



## In Contraposition to the Article: “Carotid Endarterectomy is the Best Choice for Patients with Carotid Disease”

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The Leicester study is a study with only 17 patients, and no conclusion can be drawn from its results<sup>1</sup>.

The Cavatas<sup>2</sup> study demonstrated identical results for carotid stenting and endarterectomy. As regards the mortality results in the ECST<sup>3</sup>, the possible reasons presented have to do with differences in the populations studied. In the group of patients treated with carotid stenting, all the deaths were due to CVA, whereas in the group of patients treated with endarterectomy, four deaths were due to CVA and three were due to surgical complications after the procedure. It is understood that the causes of these deaths were attributed to complications relating to the treatment strategy and not to a statistical stratagem as the authors assert<sup>4</sup>. In fact restenosis was greater in those patients treated with carotid stenting, but >70% of the patients were treated only with the balloon, and when they were submitted to carotid stenting, restenosis was close to zero, as demonstrated in the SAPPHIRE study<sup>5</sup>.

In the Lexiton I and II studies, the results were similar between the group of patients treated with carotid stenting and the other group treated with endarterectomy, which revealed that the percutaneous technique had not been superseded by endarterectomy<sup>6</sup>.

The Sapphire study<sup>5</sup> was important in the analysis of the FDA (Food and Drugs Administration), the North American agency that regulates the pharmaceutical, food and medical device industries in the USA, for the approval of carotid stenting in high risk patients. The principle of non-inferiority is established in statistics and employed in several cardiology studies, and it's not unworthy of use. We point out to the author that the fact that patients are asymptomatic does not mean that they're free of high risk.

A recent meta-analysis that analyzed a total of 1,269 patients demonstrated that in 30 days the incidence of CVA and death after carotid stenting was 8.1% (51 out of 632 patients; mean from 0.0 to 12.1%) and 6.3% after endarterectomy (40 out of 637 patients; mean from 0.0% to 9.9%), and the difference between both treatments was not statistically significant<sup>7</sup>. The mortality in this meta-analysis was different in the ACST and

Medicare studies in the USA, because the populations have different risk levels. In cardiology, the elevation of CKMB is a predictor of more adverse clinical progress in the medium to long term. The author of the paper infers the presence of commercial influences in the results of the study. I would like to warn readers against the danger of such a statement, as it poses doubts as to the seriousness of researchers and medical journals published later. The funding of studies by the industry is relatively common in evidence-based cardiology; however, we have believed in the honesty of researchers and medical journals, because if it were not so, all the information contained in such journals would have to be challenged.

The Space<sup>8</sup> study was unable to demonstrate the non-inferiority of carotid stenting in relation to endarterectomy, but its results relate to an early progress and no conclusion can be drawn about the outcomes in the medium to long term, and therefore it cannot be used isolatedly to define a procedure. The SPACE study randomized 1,183 patients over a period of 180 days after the TIA or moderate CVA (modified ranking scale of  $\leq 3$ ) demonstrating that the CVA and death rates in 30 days for patients treated with endarterectomy were 6.34% and for patients treated with carotid stenting were 6.84%, with no statistically significant difference ( $p=0.89$ ). In this case, it should be pointed out to the author that the fact that the non-inferiority of one strategy was not proven does not imply the superiority of the other strategy, as suggested in his text.

The EVA 3-S<sup>9</sup> study, in its initial phase, did not use the cerebral protection system in half of the CVAs, and presented a CVA rate in this phase of 25% in the stenting group and was interrupted to allow the incorporation of the mandatory cerebral protection required by the protocol. Most CVAs occurred in the first day, which might be associated with complications of the procedure, but the carotid angiography showed no characteristics of high risk for such a complication. Therefore, the actual reasons of the neurological complications remained unclear. It should be pointed out that 42 (before) and 36 (after) patients submitted to carotid stenting were being given only one platelet antiaggregant and not the double platelet antiaggregation therapy, as recommended in the protocol. And lastly, the editorial by Dr. Anthony Furlan<sup>10</sup>, reveals that because of a series of factors such as the little technical experience of the surgeons, the EVA 3-S study cannot be used to define the superiority of endarterectomy as a strategy over stenting.

### Key words

Endarterectomy, carotid; stents; cerebrum-protection

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### Cochrane

We believe that in patients with high surgical risk, percutaneous treatment with stenting and cerebral protection

is an established procedure (in agreement with the FDA). For moderate and low risk patients, we still lack definitive conclusions despite the existence of superiority of one technique relative to the other. Studies which are underway, such as the ICSS<sup>11</sup> study that will analyze approximately 4,000 patients, will possibly define this issue.

### Comment related to table 2

The author states the following phrase in the last paragraph of the article: "After the publication of the SPACE and the EVA-35, these considerations will probably not undergo any alterations, given that, if we add the data of these two studies to the Cochrane analysis, we will obtain stroke and death rates of 8.1% in the CAS group and of 5.9% in the ECA group, with a difference in the results ( $p=0.02$ ) (Table 2)".

Observation: initially, it is necessary to confirm whether the author used the Chi-square test directly to reach this

conclusion with  $p=0.02$ . If that is the case, it must be emphasized that the direct use of the Chi-square test is not adequate in this case, as the possible differences between the studies were not considered. One cannot ignore that the data do not have the same origin and simply consider the totaling of patients from several studies as a single group of patients. According to Thompson<sup>12</sup>, meta-analyses should incorporate a careful investigation of the potential sources of heterogeneity among the studies. Meta-analysis studies commonly use the Mantel-Haenszel test, which consists in combining results from different contingency tables. Although the sources of heterogeneity must be investigated in detail, the Mantel-Haenszel test seems more adequate than the Chi-square test to summarize the results of the studies mentioned by the author. It is worth mentioning that, as the studies do not represent the total population of the studies of the area, the DerSimonian and Laird<sup>13</sup> method, which considers the studies as random samples, could also be considered<sup>14</sup>.

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