What is the best treatment for cardiac disease?

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INTRODUCTION

The indication, implementation, evaluation and dissemination of the results of surgical treatments for carotid arteries have become more widespread and available in recent years, during a phase of enthusiasm motivated by a variety of factors.

Few surgical procedures were as well-evaluated, audited and widespread as carotid endarterectomy. But there wasn't enough evidence of a good cost-benefit ratio for it to be more widely accepted. Actually, there was and still is a great "problem" associated with carotid endarterectomy, which is the fact that this procedure ***does not provide enhanced value.***

In reality, eliminating the diagnostic arteriography - with its risk of neurological complications (0.5% -1.5%) - as well as eliminating some of the industrial steps (radiography, contrast, catheter and operator of the procedure, etc.). This resulted in economic losses for these sectors, but also offered proven benefits for patients.

In the face of economic loss, the aforementioned sectors attempted to maintain their profits and used a very intelligent strategy: they offered a "friendly suggestion" of a treatment known to be non-invasive. Representatives were quick to publicize their idea: "Why not replace an incision in the neck by a small hole in the groin, performed with local anesthesia?

The economic motivation was very strong, and logistical conditions were favorable. If the hemodynamicist navigates his catheter into the ascending aorta towards the coronary arteries for cinecoronariography, could he not expand its incursion and guide the catheter through the arch and contrast the carotid arteries? And, if the hemodynamicist finds 70% stenosis in a carotid lesion - even in an asymptomatic patient - why can't he enlarge this stenosis, which *"could be dangerous"*? These suggestions became largely accepted in the industry.

The diffusion of carotid angioplasty/stenting in the field of cardiology was first performed by Diethrich et al. [1] and Roubin et al. [2].

In the beginning, the results were unfavorable. Even so, the cardiology community believed in what they heard in medical conferences, particularly because of the ***wolf in sheep's clothing*** that was the possibility of minimally invasive surgery. However, they did not know that the surgery, which claimed to be "minimally invasive," would later become "maximally invasive." Patients were at a high risk for stroke (CVA), leading to severe brain damage (from cerebral embolization) or even death.

Obviously, a highly-charged debate began over the two techniques. They rely on different principles, so comparing them becomes difficult. However, the results for the patients - which are the most important factor - are very different, and favor the use of endarterectomy.

PROCEDURAL DIFFERENCES

In carotid endarterectomy, the vascular surgeon carefully avoids handling the carotid artery and dissects it above and below the lesion. The surgeon works only on the areas with plaque in the cases of ulcerated lesions or fresh thrombus, after heparinization and distal clamping of the internal carotid artery. This minimizes the chances of cerebral embolization, and that's the primary goal of every prophylactic treatment. After opening the artery, if the blood reflux does not present a shining flush (or, if it can't be determined), the surgeon interposes a derivation ***(internal shunt)*** that allows for the maintenance of blood flow during the procedure. With this alternative, the surgeon protects the brain and allows for the procedure to be concluded without incident. The surgeon finishes the procedure only when the removal of the atheromatous plaque is complete. The surgeon then sutures the artery using a Dacron or autologous vein *"**patch"*** to avoid stenosis in most male patients and in all female patients, since they are more susceptible to postoperative stenosis.

On the other hand, the problems of ***"carotid angioplasty/stenting"*** start with anatomically limited access, due to obstruction or stenosis of the femoral and iliac arteries, in addition to the presence of plaques and thrombi along the catheter course (thoracic and abdominal aorta). The critical point is the aortic arch, which can contain ulcerated plaque, and from which point the catheter can release fragments of thrombi or plaques that may cause cerebral embolization. Difficulties remain with the entry into the carotid ostium, particularly in the internal carotid artery.

The next difficulty comes from transposing the plaques, which may be causing a very significant stenosis, even

impeding the passage of the filter or stent or be ulcerated with free thrombus inside it - another factor that disfavors the endovascular procedure.

In ***carotid angioplasty/stenting***, the surgical strategy is completely different because, unlike an endarterectomy procedure, in which the plaque is not removed, the atheromatous plaque is ***"crushed."*** Fragments of the plaque are released, causing embolization toward the brain in 20% to 40% of patients [3-6]. To keep the plaque in its position and to decrease the chance of embolization, stent implantations (a foreign body) has recently begun to be used in critical vascular areas.

Obviously, to minimize the risk of cerebral embolization, "protective filters" were made available. These filters can reduce chances of - but cannot prevent - cerebral embolization, meaning that it is still a major problem for the patient [3-8]. In addition to occuring during surgical procedures that use carotid angioplasty/stenting (monitored by transcranial Doppler), this embolization also occurs in the postoperative in variable degrees. Rapp et al. [4] warned that more needs to be done to understand the relationship between the mechanism of repeated embolization and the early dementia found in many cases. The authors conclude that it may be premature to consider these events as unimportant or even to believe it to be impossible to reduce their frequency. This fact should still be a cause of concern. I would say that this fact is imminent because the numbers of embolization are also very different when compared to endarterectomy. The surgery is less aggressive and trauma is minimal, whereas in the endovascular technique, the surgeon is in dangerous territory, with lesions at high risk of embolization; and as it has been shown, the problem does not end when the angioplasty/stenting is complete.

The two surgical procedures (angioplasty and endarterectomy/carotid stents) can result in excessive scarring via myointimal hyperplasia, which is generally proportional to the trauma caused upon the artery and what has been implanted on it. Thus, as the trauma is more extensive with c***arotid angioplasty/stenting***, choosing this surgery will result in a degree of stenosis or occlusions that is larger than with the carotid endarterectomy.

RESULTS ANALYSIS

At this point I would like to consider the evolution of endovascular treatment of the carotid artery. Initial results were inevitably disastrous. Both Diethrich et al. [1] and Roubin et al. [2] performed indefensible procedures with compromised results. The former group performed angioplasty in asymptomatic patients with 70% stenosis, with a stroke/death rate of 10%. In 1998, the latter group performed and published results of angioplasty in elderly patients, with a stroke/death rate of 19% [9]. It must be emphasized that, in the same year, Perler et al. [10] of Johns Hopkins, published on their experience with carotid endarterectomy in elderly patients with a 2.6% stroke/death rate. A reasonable percentage of cardiologists heard Roubin's message more than Perler's, resulting in negative consequences for the patients. Initially, they were convinced of this so-called minimal-invasiveness, which was, in that case, actually a "maximal-invasiveness."

This misunderstanding was not cleared up until much later. Hobson, coordinator of the CREST study [11] in 2004, warned of the high percentage of stroke/death (12.1%) with the carotid angioplasty/stenting in elderly patients. He recommended that this procedure not be used.

Another issue worth mentioning is the high percentage of cerebral embolization using the endovascular technique [3-6]. To reduce the occurrence of this procedure, the protective filters have been proposed. In order to approve and allow the commercialization of these filters, the FDA required a randomized clinical study, showing "non-inferiority" in relation to endarterectomy.

Although the results of carotid endarterectomy were already very good, with excellent rates of stroke/death in the range of 1% to 4% [12-14], the majority of "comparative studies" showed rates of 5%, 7%, 10% of stroke/death [15-17], to the surprise of vascular surgeons. But how do we accept such different rates compared to a surgical practice that has already been proven by reliable publications and traditional services? [18.19]. The explanation is simple: due to the known limitations of endovascular treatment, the coordinator of the SAPPHIRE study invited little-known surgeons to perform the procedure in patients with a high comorbidity index, and also created a new outcome: a "chemical" myocardial infarction; or, detection of a high level of troponin.

This is the basis of SAPPHIRE study, which was widely popularized with strong marketing appeal. It was shown in conferences for only two years, with outcomes favoring the endovascular technique. Only with publication of this study in the *New England Journal of Medicine* [16], in 2004 it was possible to confirm the study's many biases, as well as the conflicts of interest proven for all eight co-authors and the author of the editorial comment.

Yadav et al. [16] compared different groups of patients. In the surgical branch, there was cardiac sub-treatment, because 6% presented previous myocardial infarctions, and, compared with the clinical branch, there was 9% less coronary angioplasties and 13% less saphenous vein bypasses.

When this study was published, it was categorically criticized by many people were committed to finding the best results for the patients. The results of carotid endarterectomy in such a study disagree with all of the

literature on the topic, along with the best and most well-established practices. The following words are from the respected Peter Bell: **"This study must be shown to students so that they know how a study should *not* be completed."**

Several studies were published at the same time, showing the mistakes of SAPPHIRE and the inadequacy for patients classified as "high-risk" patients. Mozes et al. [18], from the Mayo Clinic, published a comparative study for the group of patients considered to "high-risk" according to the criteria of the SAPPHIRE study. The authors presented a rate of stroke of 0.9% (asymptomatic) and 2.9% (symptomatic). The mortality rate was 0.2% in asymptomatic patients, and 0.5 in symptomatic patients, all of them qualified for the SAPPHIRE study.

Gasparis et al. [19] compared results in two groups of patients: one group of patients met the "high-risk" criteria according to SAPPHIRE, and the other group was considered to be "not high-risk." The authors did not find a significant difference between the two groups (1.3% and 1.1%, respectively).

But the tables turned, and several manifestations have come up in patients in recent years, showing the limitations of the endovascular technique in the treatment of patients with carotid stenosis. Diethrich et al. [1], who, years ago, enthusiastically supported endovascular treatment with 10% of complications, now declare something emblematic. In 2006, during an event in the Texas Heart, this author asserted his position on the superiority of carotid endarterectomy in carotid angioplasty/stenting [20]. In April of this year, during an event in Sao Paulo, he showed his disappointment and concern with the method [21]. He declared that the current comparative results [17, 22] showed a large difference between the results of the two techniques. The Government of France considered carotid angioplasty/stenting unsafe, and forbade the carotid endovascular procedure. U.S. government healthcare providers (Medicare and Medicaid) limited the repayment of this procedure to only very particular situations, such as cases with a high risk of endarterectomy and protocol for new device (IDE) under supervision of the FDA.

But there are other aspects to be approached.

How could the recommendation for endovascular treatment in elderly patients have been justified with a 19.2% stroke/death rate published by Mathur et al. [9], if, in the same year, Perler et al. [23] published results for elderly patients with a 2.6% stroke/death rate? This study shows results of 1036 elderly patients, with only 1.4% mortality and 1.2% stroke. Despite the discrepancy described above, it was only in 2004 that Hobson et al. [11] showed the impropriety of the endovascular technique in the elderly, with a 12.1% stroke/death rate.

Our personal experience with 79 carotid endarterectomies in elderly patients shows a stroke/death rate of 2.7%. This rate is very different from the 6.9% of the SAPPHIRE study. Other authors have shown variable results of 3% to 5% [23-25] in this age group over the years. In this group, the prevalence of carotid endarterectomies has increased, and the safest procedure must be recommended. It could be said that, if the endarterectomy is conclusively better for those patients who have more advanced atherosclerotic disease, it is clear that it is also better for those patients presenting more localized atherosclerotic disease. Today, the comparison between the two techniques in several studies shows very different rates: 9.2%, 12.1% and 19% with endovascular technique [9, 11, 26] and 2.4% to 5.5% with carotid endarterectomy.

Another major mistake that resulted in loss to the patients was the recommendation of endovascular treatment for patients who may present carotid artery occlusion. The justification for such a recommendation came from Nascet's results published in 1991 [27]. It was a study with 21 patients, with three occurrences of strokes/death (14%). These data were widely spread to support the endovascular treatment. It should be clarified that, in this study, there was surgical subtreatment; that is, internal shunts to protect the brain were not used in patients who needed them. However, arterial thrombosis, which occurred in the immediate postoperative period, does not agree with the best technique for this procedure [26.28]. In this group of patients, it is crucial to identify the experience of the surgeon and which technique is used. Through the analysis of 27 articles about carotid endarterectomy with contralateral occlusion, Samson et al. [29] noted the occurrence of stroke in 6.2% of patients in which internal shunts was not used (double, if compared to those patients who needed brain protection (3%)).

Regarding the recommendation for treatment of carotid artery disease associated with myocardial revascularization, we suggest reading the study that will be published in the next issue of the Brazilian Archives of Cardiology.

If there is, in fact, a light at the end of the tunnel, it is expected that the recommendations and results of the procedures for severe carotid artery disease will become well known by clinicians, cardiologists and neurologists, in terms of their short-, mid- and long-term effectiveness and risks.

But the commitment of the vascular surgeon is great, and includes the surgeon's proper preparation in order to obtain the best results. Wilye noted that "the body, and not the carotid artery, should be dissected" in the carotid surgery, and Perler also noted that a carotid endarterectomy should be performed with an "almost perfect" technique, because perfection is a ***divine*** virtue and is not accessible ***to humans***.

In conclusion, the carotid endarterectomy is still the procedure with the best results for well-selected patients.

This procedure respects the healing process of the tissue because it removes the plaque and does not crush and compress it with the metallic stent.

Finally, it must be remembered that: "the interest of the patient must always come first".

REFERENCES

1. Diethrich EB, Ndiaye M, Reid DB. Stenting in the carotid artery: initial experience in 110 patients. J Endovasc Surg. 1996;3(1):42-62.

2. Roubin GS, New G, Iyer SS, Vitek JJ, Al-Mubarak N, Liu MW, et al. Immediate and late clinical outcomes of carotid artery stenting in patients with symptomatic and asymptomatic carotid artery stenosis: a 5-year prospective analysis. Circulation. 2001;103(4):532-7.

3. Hammer FD, Lacroix V, Duprez T, Grandin C, Verhelst R, Peeters A, et al. Cerebral microembolization after protected carotid artery stenting in surgical high-risk patients: results of a 2-year prospective study. J Vasc Surg. 2005;42(5):847-53.

4. Rapp JH, Wakil L, Sawhney R, Pan XM, Yenari MA, Glastonbury C, et al. Subclinical embolization after carotid artery stenting: new lesions on diffusion-weighted magnetic resonance imaging occur postprocedure. J Vasc Surg. 2007;45(5):867-72.

5. Piñero P, González A, Mayol A, Martínez E, González-Marcos JR, Boza F, et al. Silent ischemia after neuroprotected percutaneous carotid stenting: a diffusion-weighted MRI study. AJNR Am J Neuroradiol. 2006;27(6):1338-45.

6. Faraglia V, Palombo G, Stella N, Taurino M, Iocca ML, Romano A, et al. Cerebral embolization in patients undergoing protected carotid-artery stenting and carotid surgey. J Cardiovasc Surg (Torino). 2007;48(6):683-8.

7. Poppert H, Wolf O, Resch M, Theiss W, Schmidt-Thieme T, Graefin von Einsiedel H, et al. Differences in number, size and location of intracranial microembolic lesions after surgical versus endovascular treatment without protection device of carotid artery stenosis. J Neurol. 2004;251(10):1198-203.

8. Schlüter M, Tübler T, Steffens JC, Mathey DG, Schofer J. Focal ischemia of the brain after neuroprotected carotid artery stenting. J Am Coll Cardiol. 2003;17:42(6):1007-13.

9. Mathur A, Roubin GS, Gomez CR, Iyer SS, Wong PM, Piamsomboon C, et al. Elective carotid artery stenting in the presence of contralateral occlusion. Am J Cardiol. 1998;81(11):1315-7.

10. Perler BA, Dardik A, Burleyson GP, Gordon TA, Williams GM. Influence of age and hospital volume on the results of carotid endarterectomy: a statewide analysis of 9918 cases. J Vasc Surg. 1998;27(1):25-31.

11. Hobson RW 2nd, Howard VJ, Roubin GS, Brott TG, Ferguson RD, Popma JJ, et al. Carotid artery stenting is associated with increased complications in octogenarians: 30-day stroke and death rates in the CREST lead-in phase. J Vasc Surg. 2004;(40):1106-11.

12. Sundt TM Jr, Ebersoldt MJ, Sharbrough FW, Piepgras DG, Marsh WR, Messick JM Jr, et al. The risk-benefit ratio of intraoperative shunting during carotid endarterectomy. Relevancy to operative and postoperative results and complications. Ann Surg. 1986;203(2):196-204.

13. Riles TS. Surgical management of internal carotid artery stenosis: preventing complications. Can J Surg. 1994;37(2):124-7.

14. Hertzer NR, O'Hara PJ, Mascha EJ, Krajewski LP, Sullivan TM, Beven EG. Early outcome assessment for 2228 consecutive carotid endarterectomy procedures: the Cleveland Clinic experience from 1989 to 1995. J Vasc Surg. 1997;26(1):1-10.

15. CAVATAS investigators. Endovascular versus surgical treatment in patients with carotid stenosis in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS): a randomised trial. Lancet. 2001;357(9270):1729-37.

16. Yadav JS, Wholey MH, Kuntz RE, Fayad P, Katzen BT, Mishkel GJ, et al. Protected carotid-artery stenting versus endarterectomy in high-risk patients. N Engl J Med. 2004;351(15):1493-501.

17. SPACE Collaborative Group, Ringleb PA, Allenberg J, Brückmann H, Eckstein HH, Fraedrich G, Hartmann M, et al. 30 day results from the SPACE trial of stent-protected angioplasty versus carotid endarterectomy in symptomatic patients: a randomised non-inferiority trial. Lancet. 2006;368(9543):1239-47.

18. Mozes G, Sullivan TM, Torres-Russotto DR, Bower TC, Hoskin TL, Sampaio SM, et al. Carotid endarterectomy in SAPPHIRE-eligible high-risk patients: implications for selecting patients for carotid angioplasty and stenting. J Vasc Surg. 2004;39(5):958-65.

19. Gasparis AP, Ricotta L, Cuadra SA, Char DJ, Purtill WA, Van Bemmelen PS, et al. High-risk carotid endarterectomy: fact or fiction. J Vasc Surg. 2003;37(1):40-6.

20. Diethrich EB. Carotid endarterectomy is better than carotid stenting for asymptomatic patients. Pro position. Tex Heart Inst J. 2006;33(2):209-10.

21. Diethrich EB. What happened to carotid stenting and will it be permanent? Anais Syllabus,CICE;2008.

22. Mas JL, Chatellier G, Beyssen B, Branchereau A, Moulin T, Becquemin JP, et al. Endarterectomy versus stenting in patients with symptomatic severe carotid stenosis. N Engl J Med. 2006;355(16):1660-71.

23. Perler BA, Willians GM. Carotid endarterectomy in the very elderly: is it worthwhile ? Surgery. 1994;116(3):479-83.

24. O'Hara PJ, Hertzer NR, Mascha EJ, Beven EG, Krajewski LP, Sullivan TM. Carotid endarterectomy in octogenarians: early results and late outcome. J Vasc Surg. 1998;27(5):860-9.

25. Rockman CB, Jacobowitz GR, Adelman MA, Lamparello PJ, Cagne PJ, Landis R, et al. The benefits of carotid endarterectomy in the octogenarian: a challenge to the resuts of carotid angioplasty and stenting. Ann Vasc Surg. 2003;17(1):9-14.

26. Bonamigo TP, Lucas ML. Análise crítica das indicações e resultados do tratamento cirúrgico da doença carotídea. J Vasc Bras. 2007;6(4):366-77.

27. European Carotid Surgery Trialists' Collaborative Group. MRC European Carotid Surgery Trial: interim results for symptomatic patients with severe (70-99%) or with mild (0-29%) carotid stenosis. Lancet. 1991;337(8752):1235-43.

28. Bonamigo TP, Weber EL, Lucas ML, Bianco C, Cardozo MA. Carotid endarterectomy in patients with contralateral occlusion: a 10-year experience. J Vasc Bras. 2004;3(1):83-91.

29. Samson RH, Showalter DP, Yunis JP. Routine carotid endarterectomy without a shunt, even in the presence of a contralateral occlusion. Cardiovasc Surg. 1998;6(5):475-84.

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