### Letter to the Editor

## Editöre Mektup

# Carotid artery stenting is not an alternative to surgery

To the Editor,

I have read the article "2 year results of carotid artery stenting (CAS)" by Arslan et al. They included 120 patients of whom 75% were neurologically symptomatic, and the rest were asymptomatic patients. They had to abort the procedure in four patients. They had one very early stroke and two late transient ischemic attacks. Furthermore, there was a 2.5% restenosis rate in 2 years. They discussed their results with the literature and came to two conclusions; (i) CAS is an alternative to carotid endarterectomy (CEA) in symptomatic and asymptomatic patients, (ii) in patients who are candidate for cardiac surgery, asymptomatic carotid lesions can be treated effectively and reliably with CAS.[1]

When the authors used the "carotid revascularization endarterectomy versus stent trial" (CREST) in their discussion, they did not mention about the subgroup analysis. In their paper, they quoted "patients being symptomatic or asymptomatic or patients' gender did not play as distinguishing factors in terms of primary endpoints." Of course, subgroup analysis did show that this not true. CAS was associated with higher stroke and death rates in symptomatic patients, females, and patients  $\geq$ 65 years compared with CEA. If these groups are removed, the only patients left in whom CAS was associated with similar stroke and death rates with CEA were asymptomatic males <65 years of age.<sup>[2]</sup> In considering carotid revascularization in asymptomatic patients, it is of utmost importance to realize that the natural risk for stroke has declined with the introduction of better medication.[3] To elucidate the effect of best medical therapy, there are two randomized controlled studies ongoing in Europe. One is the European carotid surgery trial 2 and the other is stent - protected angioplasty in asymptomatic carotid artery stenosis versus endarterectomy (Space-2). Both of these studies have a third arm consisting of medical therapy.

AHA/ASA guidelines were published according to

the CREST results which were flawed. Crest investigators in their study design simply add death, stroke, and myocardial infarction (MI) which was according to the bio markers together and came to a conclusion. The subgroup analysis showed that MI seen in the surgical group did not change the quality of life while major and minor strokes had a considerable effect on patients physical health in the CAS group. [2,4] Later, Wesley Moore, the principal investigator of CREST declared that there was a design error.<sup>[5]</sup> AHA/ASA did not take into consideration the results of the International Carotid Artery Stenting Study (ICSS). The pooled analysis of EVA-3S, Space, and ICSS showed that in patients <70 years old the 120-day stroke or death risk was 5.8% CAS and 5.7% in CEA, whereas in patients 70 years or older there was an estimated two-fold increase risk with CAS over CEA. [6] According to the recent "inter-collegiate Australasian CAS guidelines," CAS may be considered as a treatment option for patients with symptomatic severe carotid stenosis who are at high risk of stroke, but are surgically unsuitable for CEA. This includes specific patient subgroups and conditions, namely (1) postradiation therapy, (2) block dissection of the neck, (3) in situ tracheostomy, (4) recurrent stenosis following previous CEA, (5) severe cervical spine arthritis, (6) surgically inaccessible carotid stenosis (e.g., obesity and high carotid bifurcation, (7) contralateral recurrent laryngeal nerve injury, and (8) contralateral carotid artery occlusion.[7] The European society for vascular surgery guidelines is basically similar to the Australasian CAS guidelines. With level 1 evidence, they suggested surgery as the best option for symptomatic patients (A). CAS should be offered to symptomatic patients if they are at high risk for CEA, in high-volume centers with documented periprocedural stroke and death rates or inside an RCT (C). For asymptomatic patients, CAS was advised only in highvolume centers with documented low periprocedural stroke and death rates or within well-conducted clinical trials (C).[8]

The second issue in Arslan's paper was the treatment of asymptomatic carotid stenosis in patients who are candidate for coronary bypass surgery with CAS reliably and effectively.<sup>[1]</sup>

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Stroke complicates 2% of all cardiac surgery procedures and remains an important cause of mortality and permanent neurologic disability.[9] There are many reasons for stroke during cardiac operations; such as low cardiac output states, arrhythmias, embolization during aortic dissection and cannulation, extracorporeal circulation-oriented, metabolic, and disease of the carotid artery bifurcation. Surveys showed that the presence of coronary and carotid disease in the vast majority of patients is asymptomatic unilateral disease.[10] One meta-analysis showed that the risk of stroke was the lowest in patients with unilateral asymptomatic carotid stenosis (3%) and was the highest in neurologically asymptomatic patients with bilateral carotid disease (6%). The risks for asymptomatic unilateral disease did not increase with stenosis severity. Another interesting finding was the prevalence of stroke in the hemisphere ipsilateral to a nonoperated asymptomatic severe stenosis in patients with severe bilateral carotid disease undergoing a synchronous unilateral CEA + cardiac procedure was relatively low (4%). From this meta-analysis, we can deduce that no other procedure is required for the asymptomatic unilateral carotid stenosis in patients who are going to have a cardiac operation. A small minority of patients will have bilateral disease and prophylactic CEA/CAS might be considered in these patients but keeping in mind that only 1-2% of such patients will benefit from prophylaxis.[11]

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#### Authors' reply

#### Dear Editor,

Carotid artery stenosis is the most common cause of ischemic stroke and the mortality and morbidity rate is high. Although the treatment of carotid artery stenosis have begun with carotid endarterectomy (CEA), en-

dovascular carotid artery stenting (CAS) has become a favorable alternative treatment modality to CEA, in consequence of increased experience and technological advancement and as a result of guidance of randomized trials. During this period, there have been improvements in CEA techniques and medical treatment.

Carotid artery stenosis should be approached with a

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multidisciplinary attitude. Patients with carotid artery disease are treated and followed up by a council including two physicians from every department of neurology, radiology, cardiology and cardiovascular surgery in our hospital. Primary physician evaluating and following up the patients with ischemic stroke or patients with high risk of stroke is the neurologist. Patients with carotid artery stenosis are primarily evaluated by a neurologist and assessed with carotid ultrasonography, computed tomography angiography, and when needed, with conventional carotid angiography by a radiologist. Moreover, distribution of extra and intracranial arteries, presence of communicating arteries are also evaluated and patients are assessed in detail by the council. Physicians from other departments also participate in the council in case of additional comorbidities. Treatment modality is chosen according to a consensus reached by the council. After being fully informed, the opinion of the patient and his/her relatives could also direct the choice of treatment modality.

There are multiple factors affecting the choice of treatment modalities. Patient based approach may also have an additional impact on general principles of the treatment. CEA is the preferred modality when the lesion is longer than 2 cm and when it is a circular calcified lesion, ulcered and/ or thrombosed, and when it is a severe tortious lesion. On the other hand, CAS is the preferred modality when carotid artery stenosis is bilateral and/or distally located or in patients with total occlusion of contralateral carotid artery or insufficient anterior or posterior communicating arteries as well as in patients with history of radiotherapy to neck.

CAS is not opted if there are comorbidities such as significant renal disease, history of stent thrombosis, resistance to acetyl salicylic acid and clopidogrel, tendency of thrombosis in rheumatologic tests or any situation unfavorable for long term dual antiplatelet therapy, whereas CEA is not preferred when surgery constitutes a high risk due to additional diseases. Medical treatment is favored if life expectancy is short or follow up of patient is not feasible.

Intervention to carotid artery stenosis is chosen according to the present data of trials and experience of centers. There are important inadequacies in trials performed before Stenting versus Endarterectomy for Treatment of Carotid-Artery Stenosis (CREST). Em-

bolus protection device (EPD) was not used and only 26% of the patients were implanted stents in Carotid and Vertebral Artery Transluminal Angioplasty (CA-VATAS).<sup>[1]</sup> EPD use in Stent- Protected Angioplasty versus Carotid Endarterectomy (SPACE) trial is very low.<sup>[2]</sup> Physicians with adequate experience in endo-vascular intervention is 39% in Endarterectomy versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis (EVA-3S).<sup>[3]</sup> EPC was not obligatory and only symptomatic patients were included in International Carotid Stenting Study (ICSS).<sup>[4]</sup> All of these difficulties preclude a certain comparison of CAS and CEA in regard to carotid artery disease.

The most important study guiding the treatment of carotid artery stenosis in guidelines is the CREST trial. Any significant difference was not ascertained in symptomatic or asymptomatic male and female patients among CAS and CEA results with respect to primary end point of death, myocardial infarction and stroke even when the subgroup analysis of CREST was also assessed. [5] Pre-procedural stroke was more frequent in female patients and/or in symptomatic patients who were performed CAS, compared to CEA. CEA is recommended in elderly patients (>70) due to the fact that vascular tortuosity and intense calcification are more prevalent in the elderly. [5]

The experience of operator is extremely important with respect to the success of carotid artery revascularization. The physicians performing CAS were determined after the pre-selection in the CREST trial. The most successful operators were cardiologists and neuroradiologists in terms of success of procedure and complication rates according to CREST. [6] We consider our institution experienced according to annual count of procedure and complication rates.

The patients undergoing coronary bypass surgery may have carotid artery disease, which is usually unilateral. Most of these patients are not intervened regarding carotid artery disease. Carotid artery revascularization is recommended before coronary bypass surgery in patients with high pre-procedural stroke risk. Twenty five percent of our patients were asymptomatic and 80% (24 patients) of these patients was performed CAS before coronary bypass surgery. These patients were also assessed by the council and CAS was performed with the consent of cardiovascular surgeons.

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CEA is recommended with class 1A indication, whereas CAS is recommended with class 1B indication in symptomatic patients with carotid artery stenosis according to 2011 ASA/ACCF/AHA guidelines. Revascularization is recommended with class 1C indication in asymptomatic patients taking account of life expectancy of patient, other individual risk factors and preference of patient according to same guideline.<sup>[9]</sup>

As a conclusion, we consider that carotid artery revascularization should be performed in experienced centers under the decision of a council consisting neurology, radiology, cardiology and cardiovascular surgery departments in the light of contemporary guidelines; however, evaluation of individual factors should also be taken into account.

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