure is over, the patient is transferred to the operating room for CABG with no heparin reversion. Around 8 hours following CVS completion, and once bleeding due to surgery is ruled out, antiplatelet therapy with clopidogrel is restarted. (17) Today, this experience has already been applied for 47 patients, whose only neurological complication has been a transient ischemia. The four deceased patients within the first 30 days were caused by the CVS, and not by the carotid stent (one due to sepsis, two due to heart failure, and one due to surgical bleeding).

In short, I consider non-invasive CAS screening should be performed in all those patients undergoing CVS, especially in elders with multiple vessel atherosclerosis. Also, I consider that asymptomatic CAS should be treated before CVS, and that angioplasty is a very good alternative when it is performed by experienced groups in this high risk population.

BIBLIOGRAPHY

1. Fine-Edelstein JS, Wolf PA, O'Leary DH, Poehlman H, Belanger AJ, Kase CS, et al. *Precursors of extracranial carotid atherosclerosis in the Framingham Study*. Neurology 1994; 44:1046-50.

2. Cirilo F, Renzulli A, Leonardo G, Romano G, De Feo M, Della Corte A, et al. *Incidence of carotid lesions in patients undergoing coronary artery bypass graft*. Heart Views 2000; 1:402-7.

3. Bennavente O, Moher D, Pham B. *Carotid endarterectomy for asymptomatic carotid stenosis: a meta-analysis*. BMJ 1998; 317: 1477-80.

4. Chambers BR, Donnan GA. *Carotid endarterectomy for asymptomatic carotid stenosis*. Cochrane Database Syst Rev 2005; 19:CD001923.

5. Mackey AE, Abrahamowicz M, Langlois Y, Battista R, Simard D, Bourque F, et al. *Outcome of asymptomatic patients with carotid disease*. Asymptomatic Cervical Bruit Study Group. Neurology 1997; 48:896-903.

6. Sila CA, Higashida RT, Clagett GP. *Clinical decisions. Management of carotid stenosis*. N Engl J Med 2008; 358:1617-21.

7. Rothwell PM, Villagra R, Gibson R, Donders RC, Warlow CP. *Evidence of a chronic systemic cause of instability of atherosclerotic plaques*. Lancet 2000; 355:19-24.

8. Inzitari D, Eliasziw M, Gates P, Sharpe BL, Chan RK, Meldrum HE, et al. *The causes and risk of stroke in patients with asymptomatic internal-carotid-artery stenosis*. North American Symptomatic Carotid Endarterectomy Trial Collaborators. N Engl J Med 2000; 342:1693-700.

9. Taylor DW, Barnett HJ, Haynes RB, Ferguson GG, Sackett DL, Thorpe KE, et al. *Low-dose and high-dose acetylsalicylic acid for patients undergoing carotid endarterectomy: a randomized controlled trial*. ASA and Carotid Endarterectomy (ACE) Trial Collaborators. Lancet 1999; 353:2179-84.

10. Barnes RW, Nix ML, Sansonetti D, Turley DG, Goldman MR. *Late outcome of untreated asymptomatic carotid disease following cardiovascular operations*. J Vasc Surg 1985; 2:843-9.

11. Salasidis GC, Latter DA, Steinmetz OK, Blair JF, Graham AM. *Carotid artery duplex scanning in preoperative assessment for coronary artery revascularization: the association between peripheral vascular disease, carotid artery stenosis, and stroke*. J Vasc Surg 1995; 21:154-60.

12. Naylor AR, Mehta Z, Rothwell PM, et al. *Carotid artery disease and stroke during coronary artery bypass: a critical review of the literature.* Eur J Vasc Endovasc Surg 2002; 23:283-94.

13. Kougias P, Kappa JR, Sewell DH, Feit RA, Michalik RE, Imam M, et al. *Simultaneous carotid endarterectomy and coronary artery bypass grafting: results in specific patient groups*. Ann Vasc Surg 2007; 21:408-14.

14. Bucerius J, Gummert JF, Borger MA, Walther T, Doll N, Onnasch JF, et al. *Stroke after cardiac surgery: a risk factor analysis of 16,184 consecutive adult patients.* Ann Thorac Surg 2003; 75:472-8.

15. Faggioli GL, Curl GR, Ricotta JJ. *The role of carotid screening before coronary artery bypass.* J Vasc Surg 1990; 12:724-31.

16. Barnett HJ, Eliasziw M, Meldrum HE. *Evidence based cardiology: Prevention of ischaemic stroke.* BMJ 1999; 318:1539-43.

17. Mendiz O, Fava C, Valdivieso L, Dulbecco E, Raffaelli H, Lev G, et al. *Synchronous carotid stenting and cardiac surgery: an initial single-center experience.* Catheter Cardiovasc Interv 2006; 68:424-8.

Antagonist

OSVALDO FUSTINONI[1]

It is usually necessary to operate an asymptomatic internal carotid artery stenosis (CAS), generally detected through ultrasound, as a previous step toward a formally indicated cardiac surgery –in particular, myocardial revascularization surgery (MRS, or coronary artery bypass graft, CABG). This indication is grounded on the fact that such stenosis might increase the risk of cerebral ischemia if the patient undergoes surgery.

Those in favor of surgery argue that cerebrovascular risk in general and stroke risk following a CABG are higher, that CAS may cause decreased blood flow during heart surgery, and that, therefore, eliminating CAS reduces the risk of stroke –which is precisely the most frequent vascular complication of CABG. Those against this approach argue that, on the other hand, the risk of stroke due to CAS following CABG is minimun (or even lower if CAS is unilateral). This is because > 90% of such strokes are caused by aortic embolism as a result of aortic clamping performed during heart surgery, and not by CAS. Moreover, CAS is not significantly hemodynamic because decreased blood flood only occurs with CAS > 90%, and in any case, can be evaluated before. Finally, the most frequent vascular complication of carotid endarterectomy (CEA) is the acute myocardial infarction (AMI) –which is precisely the condition that CABG seeks to avoid. Only some of these arguments –for or against– have enough scientific support.

In the current state of knowledge, and on the basis of the reviewed recommendations of the American Heart Association (AHA) Stroke Council and the Argentine Society of Cardiology (SAC), indications for carotid endarterectomy (CEC) alone –that is, not combined with heart surgery– in cases of asymptomatic carotid stenosis (CAS) are the confirmed finding of a stenosis of 60-99%, *provided the surgical risk does not exceed 3%*, (1-3) because the spontaneous risk of stroke

[1] INEBA - Instituto de Neurociencias Buenos Aires. Buenos Aires, Argentina

for CAS is just 2% a year. In addition, the CEA benefit in CAS was significant only in 3 years after surgery, in a highly selected population (only 4% of tracked patients in ACAS Study were finally included). The resulting benefit, though real, is so relative that it is translated into operating 85 patients in 1 year to avoid 1 stroke, and 17 in 5 years to avoid 1 stroke. (3) For these reasons, in practice, patients with CAS who are indicated CEA are indeed a minority. According to the classification based on randomized studies, with control group and enough number of patients to set a significant difference in the group under treatment, and with low chances of false positive (alpha) or false negative (beta) errors, these are "class I and level of evidence A" or "grade A" guidelines.

Endovascular treatment (carotid stenting, CS) is currently authorized by the United States Food and Drug Administration (FDA) for use in patients whose high risk of stroke prevents them from undergoing surgery, that is, patients with formal indication of CEA but with a high surgical risk, "not eligible for NASCET – ACAS trials". These are the acronyms of the randomized studies on which the benefit of CEA for CAS is based on; the ACAS study corresponds to CAS. (3) The CS approval after the SAPPHIRE Study publication (4) was followed by controversy. CS as an alternative to CEA for standard surgical risk patients has not been approved or recommended in cases of carotid atherosclerotic stenosis.

Regarding the indication of CEA combined with cardiac surgery –in particular, coronary artery bypass graft surgery (CABG)–, the American College of Cardiology (ACC) and the American Heart Association (AHA) guidelines –2004 update–, in the section "Carotid Disease and Neurological Risk Reduction", state that carotid stenosis is "probably recommended before CABG or concomitant with CABG in patients with a symptomatic carotid stenosis or in asymptomatic patients with unilateral or bilateral internal carotid stenosis of 80% or more". (5) This is a class IIa recommendation and its level of evidence is C. This means it is controversial, with favorable evidence based only on casuistic or experts' opinions, according to the classification used by the AHA.

On the other hand, these Stroke Council/AHA guidelines state that unilateral CEA together with CABG surgery is "acceptable, with a surgical risk < 3%, and life expectancy of at least 5 years" in CEA ³ 60%, "ulcerated or not, under antiplatelet therapy or not, independently of the contralateral artery condition", in a "grade C" recommendation, that is, in this classification, based on data reported by randomized cohort studies, with control group or historic controls, or else based on anecdotal evidence from casuistics. This recommendation is not included in the "tested" CEA indications mentioned by the Stroke Council/AHA. (1)

From these references we can gather that, at present, carotid surgery combined with CABG surgery is not formally indicated in the international guidelines, and that it is controversial. *And that it is only considered "acceptable" for surgical risk < 3% and life expectancy ³ 5 years.*

CAS is a significant predictor of bad prognosis in patients undergoing CABG surgery (6), and increases the risk of vascular death, especially if it is bilateral. (7) However, there is not enough evidence that the combination of carotid surgery with cardiac surgery decreases that risk: surgical morbimortality of combined surgery is high, so it widely counteracts its supposed benefit. Casuistic data reveal morbimortality rates of 13% (8), 5.1% (9) or 11.9% (10), or 14.3% for stroke. (11) When surgeries are stratified, the rate of stroke is low (3.4%) (11), and when –once stratified– CABG is performed first, morbimortality decreases: 6% when CABG is performed first versus 13,4% when CEA is first. (10) Even when it is stated in the title of one of these studies that "combined surgery does not increase the risk of perioperative stroke", (9) its morbimortality is clearly higher than the 3% established in the Stroke Council/AHA guidelines. A meta-analysis of 16 open-label studies revealed a rate of stroke or death of 9.5% for combined surgery, and of 5.7% for stratified surgery. (12) A systematic review of 97 studies and 9,000 patients who underwent combined or stratified surgery showed a rate of AMI, stroke and death of 10-12%. (13) So far, there are no controlled studies with level of evidence A that prove the benefit of CAE combined or stratified with CABG to prevent stroke supposedly associated with cardiac surgery.

As mentioned above, since CS for high surgical risk patients undergoing CAE has been approved, it may be inferred that its use instead of CAE in patients who need CABG would suggest lower morbimortality rate than for the combined procedure. However, a systematic review of 6 studies and 277 patients undergoing stratified CS and CABG revealed 12.3% for stroke and death and 9.4% for major stroke and death. These outcomes were similar to those of combined surgery. The rate of stroke and death was 6.9% within the period between CS and CABG, and 5.6% within 30 days after CABG. The average interval between the CS and the surgery was 32 days. (14)

In short, the current level of evidence in favor of CEA/CS as the previous step to a formally indicated CABG is not enough to class I recommendation. The AHA considers combined surgery as "acceptable" – though not tested–, but only with surgical risk < 3%. Morbimortality due to CAE or CS, combined or stratified with CABG, is > 3%. So far, there is not enough evidence to *always* indicate CAS as a previous step to CABG. Rather, the current evidence shows that risk is above the supposed benefit, both for CEA and CS. If carotid surgery was recommended on the basis of already established class I indications, it should only be performed in cases of procedural risk < 3% and life expectation > 3 years. Controlled studies are nec-

essary to provide level of evidence A to determine the need to operate systematically an asymptomatic severe CAS before cardiac surgery. For the time being, they are not available. In conclusion, the asymptomatic severe carotid artery stenosis must *not* be always operated before the cardiac surgery. Rather on the contrary…

BIBLIOGRAPHY

1. Biller J, Feinberg WM, Castaldo JE, Whittemore AD, Harbaugh RE, Dempsey RJ, et al. *Guidelines for Carotid Endarterectomy: A Statement for Healthcare Professionals From a Special Writing Group of the Stroke Council, American Heart Association*. Stroke 1998; 29:554-62.

2. *Consenso de estenosis carotídea SAC*. Rev Argent Cardiol 2006; 74:160-74.

3. *Endarterectomy for asymptomatic carotid artery stenosis*. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. JAMA 1995; 273:1421-8.

4. Yadav JS, Wholey MH, Kuntz RE, Fayad P, Katzen BT, Mishkel GJ, et al; *Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy Investigators. Protected carotid-artery stenting versus endarterectomy in high-risk patients*. N Engl J Med 2004; 351:1493-501.

5. Eagle KA, Guyton RA, Davidoff R, Edwards FH, Ewy GA, Gardner TJ, et al; American College of Cardiology; American Heart Association Task Force on Practice Guidelines; American Society for Thoracic Surgery and the Society of Thoracic Surgeons. *ACC/AHA 2004 guideline update for Coronary artery bypass graft surgery: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines* (Committee to Update the 1999 Guidelines for Coronary Artery Bypass Graft Surgery). Circulation 2004; 110:1168-76.

6. Brener BJ, Brief DK, Alpert J, Goldenkranz RJ, Parsonnet V. *The risk of stroke in patients with asymptomatic carotid stenosis undergoing cardiac surgery:* a follow-up study. J Vasc Surg 1987; 5:269-79.

7. Touzé E, Warlow CP, Rothwell PM. *Risk of coronary and other nonstroke vascular death in relation to the presence and extent of atherosclerotic disease at the carotid bifurcation*. Stroke 2006; 37:2904-9.

8. 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.

9. Darling RC 3rd, Dylewski M, Chang BB, Paty PS, Kreienberg PB, Lloyd WE, et al. *Combined carotid endarterectomy and coronary artery bypass grafting does not increase the risk of perioperative stroke*. Cardiovasc Surg 1998; 6:448-52.

10. Periæ M, Huskiæ R, Neziæ D, Gradinac S, Popoviæ Z, Popoviæ AD, et al. *Combined carotid and coronary artery surgery: what have we learned after 15 years?* Cardiovasc Surg 1998; 6:156-65.

11. Giangola G, Migaly J, Riles TS, Lamparello PJ, Adelman MA, Grossi E, et al. *Perioperative morbidity and mortality in combined vs. staged approaches to carotid and coronary revascularization*. Ann Vasc Surg 1996; 10:138-42.

12. Borger MA, Fremes SE, Weisel RD, Cohen G, Rao V, Lindsay TF, et al. *Coronary bypass and carotid endarterectomy: does a combined approach increase risk? A metaanalysis*. Ann Thorac Surg 1999; 68:14-20.

13. Naylor AR, Cuffe RL, Rothwell PM, Bell PR. *A systematic review of outcomes following staged and synchronous carotid endarterectomy and coronary artery bypass*. Eur J Vasc Endovasc Surg 2003; 25:380-9.

14. Guzman LA, Costa MA, Angiolillo DJ, Zenni M, Wludyka P, Silliman S, et al. *A systematic review of outcomes in patients with staged carotid artery stenting and coronary artery bypass graft surgery*. Stroke 2008; 39:361-5.

Declaration of conflict of interests

The author does not have a conflict of interests.

AGONIST'S REPLY

Despite Dr. Fustinoni and I have agreed upon the importance of stroke as complication of CVS, we have come to opposite suggestions regarding the lack of adequate evidence about treating CAE before the CVS, and regarding the analysis of similar literature. Independently of the role we have been assigned for the controversy, I believe this happens out of extrapolating data of studies with patients who had CAE but did not requiere short-term CVS.

In this regard, it is important to point out that the expected CAE benefit should have enough time to be noticed, since, in my opinion, a CVC should not be recommended to someone whose life expectancy is lower than 3 years. Taking this fact for granted, the time element is out of our discussion.

We also agree in that the rate of complications for CAE should be lower than 3%. However, it is important to highlight that it should fit within the morbimortality of the carotid procedure in itself, and not to generalize CVC complications, since its global rate of complications is higher than 3%, at least in our community.

Therefore, if the rate of complications is adequate for a patient who will supposedly live as necessary, whether with surgery or stent, the expected benefit of CAE treatment should not be discarded.

So, if we are in a center that performs an adequate number of procedures (probably no less than 50) with positive results (morbimortality less than 3%) per year, operations must be performed before the CVC, so that its benefits can be manifested.

Treatment as well as referal should be reconsidered as a whole in the case of centers whose outcomes are different.

Dr. Oscar A. Méndiz, MD

ANTAGONIST'S REPLY

Both "contestants" recognize that CE is a predictor of bad prognosis and vascular risk for patients undergoing CABG. That is not enough to state that severe CAS should *always* be performed before cardiac surgery.

In Naylor's review (quotation 12, Dr. Méndiz), the risk of post-CABG stroke was only 2%, invariable between 1970 and 2000; 91% patients did not have significant CAS and their perioperative stroke was < 2%. This rate was 3% for unilateral CAE of 50-99% (the same as the annual spontaneous risk in CAS: 2-3%), 50% of strokes *did not* evidence CAS, and 60% of cerebral infarctions *were not* attributed only to CAS. That

is to say, *most* CAS and CABG patients *did not* have more strokes than the expected ones due to natural evolution, but they did have them *before*. The risk increased with *bilateral* CAS of 50-99% (5%) and occlusion (7-11%), but it was lower than the one reported for combined surgery. In addition, "even assuming that CAE does not imply additional risk, it would prevent only 40-50% procedural strokes".

In Guzmán's series (his quotation 14), the post-CABG stroke incidence (3.8%, not substantially different from the natural CAE risk) decreases to 1.9% in surgeries without extracorporeal circulation, and increases up to 4.8% in aortic valve surgery. It stresses the fact that post cardiac-surgical strokes occur mainly due to aortic embolism. Moreover, CAS *did not* appear as independent predictor of stroke.

Dr. Méndiz recommends to operate "almost all" CAS > 80%, on the basis of his highly specialized experience (quotation 17), but with "…a surgery-related event rate of 3%". We share this condition, but it is usually not accomplished. Thus, severe CAS surgery before cardiac surgery *cannot* be recommended *for all cases*. Extensive randomized studies are necessary to determine it, and we have also agreed on this.

Dr. Osvaldo Fustinoni, MD