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Chapter 5

Do Women Have a Higher Risk of Adverse Events after Carotid Revascularization?

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Abstract

Carotid artery stenosis is thought to cause up to 10% of ischemic strokes. Till now, the optimal treatment between carotid endarterectomy (CEA) and carotid artery stenting (CAS) remains debated, in particular for specific subgroups of patients. Available data suggest that female have higher risk of perioperative adverse events, but conflicting results comparing CEA and CAS regarding the benefit for male or female are present in the literature. A systematic review of recent publications on gender-related differences in operative risks is reported. Moreover, a consecutive cohort of 912 symptomatic and asymptomatic patients undergoing CEA (407, 44.6%) or CAS (505, 55.4%) in a single institution has been evaluated to determine the influence of gender (59.7% male vs. 40.3% female) on the outcomes after both revascularization procedures at 30 days and during 3 years of follow-up. Our experience seems to confirm literature data as regarding female higher risk of restenosis. Female patients had higher periprocedural (2.7% female vs. 0.9% male; $p < 0.05$) and long-term (11.4% female vs. 4.6% male; $p < 0.05$) restenosis rate. In conclusion, female anatomic and pathologic parameters should be taken into account for an accurate diagnosis of carotid stenosis and guidelines should be adjusted consequently.

Keywords: carotid endarterectomy, complications, gender, mortality, restenosis, stenting

1. Introduction

Carotid artery stenting (CAS) might be a potentially safe and effective therapeutic alternative to carotid endarterectomy (CEA) for carotid artery disease, especially in high-risk

patients, because CAS may avoid anesthetic and surgical risk. In this regard, the merit of using CAS has been questioned in specific subgroups of patients [1, 2]. The role of gender in the selection of the most effective carotid intervention remains a matter of debate. Historically, large randomized controlled studies looking at CEA had indicated an increased perioperative risk for women when gender subgroup analysis was performed. Additionally, all of the large CEA trials showed decreased or no benefit in women when compared to men mostly because these trials were underpowered to show any utility in the relatively small female population studied and, secondly, because the long-term benefit was undermined by the high perioperative morbidity seen in women [3, 4]. The SAPPHIRE trial was the first stenting trial to show noninferiority of CAS to CEA in high-risk patients, but the study did not compare outcomes for gender subgroups and women were underrepresented within the recruited population [5]. More recent trials reported conflicting results regarding risk of peri- and postprocedural adverse events for women and men [1, 6]. Then, reports comparing CEA and CAS failed either to analyze the influence of gender or to show a clear benefit for men or women [7].

Thus, to further inform the debate, we sought to conduct a systematic review of recent publications to assess epidemiologic and diagnostic hypotheses, which could underpin gender-related differences. Moreover, we report a retrospective observational study to determine the impact of gender on the outcomes of both carotid interventions in our institution.

2. Gender: stroke epidemiology and carotid disease

2.1. Gender differences in stroke epidemiology

An extensive review on gender differences in stroke epidemiology has shown that stroke is more common in men than in women and male patients are on average younger than female when they are affected by their first stroke [8]. Western European studies demonstrated that stroke incidence was about 30% higher in men than in women, but the strokes that did occur in women tended to be more severe [9]. During the last decade, an extensive number of papers have been published on epidemiological differences between genders.

A systematic review around gender differences in stroke epidemiology, presented by Appelros et al., including 59 incidence studies from 19 countries and 5 continents, showed that the mean age at first-ever stroke was 68.6 years among men and 72.9 years among women [10]. Stroke incidence and prevalence rates were 33 and 41% higher in male than in female, respectively, with large variations between age bands and between populations. The incidence rates of brain infarction and intracerebral hemorrhage were higher among men, whereas the rate of subarachnoid hemorrhage was higher among women, although this difference was not statistically significant. Stroke tended to be more severe in women with a 1-month case fatality of 24.7% compared with 19.7% for men.

The lower stroke incidence in women has been analyzed in systematic reviews in the last decades. A plausible reason might be the protective role of ovarian estrogen on the cerebral

circulation [11–13], even if randomized trials currently recommend that postmenopausal hormone therapy should not be used in the primary prevention of stroke [14].

Other possible factors might be genetic factors, but no evidence for this expectation was found in the literature. Conversely, a recent systematic review showed that women with stroke have a higher familiarity of stroke than men [15].

Numerous studies have shown that blood pressure value was higher in men than women of same age [16, 17]. Moreover, peripheral artery disease [18, 19], ischemic heart disease [18, 20–22], and cigarette consumption [18–20, 23, 24] are more frequent among male stroke patients. Women have been shown to be at higher risk than men for atrial fibrillation-related cardioembolic stroke [22, 25–28]. The Swedish Stroke Register has shown that women with atrial fibrillation receive oral anticoagulant therapy less often than men [24]. The higher prevalence of embolic strokes among women could justify their higher stroke severity.

2.2. Diagnostic criteria for carotid stenosis by gender

The North American Symptomatic Carotid Endarterectomy Trial (NASCET) investigators standardized the method of quantifying the degree of carotid stenosis, and they considered arteriography the most predictable method for evaluating carotid stenosis [29].

Carotid duplex ultrasound scan (DUS) compares favorably with arteriography, and many physicians are using carotid DUS as the definitive diagnostic procedure before CEA even if it is mandatory to submit the patient to computer tomography angiography (CTA) or magnetic resonance angiography (MRA) for CAS to explore arch anatomy [30, 31]. Diagnostic criteria for carotid DUS have been accepted as predictable from laboratories accredited by the Intersocietal Commission for the Accreditation of Vascular Laboratories with ongoing quality programs.

Nevertheless, carotid DUS frequently resulted in overestimation of disease severity in women. This underlined the issue that women may have higher velocities in their carotid arteries than men for similar carotid stenosis. The question is: Are we overdiagnosing disease in women according to gender differences in carotid stenosis? The purpose of Comerota's study was to examine whether there were velocity differences based on gender in patients with carotid artery disease and whether different velocity criteria should be used in women, especially at clinically relevant thresholds of disease [32].

Patients who underwent carotid arteriography and carotid DUS were the basis for this study. Data from 1019 carotid bifurcations were available. Comparison was performed on the basis of 938 carotid arteries. Analyses were made in 536 male and 402 female carotid arteries. Arteriography was performed on average 23 days after the ultrasound examination, with 74% of arteriographic examinations performed within 30 days and 95% performed within 82 days of carotid DUS. Additionally, the single most diseased artery per patient was analyzed by gender. Peak systolic velocity (PSV) and end-diastolic velocity (EDV) were averaged for data subsets according to 10% intervals of internal carotid artery (ICA) stenoses. For all intervals, PSV and EDV averaged 9 and 6% higher in women than in men. Significant gender differences existed between PSV and EDV for 60 and 70% stenoses. For 70% stenosis, PSV averaged 285 $\pm$ 16 cm/s in women and

236 ± 11 cm/s in men ($p = 0.01$) and EDV averaged 79 ± 7 cm/s in women and 77 ± 6 cm/s in men ($p = 0.03$). For 60% stenosis, PSV averaged 228 ± 14 cm/s in women and 189 ± 11 cm/s in men ($p = 0.03$) and EDV averaged 68 ± 6 cm/s in women and 51 ± 4 cm/s in men ($p = 0.01$).

Williams et al. demonstrated that the diameter of the common carotid arteries (CCA), ICA, and external carotid arteries (ECA) were considerably smaller in women compared to those in men [33]. Schultz et al. showed a remarkable gender-specific difference in the distribution of atherosclerotic plaque. They reviewed 5395 arteriograms from the European Carotid Surgery Trial and compared diameter ratios of the ICA, CCA, and ECA with minimal disease to obtain a real relationship between vessels [34]. Among the 2930 arteriograms available for review, the mean ICA/CCA, ICA/ECA, and outflow/inflow area ratios were larger in women than in men ($p < 0.0001$). In addition, there were differences in the distribution of carotid plaque, with men more likely to have maximal stenosis in the ICA and women having a greater degree of plaque within the carotid bulb. Moreover, women appeared to have more severe disease in the ECA, which would also bias the distribution of existing flow velocity through the patent ICA.

Hansen et al. showed changes in arterial wall compliance in women who display higher age-related stiffness of their arteries and develop a higher degree of pulsatility with a higher velocity for any given blood pressure [35, 36].

Moreover, the natural history of carotid atherosclerosis emerges to be divergent in women compared with men. Independently from age, the risk for stroke is higher in men than in women [37]. The risk for stroke is greater in men with similar degrees of carotid stenosis [4, 29, 38] due to the fact that men have greater prevalence of high-risk carotid plaques. Joakimsen et al. showed that atherosclerotic lesions in men were more instable and ultrasound characteristics showed soft and lipid-rich plaques, with more common intraplaque hemorrhage. These characteristics are associated with an increased risk for ischemic events, including myocardial infarction (MI) and stroke [39–41].

According to those anatomic and pathologic gender-related differences, the higher velocity profiles observed in women compared with men could be explained. It needs to be adjusted in guidelines for an accurate and proper diagnosis in carotid stenosis in the near future.

2.2.1. Women gender-specific parameters

- Considerably smaller carotid diameter.
- Higher arterial velocity in carotid artery: PSV and EDV.
- Different distribution of atherosclerotic plaque with greater degree of plaque within the carotid bulb and more severe disease in the ECA.
- Different arterial wall compliance with higher age-related stiffness and higher degree of pulsatility.
- Presence of artifacts increasing arterial velocity (anemia).

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3. Carotid revascularization: gender differences

3.1. Carotid revascularization outcomes in women compared with men

The literature shows that women have a higher risk of perioperative adverse events during carotid revascularization. In the Asymptomatic Carotid Atherosclerosis Study (ACAS), women had a higher rate of perioperative events (3.6% female [F] vs. 1.7% male [M]) during CEA [42] with a lower rate of events for female (8.7% F vs. 12.1% M) treated with best medical therapy. This result shows a lower 5-year risk reduction for female (17%) compared with male (66%).

The Asymptomatic Carotid Surgery Trial (ACST) suggested a lower long-term benefit of surgery for female, with male collecting a higher 5-year risk reduction than female (8.21% M vs. 4.08% F) [43]. In the International Carotid Stenting Study (ICSS), female had a higher 120-day event rate for CEA (7.6% F vs. 4.2% M) but a lower rate for CAS (8.0% F vs. 8.7% M) [44]. Reverse results was found in the Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST) [6]. In this study, 2502 patients were randomly assigned to CEA (n = 1240) or CAS (n = 1262), 872 (34.9%) of whom were female. Rates of the primary endpoint for CAS compared with CEA were 6.2% vs. 6.8% in male (hazard ratio [HR] 0.99, 95% confidence interval [CI] 0.66–1.46) and 8.9% vs. 6.7% in female (HR 1.35, 95% CI 0.82–2.23). There was no significant interaction in the primary endpoint between genders (interaction $p = 0.34$). Periprocedural events occurred in 35 (4.3%) of 807 males assigned to CAS compared with 40 (4.9%) of 823 assigned to CEA (HR 0.90, 95% CI 0.57–1.41) and 31 (6.8%) of 455 females assigned to CAS compared with 16 (3.8%) of 417 assigned to CEA (HR 1.84, 95% CI 1.01–3.37; interaction $p = 0.064$).

In 2014, Jim et al. presented data from the Society for Vascular Surgery Vascular Registry to determine the effect of gender on outcomes after carotid revascularization [45]. There were 9865 patients (40.6% female) who underwent CEA (n = 6492) and CAS (n = 3373). The primary end point was a composite of death, stroke, and MI at 30 days. There were no differences in age and ethnicity between genders, but males were more likely to be symptomatic (41.6% M vs. 38.6% F; $p < 0.003$). There was a higher prevalence of hypertension and chronic obstructive pulmonary disease in female, whereas male had a higher prevalence of coronary artery disease, history of MI, and smoking history. For disease etiology in CAS, restenosis was more common in female (28.7% F vs. 19.7% M; $p < 0.0001$) and radiation was higher in male (6.2% M vs. 2.6% F; $p < 0.0001$). Comparing by gender, there were no statistically significant differences in the primary endpoint for CEA (4.07% F vs. 4.06% M) or CAS (6.69% F vs. 6.80% M). There were no differences after stratification by symptomatology and multivariate risk adjustment. These divergent results seem to be associated with different factors. In the last decades, best medical therapy improved significantly with a wide disposability of statins and antiplatelets with beneficial results on patient outcomes [46]. Another factor seems the fact that females were underrepresented in carotid randomized controlled trials [6].

4. Do women have a higher risk of adverse events after carotid revascularization in our experience?

4.1. Study design

A database of 912 consecutive patients with symptomatic or asymptomatic carotid artery stenosis undergoing CEA or CAS for carotid revascularization in the Department of Surgery of a single Institution from 2010 to 2017 was analyzed. Carotid stenosis was ≥80% for asymptomatic or ≥50% for symptomatic patients, as detected by DUS and confirmed by CTA or MRA using NASCET criteria [29].

The choice of revascularization technique (CAS/CEA) was based on general guideline recommendations, for example, European Society for Vascular Surgery (ESVS), American College of Cardiology and American Heart Association (ACC/AHA), and the team center experience according to morphologic and clinical data indicating best suitability with the aim of performing CAS and CEA with low procedural risks. Usually, patients with unfavorable aortic arch anatomy, severe peripheral vascular disease precluding femoral access, or extremely tortuous carotid anatomy were excluded from CAS. Similarly, unstable plaque, known allergies to aspirin, clopidogrel, or contrast media, and renal insufficiency (creatinine ≥1.5 mg/dL) were considered exclusion criteria for CAS.

4.2. CAS and CEA protocols

For CAS, the patient was given dual antiplatelet therapy beginning 1 day before the procedure. All patients received a 300 mg loading dose of clopidogrel 1 hour before the procedure.

Clinical investigation included a baseline assessment of a physical examination, carotid DUS of the supra-aortic vessels, procedural angiography, and neurological assessment measured using the National Institutes of Health Stroke Scale (NIHSS) [47]. All aortic arch types were included.

All procedures were performed following a standardized protocol in the operating room, equipped with a portable imaging fluoroscopic C-arm (OEC 9900 elite; GE Medical Siemens, Waukesha, WI, USA), by a single vascular team. Two skilled operators with high volume experience (>50 CEA/CAS procedures per year as first operator) performed all procedures [48–50]. Iodinated or gadolinium contrast was used in patients with normal creatinine level or creatinine >1.5 mg/dL (132 mmol/L), respectively. All patients received an intravenous heparin bolus (100 units/kg heparin) to achieve intraoperative anticoagulation (activated clotting time (ACT) ≥ 250 s throughout the procedure). In our center, with increasing experience, the number of CAS increased over time allowing CEA to be used for fewer and more complex cases in recent years. All procedures were carried out via femoral access. The introducer sheath (8 Fr) and guiding catheters (Zuma, Medtronic, MN, USA; Flexor, Cook Medical, IN, USA; Mach 1, Boston Scientific Corporation, MA, USA) ranged from 6 to 8 Fr, using inner catheters (coaxial method) with different shapes according to the anatomy of the arch (Imager II, Boston Scientific Corporation). Variable models of carotid stents (open-cell, closed-cell, hybrid, and micromesh

stents) were employed, as a function of lesion characteristics and vessel anatomy. Temporary distal (Emboshield NAV6, Abbott Vascular, Santa Clara, CA, USA) or proximal (Mo.Ma, Medtronic, Minneapolis, MI, USA) cerebral protection devices were used as per internal protocol. Predilation was performed at the operator's discretion, with 2.0–4.0 mm TREK coronary balloons (Abbott Vascular). Postdilation was performed with a 4.5- or 5.5-mm diameter Rx Viatrac 14 Plus balloons (Abbott Vascular). CAS postoperative medical therapy included clopidogrel (75 mg once daily) for 1 month and aspirin (100 mg once daily) for a lifelong period.

For CEA, patients were usually maintained on aspirin therapy. CEA was performed under local anesthesia under electroencephalography (EEG) monitoring or transcutaneous oxygen saturation monitoring. Dacron or bovine pericardium graft angioplasty, or eversion endarterectomy were performed.

4.3. Procedural follow-up

Postprocedural patient evaluation was performed at the periprocedural (30 days) and at the postprocedural periods, at 3 months, 6 months, and yearly thereafter within 3 years, by a neurologist and a vascular surgeon.

Patient data were captured using a paper case report form. Symptoms status and exact information about clinical adverse events were obtained. Carotid DUS of the supra-aortic vessels was obtained to determine the degree of carotid stenosis.

4.4. Endpoints, definitions, and statistical analysis

Primary endpoints were rates of death; stroke; MI; a composite of the incidence of any stroke, MI, or death; and restenosis within 30 days. Secondary endpoints were rates of death; stroke; MI; a composite of the incidence of any stroke, MI, or death; and restenosis, during the follow-up period, within 36 months after the procedure.

For the composite of any stroke, MI, or death, patients might have had more than one event. For example, fatal stroke events are included in both death and stroke outcomes, and subjects might have had both an ipsilateral and a subsequent contralateral stroke. The diagnosis and quantification of restenosis was performed using carotid DUS. Carotid restenosis was set at ≥40% [51, 52].

Categorical variables were reported as number and percentages. For numeric variables, minimum, maximum, mean, and standard deviation were calculated. Continuous data are presented as percentages or mean ± standard deviation (SD). Rates for comorbidities, complications, and 30-day outcomes were compared between male and female patients and between those undergoing CAS and CEA by χ^2 test. Survival, stroke, MI, and restenosis rates were calculated using Kaplan-Meier analysis to compensate for patient dropouts and were reported using current Society for Vascular Surgery (SVS) criteria [53]. Standard errors (SE) are reported in Kaplan-Meier analyses. The log-rank test was used to determine differences among patients submitted to CEA and CAS.

A value of $p < 0.05$ was considered statistically significant for all measurements. All analyses were performed using STATA™ (STATA Corp., version 14.0, College Station, TX, USA).

The study was approved by the local Ethic Committee of Istituto Auxologico Italiano (statement CE 30.05.2006). Written consent was obtained from all patients before both CAS and CEA revascularization.

4.5. Results

From 2010 to 2017, a total of 912 patients underwent interventions for carotid stenosis. There were 544 (59.7%) males and 368 (40.3%) females. Mean age was 71.1 ± 8.6 and 69.4 ± 9.0 for male and female patients, respectively. About 193 (35.4%) male and 128 (34.7%) female patients were symptomatic. Of the 912 carotid revascularizations, 407 (44.6%) were by CEA and 505 (55.4%) were by CAS. Demographic and baseline characteristics of study participants after separation by gender and procedure are presented in **Table 1**. Female patients were older (72.1 ± 9.0 F vs. 68.4 ± 8.6 M, $p < 0.05$) and more likely to have a history of hypertension (79.7% F vs. 72.5% M, $p < 0.05$) and hyperlipidemia (74.4% F vs. 69.2% M, $p < 0.05$) with respect to male patients. Male patients were more likely to be smokers (35.0% M vs. 33.3% F, $p < 0.05$) and to have history of MI (19.7% M vs. 17.5% F, $p < 0.05$), chronic renal insufficiency (20.5% M vs. 11.9% F, $p < 0.05$), and CAD (28.0% M vs. 26.1% F, $p < 0.05$). The distribution of comorbidities within the two procedural groups was similar. For CAS patients, men were more likely to have diabetes (37.9% M vs. 33.5% F, $p < 0.05$) and chronic renal insufficiency (18.0% M vs. 13.8% F, $p < 0.05$) and women had a higher prevalence of hypertension (89.5% F vs. 71.5% M, $p < 0.05$) and hyperlipidemia (82.9% F vs. 72.0% M, $p < 0.05$). For CEA patients, men tended to have a higher prevalence of history of MI (20.3% M vs. 16.0% F, $p < 0.05$) and chronic renal

	M (n = 544)	F (n = 368)	CEA (n = 407)		CAS (n = 505)	
			M (n = 326)	F (n = 200)	M (n = 241)	F (n = 145)
Age, mean ± SD	68.4 ± 8.6	72.1 ± 9.0	68.9 ± 8.5	71.5 ± 9.3	68.0 ± 8.7	72.8 ± 8.6
Symptomatic, n (%)	193 (35.4%)	128 (34.7%)	108 (33.1%)	70 (34.9%)	85 (35.0%)	58 (40.1%)
Smokers, n (%)	191 (35.0%)	123 (33.3%)	109 (33.4%)	77 (38.8%)	82 (33.8%)	45 (31.3%)
Hypertension, n (%)	395 (72.5%)	293 (79.7%)	222 (68.0%)	164 (82.0%)	173 (71.5%)	129 (89.5%)
Diabetes, n (%)	172 (31.7%)	127 (34.5%)	81 (24.8%)	78 (39.3%)	91 (37.9%)	48 (33.5%)
Hyperlipidemia, n (%)	376 (69.2%)	274 (74.4%)	202 (62.0%)	154 (77.1%)	174 (72.0%)	120 (82.9%)
CAD, n (%)	152 (28.0%)	96 (26.1%)	86 (26.4%)	55 (27.5%)	66 (27.3%)	41 (28.5%)
History of stroke, n (%)	133 (24.5%)	78 (21.3%)	71 (21.9%)	44 (21.8%)	62 (25.6%)	35 (24.0%)
History of MI, n (%)	107 (19.7%)	64 (17.5%)	66 (20.3%)	32 (16.0%)	41 (17.0%)	32 (22.4%)
Chronic renal insufficiency, n (%)	112 (20.5%)	44 (11.9%)	68 (20.9%)	24 (12.0%)	43 (18.0%)	20 (13.8%)
CHF, n (%)	54 (9.8%)	42 (11.5%)	29 (8.8%)	19 (9.5%)	25 (10.3%)	23 (16.1%)
COPD, n (%)	105 (19.4%)	54 (14.6%)	61 (18.6%)	30 (15.1%)	45 (18.5%)	24 (16.5%)
Cancer history, n (%)	101 (18.6%)	72 (19.5%)	53 (16.3%)	37 (18.5%)	48 (19.7%)	35 (24.1%)

M: male; F: female; CEA: carotid endarterectomy; CAS: carotid artery stenting; SD: standard deviation; CAD: coronary artery disease; MI: myocardial infarction; CHF: congestive heart failure; and COPD: chronic obstructive pulmonary disease.

Table 1. Baseline characteristics of study participants (n = 912).

insufficiency (20.9% M vs. 12.0% F, $p < 0.05$), whereas women had a higher prevalence of hypertension (82.0% F vs. 68.0% M, $p < 0.05$), diabetes (39.3% F vs. 24.8% M, $p < 0.05$), and hyperlipidemia (77.1% F vs. 62.0% M, $p < 0.05$).

Patients were required to undergo DUS and neurological examination at 1 month and subsequently at 3, 6, 12, 24, and 36 months after the procedure.

Periprocedural outcome measures in male patients compared with female patients are reported in **Table 2**. The death rate in the overall population was 0.3% (3/912), with no significant differences in rates between the two groups (0.4% M vs. 0.3% F) and between the two procedures (0.5% CEA vs. 0.2% CAS). Periprocedural outcomes were similar for male and female patients for 30-day death, stroke, MI, and a composite of any stroke, MI, or death rates. Female patients had higher periprocedural restenosis rate (2.7% F vs. 0.9% M; $p < 0.05$). Periprocedural outcomes were similar for CEA and CAS for 30-day death, stroke, and MI rates. Female patients undergoing CEA had a higher 30-day rate of any stroke, MI, or death (5.5% F vs. 3.1% M, $p < 0.05$). Female patients undergoing CAS had a higher 30-day rate of any stroke, MI, or death (7.6% F vs. 5.4% M, $p < 0.05$) and restenosis (4.8% F vs. 1.2% M, $p < 0.05$).

For long-term follow-up, 95, 91, 78, 75, and 62% of patients attended their 3-, 6-, 12-, 24-, and 36-month follow-up appointments, respectively. Patients were not able to attend follow-up mainly because they moved to remote locations or because they declined further visits for personal reasons. Most recent patients could not attend their 24- and 36-month appointments yet.

Long-term outcomes were similar for male and female patients for 36-month death and stroke. Male patients experienced a slightly higher rate of MI. Female patients had higher long-term restenosis rate (11.4% F vs. 4.6% M; $p < 0.05$). Female patients undergoing CEA had a higher 36-month rate of stroke (14.0% F vs. 6.7% M; $p < 0.05$) and restenosis (11.5% F vs. 2.5% M,

	M (n = 544)	F (n = 368)	CEA (n = 407)		CAS (n = 505)	
			M (n = 326)	F (n = 200)	M (n = 241)	F (n = 145)
Short-term (≤30 days) outcomes, n (%)						
Death	2 (0.4%)	1 (0.3%)	1 (0.3%)	1 (0.5%)	1 (0.4%)	0 (0.0%)
Stroke	7 (1.3%)	5 (1.4%)	2 (0.6%)	3 (1.5%)	5 (2.1%)	2 (1.4%)
MI	13 (2.4%)	10 (2.7%)	6 (1.8%)	5 (2.5%)	7 (2.9%)	5 (3.5%)
Stroke, MI, or death	9 (1.7%)	6 (1.6%)	10 (3.1%)	11 (5.5%)	13 (5.4%)	11 (7.6%)
Restenosis	5 (0.9%)	10 (2.7%)	2 (0.6%)	3 (1.5%)	3 (1.2%)	7 (4.8%)
Long-term (>30 days) outcomes, n (%)						
Death	37 (6.8%)	35 (9.5%)	17 (5.2%)	12 (6.0%)	20 (8.3%)	23 (15.9%)
Stroke	52 (9.6%)	59 (16.0%)	22 (6.7%)	28 (14.0%)	30 (12.4%)	31 (21.4%)
MI	38 (7.0%)	22 (6.0%)	20 (5.1%)	11 (4.1%)	18 (6.4%)	11 (5.2%)
Stroke, MI, or death	101 (18.6%)	87 (23.7%)	45 (13.8%)	46 (23.1%)	56 (23.2%)	41 (28.4%)
Restenosis	25 (4.6%)	42 (11.4%)	8 (2.5%)	23 (11.5%)	17 (7.0%)	19 (13.1%)

M: male; F: female; CEA: carotid endarterectomy; CAS: carotid angioplasty and stenting; and MI: myocardial infarction.

Table 2. Periprocedural (30 days) outcomes after carotid revascularization in male and female patients receiving CEA or CAS.

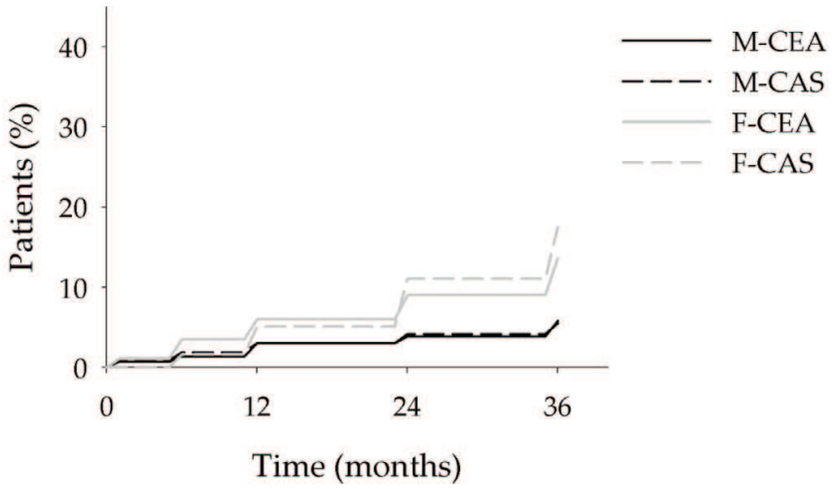
$p < 0.05$). No significant differences in long-term outcomes were observed between male and female patients undergoing CAS (**Table 2**).

The 36-month risk of any cause mortality was 5.6 (1.6)% (mean (SD)) for male patients and 15.2 (3.3)% for female patients, with a significant difference in Kaplan-Meier estimates at 36 months between the two groups according to log-rank test. Female patients undergoing CAS experience lower 3-year freedom from death rate, with no significance difference with respect to the other groups (82.5% vs. 94.5, 94.2, and 86.4% for F-CAS, M-CAS, M-CEA, and F-CEA patients, respectively, $p > 0.05$; **Figure 1**).

The risk of stroke at 36 months was 10.8 (2.2)% for male and 21.4 (3.7)% for female ($p < 0.05$). Male patients undergoing CEA had a higher 36-month freedom from stroke rate as compared to the other groups (91.6% vs. 85.8, 82.2, and 73.7% for M-CEA, M-CAS, F-CEA, and F-CAS patients, respectively, $p < 0.05$) with a significant difference in the comparison between M-CEA and F-CAS (**Figure 2**).

Male patients had a greater risk of MI than female patients. The 12-, 24-, and 36-month estimates of MI rates were 4.9 (1.4)%, 6.0 (1.6)%, and 7.6 (1.8)% for male and a constant rate equal to 5.8 (2.0)% for female ($p > 0.05$). There were no differences in the risk of experiencing a MI during follow-up among male and female patients undergoing CEA or CAS (**Figure 3**).

The overall risk of any stroke, MI, or death was equal to 20.4 (2.8)% for male patients and 30.9 (4.2)% for female patients ($p < 0.05$). The 3-year freedom from any stroke, MI, or death was 84.4, 72.6, 72.2, and 64.9% for M-CEA, M-CAS, F-CEA, and F-CAS patients, respectively, with significant differences in the comparison between M-CEA and F-CAS (**Figure 4**).



Months	0	1	3	6	12	24	36
M-CEA	326	326	326	308	292	244	230
M-CAS	241	241	241	228	217	182	171
F-CEA	200	200	200	189	176	146	135
F-CAS	145	145	145	139	130	107	96

Figure 1. Mortality. Male and female patients submitted to CEA or CAS who survived during follow-up. Error bars are omitted for clarity. Standard errors did not exceed 10% at all-time intervals that were analyzed. The number of patients at risk at each time interval is shown below the figure.

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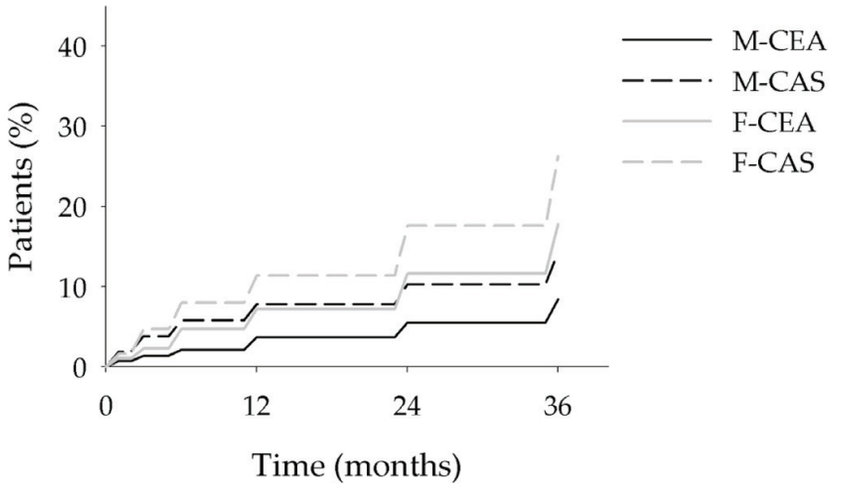
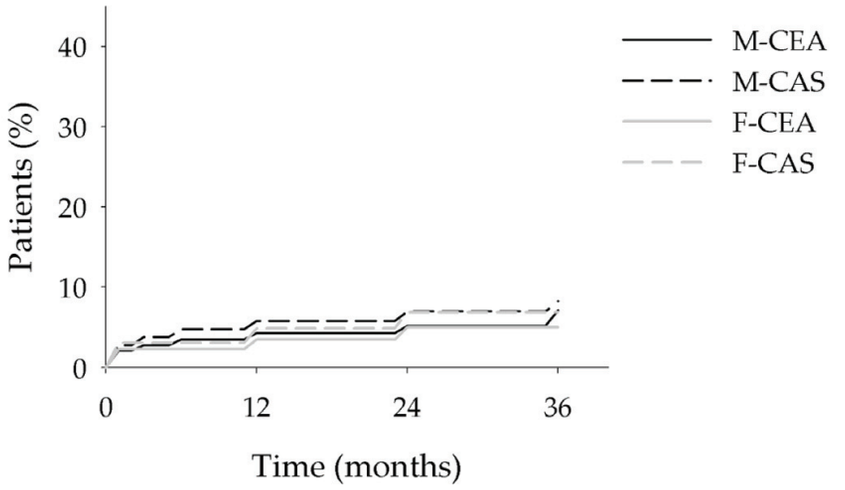


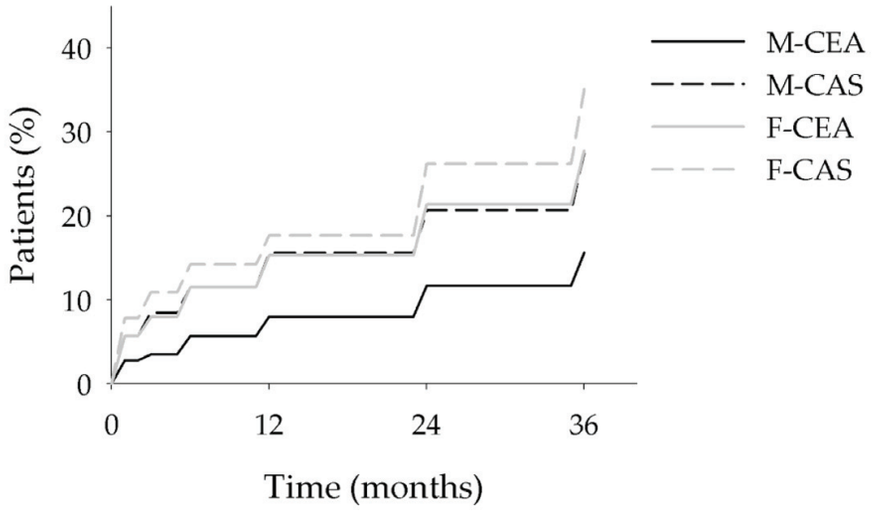
Months	0	1	3	6	12	24	36
M-CEA	326	326	324	306	290	242	226
M-CAS	241	241	236	221	207	171	157
F-CEA	200	200	197	187	173	144	130
F-CAS	145	145	143	132	121	98	87

Figure 2. Stroke. Male and female patients submitted to CEA or CAS who experienced a stroke during follow-up. Error bars are omitted for clarity. Standard errors did not exceed 10% at all-time intervals that were analyzed. The number of patients at risk at each time interval is shown below the figure.



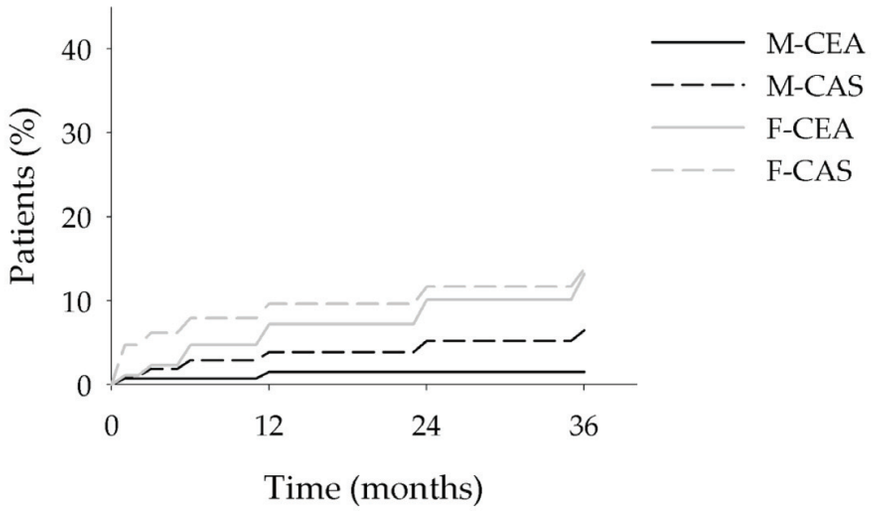
Months	0	1	3	6	12	24	36
M-CEA	326	326	319	301	285	239	226
M-CAS	241	241	234	221	210	176	164
F-CEA	200	200	200	201	178	150	150
F-CAS	145	145	145	146	128	107	107

Figure 3. Myocardial infarction (MI). Male and female patients submitted to CEA or CAS who experienced a MI during follow-up. Error bars are omitted for clarity. Standard errors did not exceed 10% at all-time intervals that were analyzed. The number of patients at risk at each time interval is shown below the figure.



Months	0	1	3	6	12	24	36
M-CEA	326	326	317	299	278	228	207
M-CAS	241	241	228	210	194	153	135
F-CEA	200	200	189	176	160	128	112
F-CAS	145	145	135	123	112	89	75

Figure 4. Stroke, MI, or death. Male and female patients submitted to CEA or CAS who experienced any stroke, MI, or death during follow-up. Error bars are omitted for clarity. Standard errors did not exceed 10% at all-time intervals that were analyzed. The number of patients at risk at each time interval is shown below the figure.



Months	0	1	3	6	12	24	36
M-CEA	326	326	326	326	294	294	294
M-CAS	241	238	237	223	212	178	166
F-CEA	200	200	198	187	173	144	132
F-CAS	145	145	139	130	121	100	93

Figure 5. Restenosis. Male and female patients submitted to CEA or CAS who experienced a restenosis during follow-up. Error bars are omitted for clarity. Standard errors did not exceed 10% at all-time intervals that were analyzed. The number of patients at risk at each time interval is shown below the figure.

During follow-up, female patients exhibited higher restenosis risk with respect to male [2.5 (1.0)%, 3.0 (1.1)%, and 3.6 (1.3)% vs. 8.2 (2.3)%, 10.8 (2.7)%, and 13.5 (3.0)% for 12-, 24-, and 36-month rates, for male and female patients, respectively ($p < 0.05$)]. Male patients undergoing CEA experienced higher freedom from restenosis rates at 3 years (98.5% vs. 93.5%, 86.8%, and 86.2%, for M-CEA, M-CAS, F-CEA, and F-CAS patients, respectively) with significant differences in the comparisons between M-CEA and F-CAS and between M-CEA and F-CEA (**Figure 5**).

5. Conclusion

Stroke has been shown to be more common in male than in female. Male patients are affected by first stroke on average in younger age with respect to female [8]. Stroke incidence was demonstrated to be about 30% higher in men than in women in Western European studies, but strokes in women tend to be more severe [9].

During the last decade, an extensive number of papers have been published on epidemiological differences between gender. The lower stroke incidence in female has been analyzed in systematic reviews in the last decades. Plausible reasons might be the protective role of ovarian estrogen on the cerebral circulation [11–13], genetic factors [15], sensitivity for antiplatelet therapy [54], lower blood pressure values [16, 17], lower frequency of peripheral artery diseases [18, 19], ischemic heart diseases [20–22], and cigarettes consumption [23, 24] in female patients with respect to male patients.

Carotid revascularization outcomes in female compared with male showed that the former have a higher risk of perioperative adverse events [55]. The ACAS reported a higher rate of perioperative events for female with respect to male (3.6% F vs. 1.7% M) during CEA [42] with a lower rate of events for female (8.7% F vs. 12.1% M) treated with best medical therapy. Moreover, this study showed a lower 5-year risk reduction for female (17% F vs. 66% M). In more recent trials, carotid revascularization outcomes were similar between genders, but restenosis was more common in female [6, 45].

In the study presented herein, 912 consecutive patients with symptomatic and asymptomatic carotid artery stenosis underwent CEA (44.6%) or CAS (55.4%) in a single institution. The death rate in the overall population was 0.3% (3/912), with no significant differences in rates between male and female patients (0.4% M vs. 0.3% F) and between the two procedures (0.5% CEA vs. 0.2% CAS).

Periprocedural outcomes were similar for male and female patients for 30-day death, stroke, MI, and a composite of any stroke, MI, or death rates. Female patients had higher periprocedural restenosis rate (2.7% F vs. 0.9% M; $p < 0.05$). Periprocedural outcomes were similar for CEA and CAS for 30-day death, stroke, and MI rates.

Female patients undergoing CEA had a higher 30-day rate of any stroke, MI, or death (5.5% F vs. 3.1% M, $p < 0.05$). Female patients undergoing CAS had also a higher 30-day risk of restenosis (4.8% F vs. 1.2% M, $p < 0.05$).

Long-term outcomes were similar for male and female patients for 36-month death and stroke. Female patients had higher long-term restenosis rate (11.4% F vs. 4.6% M; $p < 0.05$). Female

patients undergoing CEA had a higher 36-month rate of stroke (14.0% F vs. 6.7% M; $p < 0.05$) and restenosis (11.5% F vs. 2.5% M, $p < 0.05$). No significant differences in long-term outcomes were observed between male and female patients undergoing CAS. Our monocentric experience seems to confirm literature data as regarding female higher risk of restenosis during CEA. These gender-associated differences should be taken into account for the treatment of carotid artery disease.

In light of this, in the near future, female anatomic and pathologic parameters should be used, such as carotid diameter which is considerably smaller in female than in male, thus determining higher arterial velocity in carotid artery. The greater degree of atherosclerotic plaque within the carotid bulb, the higher age-related arterial wall stiffness and degree of pulsatility, and the presence of artifacts increasing arterial velocity should be taken into account for an accurate diagnosis of carotid stenosis and guidelines should be adjusted consequently.

Gender subgroup analyses from large randomized trials, such as ACST-2, an international randomized trial comparing CEA with CAS for long-term stroke prevention, which planned the recruitment of 3600 patients by the end of 2019 [56–58], may report interesting and important results on the impact of gender on the peri- and postprocedural outcomes after carotid revascularization procedures.

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References

[1] Carotid Stenting Trialists' Collaboration, Bonati LH, Dobson J, Algra A, Branchereau A, Chatellier G, et al. Short-term outcome after stenting versus endarterectomy for symptomatic carotid stenosis: A preplanned meta-analysis of individual patient data. Lancet. 2010;**376**:1062-1073. DOI: 10.1016/S0140-6736(10)61009-4

[2] Eckstein H-H, Ringleb P, Allenberg J-R, Berger J, Fraedrich G, Hacke W, et al. Results of the stent-protected angioplasty versus carotid endarterectomy (SPACE) study to treat symptomatic stenoses at 2 years: A multinational, prospective, randomised trial. Lancet Neurology. 2008;**7**:893-902. DOI: 10.1016/S1474-4422(08)70196-0

[3] Collaborators NASCET. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. The New England Journal of Medicine. 1991; **325**:445-453. DOI: 10.1056/NEJM199108153250701

[4] 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**:1235-1243. DOI: 10.1016/0140-6736(91)92916-P

[5] Yadav J, Wholey M, Kuntz R, Fayad P, Katzen B, Mishkel G, et al. Protected carotid artery stenting versus endaerterectomy in high risk patients. The New England Journal of Medicine. 2004;**351**:1493-1501. DOI: 10.1056/NEJMoa1208410

[6] Howard VJ, Lutsep HL, Mackey A, Demaerschalk BM, Sam AD, Gonzales NR, et al. Influence of sex on outcomes of stenting versus endarterectomy: A subgroup analysis of the carotid revascularization endarterectomy versus stenting trial (CREST). Lancet Neurology. 2011;**10**:530-537. DOI: 10.1016/S1474-4422(11)70080-1

[7] Goldstein LJ, Khan HU, Sambol EB, Kent KC, Faries PL, Vouyouka AG. Carotid artery stenting is safe and associated with comparable outcomes in men and women. Journal of Vascular Surgery. 2009;**49**:315-324. DOI: 10.1016/j.jvs.2008.08.110

[8] Wyller TB. Stroke and gender. The Journal of Gender-Specific Medicine. 1999;**2**:41-45

[9] Sudlow CL, Warlow CP. Comparing stroke incidence worldwide: What makes studies comparable? Stroke. 1996;**27**:550-558

[10] Appelros P, Stegmayr B, Terent A. Sex differences in stroke epidemiology: A systematic review. Stroke. 2009;**40**:1082-1090. DOI: 10.1161/STROKEAHA.108.540781

[11] Murphy SJ, McCullough LD, Smith JM. Stroke in the female: Role of biological sex and estrogen. ILAR Journal. 2004;**45**:147-159

[12] Krause DN, Duckles SP, Pelligrino DA. Influence of sex steroid hormones on cerebrovascular function. Journal of Applied Physiology. 2006;**101**:1252-1261. DOI: 10.1152/japplphysiol.01095.2005

[13] Alonso de Leciñana M, Egido JA, Fernández C, Martínez-Vila E, Santos S, Morales A, et al. Risk of ischemic stroke and lifetime estrogen exposure. Neurology. 2007;**68**:33-38. DOI: 10.1212/01.wnl.0000250238.69938.f5

[14] Goldstein LB, Adams R, Alberts MJ, Appel LJ, Brass LM, Bushnell CD, et al. Primary prevention of ischemic stroke: A guideline from the American Heart Association/American Stroke Association Stroke Council: Cosponsored by the Atherosclerotic Peripheral Vascular Disease Interdisciplinary Working Group; Cardiovascular Nursing Council. Stroke. 2006;**37**:1583-1633. DOI: 10.1161/01.STR.0000223048.70103.F1

[15] Touze E, Rothwell PM. Sex differences in heritability of ischemic stroke: A systematic review and meta-analysis. Stroke. 2008;**39**:16-23. DOI: 10.1161/STROKEAHA.107.484618

[16] Khoury S, Yarows SA, O'Brien TK, Sowers JR. Ambulatory blood pressure monitoring in a nonacademic setting. Effects of age and sex. American Journal of Hypertension. 1992;**5**: 616-623

[17] Wiinberg N, Høegholm A, Christensen HR, Bang LE, Mikkelsen KL, Nielsen PE, et al. 24-h ambulatory blood pressure in 352 normal Danish subjects, related to age and gender. American Journal of Hypertension. 1995;**8**:978-986. DOI: 10.1016/0895-7061(95)00216-2

[18] Arboix A, Oliveres M, García-Eroles L, Maragall C, Massons J, Targa C. Acute cerebrovascular disease in women. European Neurology. 2001;**45**:199-205. DOI: 10.1159/000052130

[19] Roquer J, Campello AR, Gomis M. Sex differences in first-ever acute stroke. Stroke. 2003; **34**:1581-1585. DOI: 10.1161/01.STR.0000078562.82918.F6

[20] Jorgensen HS, Weber U, Nakayama H, Kammersgaard LP, Olsen TS. Differences in risk factor distribution, initial stroke severity, and outcome in men and women. The Copenhagen Stroke Study. Cerebrovascular Diseases. 1999;**9**(Suppl 1):9-19

[21] Holroyd-Leduc JM, Kapral MK, Austin PC, Tu JV. Sex differences and similarities in the management and outcome of stroke patients. Stroke. 2000;**31**:1833-1837

[22] Fang MC, Singer DE, Chang Y, Hylek EM, Henault LE, Jensvold NG, et al. Gender differences in the risk of ischemic stroke and peripheral embolism in atrial fibrillation: The AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. Circulation. 2005;**112**:1687-1691. DOI: 10.1161/CIRCULATIONAHA.105.553438

[23] Worrall BB, Johnston KC, Kongable G, Hung E, Richardson D, Gorelick PB. Stroke risk factor profiles in African American women: An interim report from the African-American Antiplatelet Stroke Prevention Study. Stroke. 2002;**33**:913-919

[24] Glader E-L, Stegmayr B, Norrving B, Terént A, Hulter-Asberg K, Wester P-O, et al. Sex differences in management and outcome after stroke: A Swedish national perspective. Stroke. 2003;**34**:1970-1975. DOI: 10.1161/01.STR.0000083534.81284.C5

[25] Stroke Prevention in Atrial Fibrillation Investigators. Risk factors for thromboembolism during aspirin therapy in patients with atrial fibrillation: The stroke prevention in atrial

fibrillation study. Journal of Stroke and Cerebrovascular Diseases. 1995;**5**:147-157. DOI: 10.1016/S1052-3057(10)80166-1

[26] Stewart S, Hart CL, Hole DJ, McMurray JJV. A population-based study of the long-term risks associated with atrial fibrillation: 20-year follow-up of the Renfrew/Paisley study. The American Journal of Medicine. 2002;**113**:359-364

[27] Wang TJ, Massaro JM, Levy D, Vasan RS, Wolf PA, D'Agostino RB, et al. A risk score for predicting stroke or death in individuals with new-onset atrial fibrillation in the community. Journal of American Medical Association. 2003;**290**:1049. DOI: 10.1001/jama.290.8.1049

[28] Friberg J, Scharling H, Gadsbøll N, Truelsen T, Jensen GB, Copenhagen City Heart Study. Comparison of the impact of atrial fibrillation on the risk of stroke and cardiovascular death in women versus men (The Copenhagen City Heart Study). The American Journal of Cardiology. 2004;**94**:889-894. DOI: 10.1016/j.amjcard.2004.06.023

[29] Collaborators NASCET. Beneficial effects of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. The New England Journal of Medicine. 1991; **325**:445-453

[30] Flanigan DP, Schuler JJ, Vogel M, Borozan PG, Gray B, Sobinsky KR. The role of carotid duplex scanning in surgical decision making. Journal of Vascular Surgery. 1985;**2**:15-25. DOI: 10.1016/0741-5214(85)90171-5

[31] Zwolak RM. Carotid endarterectomy without angiography: Are we ready? Vascular Surgery. 1997;**31**:1-9. DOI: 10.1177/153857449703100101

[32] Comerota AJ. Gender differences in carotid stenosis: Are we overdiagnosing disease in women? Vascular. 2006

[33] Ford CS, Howard VJ, Howard G, Frye JL, Toole JF, McKinney WM. The sex difference in manifestations of carotid bifurcation disease. Stroke. 1986;**17**:877-881. DOI: 10.1161/01.STR.17.5.877

[34] Scheel P, Ruge C, Schöning M. Flow velocity and flow volume measurements in the extracranial carotid and vertebral arteries in healthy adults: Reference data and the effects of age. Ultrasound in Medicine & Biology. 2000;**26**:1261-1266. DOI: 10.1016/S0301-5629(00)00293-3

[35] Schulz UG, Rothwell PM. Sex differences in carotid bifurcation anatomy and the distribution of atherosclerotic plaque. Stroke. 2001;**32**:1525-1531

[36] Hansen F, Mangell P, Sonesson B, Länne T. Diameter and compliance in the human common carotid artery—variations with age and sex. Ultrasound in Medicine & Biology. 1995;**21**:1-9

[37] Brass LM, Pavlakis SG, DeVivo D, Piomelli S, Mohr JP. Transcranial Doppler measurements of the middle cerebral artery. Effect of hematocrit. Stroke. 1988;**19**:1466-1469. DOI: 10.1161/01.STR.19.12.1466

[38] Barnett HJM, Taylor DW, Eliasziw M, Fox AJ, Ferguson GG, Haynes RB, et al. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. The New England Journal of Medicine. 1998;**339**:1415-1425. DOI: 10.1056/NEJM199811123392002

[39] Barnett HJM, Meldrum HE, Eliasziw M, North American Symptomatic Carotid Endarterectomy Trial (NASCET) collaborators. The appropriate use of carotid endarterectomy. Canadian Medical Association Journal. 2002;**166**:1169-1179

[40] Joakimsen O, Bonaa KH, Stensland-Bugge E, Jacobsen BK. Age and sex differences in the distribution and ultrasound morphology of carotid atherosclerosis: The Tromsø Study. Arteriosclerosis, Thrombosis, and Vascular Biology. 1999;**19**:3007-3013. DOI: 10.1161/01.ATV.19.12.3007

[41] Fuster V. Elucidation of the role of plaque instability and rupture in acute coronary events. The American Journal of Cardiology. 1995;**76**:24C-33C

[42] Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. Endarterectomy for asymptomatic carotid artery stenosis. Journal of American Medical Association. 1995;**273**:1421-1428

[43] Halliday A, Mansfield A, Marro J, Peto C, Peto R, Potter J, et al. Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: Randomised controlled trial. Lancet. 2004;**363**:1491-1502. DOI: 10.1016/S0140-6736(04)16146-1

[44] International Carotid Stenting Study investigators, Ederle J, Dobson J, Featherstone RL, Bonati LH, van der Worp HB, et al. Carotid artery stenting compared with endarterectomy in patients with symptomatic carotid stenosis (International Carotid Stenting Study): An interim analysis of a randomised controlled trial. Lancet (London, England). 2010;**375**:985-997. DOI: 10.1016/S0140-6736(10)60239-5

[45] Jim J, Dillavou ED, Upchurch GR, Osborne NH, Kenwood CT, Siami FS, et al. Gender-specific 30-day outcomes after carotid endarterectomy and carotid artery stenting in the Society for Vascular Surgery Vascular Registry. Journal of Vascular Surgery. 2014;**59**:742-748. DOI: 10.1016/J.JVS.2013.09.036

[46] National Cholesterol Education Program (NCEP). Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III). Third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III) final report. Circulation. 2002;**106**:3143-3421

[47] Lyden P, Brott T, Tilley B, Welch KM, Mascha EJ, Levine S, et al. Improved reliability of the NIH stroke scale using video training. NINDS TPA Stroke Study Group. Stroke. 1994;**25**:2220-2226. DOI: 10.1161/01.STR.25.11.2220

[48] Casana R, Tolva V, Odero A Jr, Malloggi C, Paolucci A, Triulzi F, et al. Safety and efficacy of the new micromesh-covered stent CGuard in patients undergoing carotid artery

stenting: Early experience from a single Centre. European Journal of Vascular and Endovascular Surgery. 2017;**54**:681-687. DOI: 10.1016/J.EJVS.2017.09.015

[49] Casana R, Halliday A, Bianchi P, Fresa E, Silani V, Parati G, et al. Carotid artery stenting in patients with acute coronary syndrome: A possible primary therapy for symptomatic carotid stenosis. Journal of Endovascular Therapy. 2013;**20**:546-551. DOI: 10.1583/13-4244.1

[50] Tolva V, Bertoni GB, Bianchi PG, Keller GC, Casana R. Immediate surgery for acute internal carotid artery dissection and thrombosis during filter deployment prior to stenting: A case report. Vascular. 2013;**21**:247-250. DOI: 10.1177/1708538113478774

[51] Parlani G, De Rango P, Cieri E, Verzini F, Giordano G, Simonte G, et al. Diabetes is not a predictor of outcome for carotid revascularization with stenting as it may be for carotid endarterectomy. Journal of Vascular Surgery. 2012;**55**:79-89. DOI: 10.1016/j.jvs.2011.07.080

[52] Faught WE, Mattos M, van Bemmelen PS, Hodgson KJ, Barkmeier LD, Ramsey DE, et al. Color-flow duplex scanning of carotid arteries: New velocity criteria based on receiver operator characteristic analysis for threshold stenoses used in the symptomatic and asymptomatic carotid trials. Journal of Vascular Surgery. 1994;**19**:818-828. DOI: 10.1016/S0741-5214(94)70006-0

[53] Baker JD, Rutherford RB, Bernstein EF, Courbier R, Ernst CB, Kempczinski RF, et al. Suggested standards for reports dealing with cerebrovascular disease. Journal of Vascular Surgery. 1988;**8**:721-729

[54] den Hartog AG, Algra A, Moll FL, de Borst GJ. Mechanisms of gender-related outcome differences after carotid endarterectomy. Journal of Vascular Surgery. 2010;**52**:1062-1071.e6. DOI: 10.1016/j.jvs.2010.03.068

[55] Bisdas T, Egorova N, Moskowitz AJ, Sosunov EA, Marin ML, Faries PL, et al. The impact of gender on in-hospital outcomes after carotid endarterectomy or stenting. European Journal of Vascular and Endovascular Surgery. 2012;**44**:244-250. DOI: 10.1016/J.EJVS.2012.06.009

[56] de Waard DD, Halliday A, de Borst GJ, Bulbulia R, Huibers A, Casana R, et al. Choices of stent and cerebral protection in the ongoing ACST-2 trial: A descriptive study. European Journal of Vascular and Endovascular Surgery. 2017;**53**:617-625. DOI: 10.1016/j.ejvs.2016.12.034

[57] Halliday A, Bulbulia R, Gray W, Naughten A, den Hartog A, Delmestri A, Wallis C, le Conte S, Macdonald S. Status update and interim results from the asymptomatic carotid surgery trial-2 (ACST-2). European Journal of Vascular and Endovascular Surgery. 2013;**46**:510-518. DOI: 10.1016/j.ejvs.2013.07.020

[58] Huibers A, Halliday A, Bulbulia R, Coppi G, de Borst GJ. Antiplatelet therapy in carotid artery stenting and carotid endarterectomy in the asymptomatic carotid surgery trial-2. European Journal of Vascular and Endovascular Surgery. 2016;**51**:336-342. DOI: 10.1016/J.EJVS.2015.11.002

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