Periprocedural Complication Rate of Carotid Endarterectomy versus Carotid Angioplasty and Stenting: A Retrospective Study and Review of the Literature

Avi Gadoth MD[1*], Eitan Auriel MD MSc[1,2*], Hila Shaim[3] and Natan M. Bornstein MD[1,2]

[1]Department of Neurology and [2]Stroke Unit, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel
[3]Medical Faculty Heidelberg, Ruprecht Karl University Heidelberg, Heidelberg, Germany

ABSTRACT: **Background:** In the past, carotid endarterectomy (CEA) was the only modality for invasive intervention in cases of carotid stenosis. Due to improvements in endovascular techniques (stenting), there is a growing debate regarding the preferred procedure for carotid intervention.

Objectives: To compare the 30 day complication rate after CEA and carotid angioplasty and stenting (CAS) in a tertiary medical center in Israel between the years 2008 and 2010.

Methods: We reviewed the medical charts of all the patients who underwent either CEA or CAS of the internal carotid artery due to symptomatic and asymptomatic stenosis during the period 2008–2010 (total of 128 patients).

Results: There was no difference between the groups in the rate of severe complications in the peri-procedural period. Mild complications were non-significantly more common in the CEA group (17%) compared to the CAS group (7.1%).

Conclusions: There was no significant difference in the mild and severe complications rate between CEA and CAS in the peri-procedural period.

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Stroke is the third most common cause of death worldwide [1]. According to the National Acute Stroke Israeli Survey (NASIS), data show that approximately 15,000 patients were hospitalized during 2010 for stroke. The estimated death/hospitalization ratio for stroke was 0.063:1 (6.3%) [2]. Atherosclerotic lesions in the extracranial internal carotid arteries account for ischemic stroke in about 20% of cases. These are usually caused by arterio-arterial embolism and, significantly less commonly, by hemodynamic factors [3].

In the past, carotid endarterectomy was the only modality for invasive intervention in cases of severe, mostly symptomatic, carotid stenosis. As a result of improvements in endovascular techniques (stenting), there is a growing debate regarding the preferred procedure for carotid intervention in these patients. The complications associated with both procedures – CEA and stenting – are classified as mild and severe, as well as peri-procedural and long-term.

Six large randomized studies have compared CEA to carotid angioplasty and stenting with regard to the safety of both procedures [4-9]. The studies were not identical in several aspects, and the inclusion criteria were different, with only some of the studies including asymptomatic patients. In contrast to other studies, the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy study (SAPPHIRE) [5] included only high risk surgical patients, there was a difference in the credential requirements of the surgeons and interventionists, and there were differences in the devices and methods used.

Two studies – the EVA-3S trial (Endarterectomy versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis) trial and the ICSS (International Carotid Stenting Study) [6,9] – showed peri-procedural inferiority of CAS compared with CEA. One study, SAPPHIRE [5], showed a higher rate of peri-procedural complications in CEA compared with CAS, but this was mostly due to myocardial infarction, which was included as part of the primary outcome. When evaluating the rate of severe complications without myocardial infarction the peri-procedural complication rate was similar for both modalities.

Three studies – CAVATAS (Carotid and Vertebral Artery Transluminal Angioplasty Study), SPACE (Stent-Protected Angioplasty versus Carotid Endarterectomy) and CREST (Carotid Revascularization Endarterectomy versus Stenting Trial) [4,7,8] – yielded the same severe complication rate for both modalities.

Currently, no consensus has been reached on whether CAS is as safe as CEA for internal carotid artery intervention. In the present study we compared the 30 day complication

*The first two authors contributed equally to this article

CEA = carotid endarterectomy
CAS = carotid angioplasty and stenting
SAPPHIRE = Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy

rate after CEA and CAS in a tertiary medical center in Israel for the period 2008–2010.

PATIENTS AND METHODS

We reviewed the medical charts of all patients who underwent either CEA or CAS of the internal carotid artery due to symptomatic and asymptomatic stenosis between the years 2008 and 2010 (total 128 patients), focusing on the operative and perioperative 30 day complication rate following both procedures.

The complications were classified as mild and severe. Mild complications included hematoma, wound infection, lung or urinary tract infections, cranial nerve paresis, mild arrhythmias and larynx edema. Severe complications included myocardial infarction, stroke, death, sepsis and ventricular fibrillation. Pre-existing medical conditions were evaluated using the hospitalization charts.

The patients who underwent CEA or CAS were either patients with severe internal carotid artery stenosis (70%–99%), either symptomatic or asymptomatic, or symptomatic patients with moderate carotid artery stenosis (50–69%).

The decisions to intervene and which procedure was preferable for each patient were made by a multidisciplinary expert panel comprising vascular neurologists, vascular surgeons and a cardiologist who is also an endovascular interventionist. Patients who underwent CEA were operated by experienced vascular surgeons. Endovascular procedures were performed either by a cardiologist who was trained to perform the procedure or by a neuroendovascular specialist. Protective devices were used in all endovascular procedures.

We used chi-square test in the statistic analysis of the results for categorical variables and the Student *t*-test for continuous variables as appropriate.

RESULTS

Between 2008 and 2010 a total of 128 patients underwent intervention due to internal carotid artery stenosis: CAS in 28 patients and CEA in 100 patients. The patients' mean age was 69.5 ± 10.22 years in the CEA group and 64.5 ± 8.63 years in the CAS group ($P = 0.012$); 75% in the CEA group were males compared to 89.3% of the CAS group; 56% and 64% in the CEA and CAS groups respectively were symptomatic. Pre-existing conditions were similar in both groups [Table 1]. Hypertension was the most frequent risk factor in both groups. The clinical and demographical characteristics of the study population are summarized in Table 1.

There was no difference between both groups in the rate of severe complications in the peri-procedural period (7% and 7.1% for CEA and CAS respectively). Mild complications were non-significantly more common in the CEA group (17%) than in the CAS group (7.1%) [Table 2].

Table 1. Clinical and demographical characteristics of the study population

	Endarterectomy (n=100)	CAS (n=28)	*P* value
Age (yrs)	69.47 (47–86)	64.57 (45–83)	0.012
Female	25%	10.7 %	› 0.1
Symptomatic	56%	64.3 %	› 0.1
Ischemic heart disease	47%	64.3 %	› 0.1
Hypertension	78%	64.3 %	› 0.1
Hyperlipidemia	70%	50%	› 0.5
Heart failure	2%	3.6%	› 0.5
Smoking	20%	17.9%	› 0.5
Chronic renal failure	19%	14.3%	› 0.5
Diabetes mellitus	40%	32.1%	› 0.1
Peripheral vascular disease	13%	3.6%	› 0.1
Cancer	6%	0%	0.1
Atrial fibrillation	8%	0%	0.1

Table 2. Peri-procedural complication rate for both CEA and CAS

	Endarterectomy	CAS	*P* value
Mild complications (%)	17	7.1	› 0.1
Severe complications (%)	7	7.1	› 0.5

When excluding myocardial infarction as a primary endpoint the rate of severe complications in the CAS group remained 7.1% but decreased to 4% in the CEA group ($P < 0.01$). When subdividing the CEA group into symptomatic and asymptomatic patients, there was no significant difference in the rate of severe complications between the groups. There was also no significant difference in mild complications. In the CAS group, all complications occurred in the symptomatic patients.

When comparing the complications rate in symptomatic patients between the CEA and CAS groups, there was no significant difference between the rates of severe and mild complications. When subdividing the patients by age, there was a significant difference in the CAS group in severe complications rate between patients aged 70 years and older (22%) and those younger than 70 years (0%) ($P < 0.05$). There was a non-significant higher severe complications rate for patients aged 70 and higher in the CAS group compared to the CEA group.

If myocardial infarction had not been included as a primary outcome in our study, the severe complications rate in symptomatic patients ≥ 70 years old in the CEA group would have declined to 3.57% and in the CAS group to 7.1% ($P < 0.02$).

The severe complications rate in the CEA group included one death, three strokes and three myocardial infarctions,

one of which was non-ST elevation MI. Among the severe complications in the CAS group were two strokes. There were more cases of cranial nerve damage following CEA than CAS (eight events vs. none).

DISCUSSION

The present work was a retrospective, non-randomized study that analyzed the records of all patients who underwent either CEA or CAS due to internal carotid artery stenosis during the period 2008–2010. We did not find any differences in the rate of severe complications up to 30 days following the procedure between the two groups.

The first large randomized control study that compared both modalities was the CAVATS study [4] which, similar to our work, showed no difference in the severe complications rate between CEA and CAS. However, one important limitation of that study was that it began in 1992 when CAS was a new technique with which interventionists had little experience and a technology that was under development. One can claim that nowadays with experienced interventionists and advanced technology and equipment the results might have been different and would potentially show reduced complications in the CAS group.

Both the SAPPHIRE study [5], which included only high risk surgical patients, and the CREST study [8] found that MI was more prevalent during the peri-procedural period in the CEA group. When excluding MI as a primary outcome in the SAPPHIRE study the results show the same prevalence for severe complications in the peri-procedural period for both groups. When excluding MI as a primary outcome in the CREST study, the results show significantly fewer severe complications in the CEA group. Similarly, in our study, when excluding MI as a primary endpoint the severe complications rate in the CAS group remains at 7.1% but decreases to 4% in the CEA group ($P < 0.01$).

These findings, together with our results, emphasize the importance of careful patient selection regarding high surgical risk patients and pre-existing medical conditions. It is worth mentioning that unlike our study, the patients in the SAPPHIRE study were all high risk surgery patients and therefore the comparison with our study is limited.

The SPACE study [7], in agreement with ours, found no significant difference in the severe complications rate between both groups (6.84% with carotid artery stenting and 6.34% with carotid endarterectomy). However, it failed to prove non-inferiority of carotid artery stenting compared with carotid endarterectomy for the peri-procedural complications rate. The major difference between our study and the SPACE study is that in the latter, MI was not defined as a primary endpoint and therefore the two studies are difficult to compare.

MI = myocardial infarction

CREST = Carotid Revascularization Endarterectomy versus Stenting Trial
SPACE = Stent-Protected Angioplasty versus Carotid Endarterectomy

Table 3. Summary of large prospective randomized control studies

	Symptom-atology	Periprocedural minor complications	Peri-procedural major complications	Surgeons and interventionist inclusion criteria	Use of protective device
CAVATAS [4]	Not addressed	More in CEA	Same	Record of interventionists reviewed by a committee, no definition regarding number of procedures	No protective device
SAPPHIRE [5]	Both	More in CEA	More in CEA with MI as primary endpoint. Without MI as primary endpoint results were the same	The experience of surgeons had to meet the criteria of the American Heart Association with respect to acceptable rates of complications during and after carotid endarterectomy, and the experience of interventional physicians had to be equal to or superior to the published results of carotid stenting (i.e., an incidence of periprocedural stroke or death of less than 6%)	Protective device was used
EVA-3S [6]	Symptomatic	Same, more cranial nerve palsies in CEA	More in CAS	Surgeons had at least 25 procedures in the year before the study. Interventionists had at least 12 carotid endovascular procedures or 35 supra-aortic procedures with at least five of them in the carotid	Protective device was used
SPACE [7]	Symptomatic	NA	Same	Surgeons had at least 25 procedures. Mortality and morbidity rates were reviewed by a committee. Interventionists had to have at least 25 consecutive successful procedures.	27% were with protective device
CREST [8]	Both	More cranial nerve palsies in CEA	Same CAS – more stroke CEA – more MIs	Surgeons with at least 12 procedures per year and low complication rate. Interventionists' records were reviewed by a committee	Protective device mandatory (96%)
ICSS [9]	Symptomatic	More in CEA	More in CAS	Surgeons and interventionists with at least 50 procedures. Protection	Protective device not mandatory

CAVATAS = Carotid and Vertebral Artery Transluminal Angioplasty Study, SAPPHIRE = Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy, EVA-3S = Endarterectomy versus Angioplasty Symptomatic Severe Carotid Stenosis, SPACE = Stent-Protected Angioplasty versus Carotid Endarterectomy, CREST = Carotid Revascularization Endarterectomy versus Stenting Trial, ICCS = International Carotid Stenting Sudy

In contrast to our study, EVA-3 [6] and ICSS [9], both large prospective randomized studies, showed more periprocedural severe complications in the CAS group. In both studies there were strict requirements regarding surgeons and endovascular specialists [Table 3] for participation in the study. In EVA-3 the use of a protection device was mandatory in contrast to ICSS. It is important to emphasize that our study was a small retrospective, non-randomized study and the procedures (CEA and CAS) were performed by three different groups: vascular surgeons, cardiologists and neuroradiologists. Since our study was retrospective we could not implement strict enrollment criteria for interventionists as in the other randomized studies.

In a meta-analysis including symptomatic patients from the EVA-3S, SPACE and ICSS studies, the investigators assessed the difference in severe complications according to age. The data showed a significantly higher risk for severe complications in the CAS group compared to the CEA group (10.5% vs. 4.4%, $P = 0.0078$) for patients 70 years and older, but there was no significant difference in the severe complications rate in patients under age 70 (5.1% for CAS and 4.5% for CEA) [10]. Our data showed significant differences in the CAS group in the severe complications rate between patients older than 70 (22%) and younger than 70 (0%) ($P < 0.05$). The data also showed a non-significant higher severe complications rate for symptomatic patients ≥ 70 years old in the CAS group compared to the CEA group.

The meta-analysis did not include MI as a primary outcome. If not including MI as a primary outcome in our study, the severe complications rate in symptomatic patients aged ≥ 70 in the CEA group would have declined to 3.57% and in the CAS group it would have remained the same (since there were no MIs in this group). The difference now between the CEA and CAS groups becomes significant ($P < 0.02$).

CONCLUSIONS

Our results show no significant difference in the mild and severe complications rate between CEA and CAS in the periprocedural period. Symptomatic patients ≥ 70 years are more likely to have severe complications if undergoing CAS. For patients younger than 70 years old the severe complications rate is the same.

Our results should be viewed cautiously since our study is retrospective and involved a small number of patients, especially in the CAS group. On the other hand, we provide recent data from procedures performed by experienced physicians using the most advanced equipment. The long-term outcome of these procedures was not explored in our study and should be taken into consideration when choosing the suitable procedure.

Corresponding author:
Dr. A. Gadoth
Dept. of Neurology, Tel Aviv Sourasky Medical Center, 6 Weizmann St., Tel Aviv 64239, Israel
Phone: (972-3) 697-3424
Fax: (972-3) 697-4318
email: avigadoth@gmail.com

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