Carotid Artery Stenting in Clinical Practice: Does Sex Matter? Results From the Carotid Artery Stenting Registry of the Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte (ALKK)

Nicolas Werner, MD; Uwe Zeymer, MD, FESC; Bernd Mark, MD; Matthias Hochadel, PhD; Karl Eugen Hauptmann, MD; Jens Jung, MD; Ellen Hoffmann, MD, FESC; Albrecht Elsässer, MD; Thomas Fürste, MD; Matthias Leschke, MD; Harald Mudra, MD; Ralf Zahn, MD, FESC; for the *Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte (ALKK)*.

Herzzentrum (Werner, Zeymer, Mark, Zahn), Kardiologie, Ludwigshafen, Städtisches Klinikum; Stiftung Institut für Herzinfarktforschung an der Universität Heidelberg (Zeymer, Hochadel), Ludwigshafen; Krankenhaus der Barmherzigen Brüder (Hauptmann), Kardiologie, Trier; Klinikum Worms (Jung), Kardiologie, Worms; Klinikum München-Bogenhausen (Hoffmann), Klinik für Kardiologie, München; Klinikum Oldenburg (Elsässer), Kardiologie, Oldenburg; Klinikum Siloah (Fürste), Kardiologie, Hannover; Klinikum Esslingen (Leschke), Kardiologie, Esslingen; Klinikum München-Neuperlach (Mudra), Klinik für Kardiologie, München, Germany

ABSTRACT

Background: Carotid artery stenting (CAS) is increasingly used for treatment of severe carotid artery stenosis, but only few procedural risk factors for complications of CAS are clearly defined yet. A possible impact of the patient's gender on the outcome of patients undergoing CAS has not been investigated properly and only little information about this topic is available so far.

Methods: We analysed data of the German prospective, multicenter CAS Registry of the *Arbeitsgemeinschaft leitende kardiologische Krankenhausärzte*.

Results: From July 1996 to May 2009 5130 patients underwent CAS at 35 German hospitals and were enrolled into the prospective ALKK CAS Registry. Therefrom 1443 (28.1%) patients were female. There was no significant time-related difference in the proportion of women undergoing CAS over the years. Women undergoing CAS were significantly older than men (73 years vs. 70 years, $p < 0.01$) and had a longer in hospital stay in comparison to men ($p < 0.01$). The majority of patients treated with CAS was between 60 and 80 years of age (~73%). No significant differences between women and men could be found regarding in-hospital events like death (0.5% vs. 0.5%, $p = 0.99$), major or minor stroke (1.7% vs. 1.6%, $p = 0.97$; 1.0% vs. 1.6%, $p = 0.12$), TIA (2.8% vs. 2.6%, $p = 0.64$), amaurosis fugax (0.3% vs. 0.5%, $p = 0.25$), intracranial bleeding (0.5% vs. 0.3%, $p = 0.43$), myocardial infarction (0.1% vs. 0.0%, $p = 0.48$) or all non-fatal strokes and all death (3.0% vs. 3.4%, $p = 0.47$). 30 day event rates did not show gender related differences in the combined endpoint of the outcome of patients undergoing CAS, as well ($\bar{q} n = 31/882$ [3.5%] vs. $\bar{o} n = 109/2273$ [4.8%], $p = 0.12$).

Conclusion: Our results do not suggest any gender-related differences in success rates and complications in CAS. In clinical practice approximately 30% of patients treated with CAS are women.

Introduction

About 5%–12% of new strokes are caused by carotid stenosis with lesions amenable to revascularization. Symptomatic as well as high-grade asymptomatic carotid artery stenoses

are associated with an increased risk of subsequent ipsilateral ischemic events. Carotid endarterectomy (CEA) was the first intervention that showed a reduction of the risk of further ischemic events beyond optimal medical therapy.^{1–6} Carotid artery stenting (CAS) has become an alternative to CEA, especially in some high-risk subgroups of patients.⁷ The early encouraging results of the Stenting and Angioplasty With Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial, showing no

The institutions and people who participated in the ALKK CAS Registry are listed in Zahn et al.¹⁶ The authors have no funding, financial relationships, or conflicts of interest to disclose.

significant difference in long-term outcomes between CAS and CEA in patients at high surgical risk,⁸ generated a further development of the technique of CAS and inspired more studies to be undertaken. In addition, the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS) in 2001 demonstrated no significant difference between CAS and CEA in the rate of stroke or death within 30 days and during the 3-year follow-up.⁹

In contrast, 2 following randomized trials, Stent-Supported Percutaneous Angioplasty of the Carotid Artery vs Endarterectomy (SPACE) and Endarterectomy vs Angioplasty in Patients with Symptomatic Severe Carotid Stenosis (EVA 3-S) could not affirm noninferiority of CAS compared with CEA in symptomatic patients at low surgical risk.^{10–13} Recently, 4-year results of the Carotid Revascularization Endarterectomy vs Stenting (CREST) trial, comparing symptomatic and asymptomatic patients at low surgical risk with severe carotid stenosis to undergo CEA or CAS, showed no significant differences in the combined endpoint for stroke, myocardial infarction (MI), or death between both groups.¹⁴ Nevertheless, the periprocedural rates of individual components of the combined endpoint differed significantly between the stent and the endarterectomy group, with a significantly lower periprocedural stroke rate in the endarterectomy group (2.3% vs 4.1%, $P = 0.01$) and a significantly increased risk of periprocedural MI in the endarterectomy group (2.3% vs 1.1%, $P = 0.03$).¹⁴

Carotid artery stenting is still an evolving intervention with a rapid development of new techniques. The risk for procedure-related complications and clinical outcome in CAS may depend on various factors, for example the center experience, the patient's age, and previous intervention on the vessel.¹⁵ Knowing these risk factors may lower the risk for periprocedural complications in the future and make CAS an even safer procedure. A possible impact of the patient's sex on the outcome of the CAS in clinical practice has not been investigated in detail, and only little information about this topic is available so far. To determine the influence of the sex on CAS, we analyzed the data of the prospective Carotid Artery Stenting (CAS) Registry of the German Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte (ALKK).

Methods

The ALKK is an ongoing registry that was initiated 1996 to document current indications and outcomes of CAS as well as to improve quality of CAS by simple quality measurements. All interventions were prospectively enrolled in the registry.¹⁶ All complications occurring in the catheterization laboratory and during the in-hospital phase were prospectively documented. All data from the initiation in 1996 until the end of May 2009 were analyzed for this report. All data were collected prospectively and analyzed centrally.

Patient Selection

For this analysis, we retrospectively created 2 groups of patients according to sex. All patients undergoing CAS for carotid stenosis at the participating hospitals enrolled in this registry from the initiation in 1996 until end of May 2009 were analyzed for this report. Patients with

symptomatic stenoses had a history of ipsilateral stroke, ≥ 1 transient ischemic attack (TIA), or an episode of amaurosis fugax. In these patients an angiographically documented stenosis $\geq 70\%$, according to the diagnostic criteria of the North American Symptomatic Carotid Endarterectomy Trial (NASCET),³ was suggested to be an indication for an intervention. In case of asymptomatic patients, a stenosis $\geq 80\%$ was suggested as an indication for intervention, especially in the presence of contralateral occlusion, before major surgery or documented progression of the stenosis. The decision to treat a given patient was left to the treating physician. The risks and benefits of CAS were explained to the patients. The operator informed them that they were undergoing an investigational procedure, told them about the proven efficacy of CEA in randomized trials, and offered them that treatment as an alternative.

Definitions

Amaurosis fugax was defined as a retinal ischemia with transient monocular blindness and a TIA as a focal neurological deficit that resolved spontaneously within 24 hours. The diagnosis of stroke was merely a clinical one and was defined as loss of neurological function caused by an ischemic or hemorrhagic event with residual symptoms at least 24 hours after onset; a minor stroke was diagnosed if symptoms disappeared within 1 week after onset, and a major stroke was diagnosed if symptoms persisted for >1 week after onset. No quantification of the severity of stroke (such as the National Institutes of Health classification),¹⁷ besides its reversibility, was made. Until 2008, no differentiation between ischemic strokes, hemorrhagic strokes, and strokes with unknown etiology was made. Since January 2008, these entities have been evaluated separately. Endpoints were evaluated by a neurologist either immediately at the occurrence of symptoms or routinely at the end of the hospital stay. There was no routine use of cranial computed tomography or magnetic resonance imaging scanning after CAS. We did not separately evaluate 30-day follow-up endpoints until 2008. Since then, 30-day event rates were collected prospectively. We also tried to get a follow-up of patients treated before this point in time to determine 30-day event rates, which were calculated by the Kaplan-Meier method. Completeness of these data was achieved in 61.5% of all enrolled patients (61.1% of all women and 61.6% of all men). The combined clinical endpoint of all death and strokes was prospectively defined as the primary endpoint.

Different angiographic appearances of the stenosis were defined as follows: (1) ulcer, an excavation at the site of the stenosis; and (2) visible thrombus, a round-shaped filling defect at the stenosis site, either mobile or not mobile. Quantification of the severity of the stenosis was performed by using the NASCET method.³ The use of a quantitative angiographic measurement or just "eye-balling" was left to the discretion of the treating physician.

CAS Procedure

The CAS procedure was performed according to the standard protocol of each participating center. As the ALKK is an association of cardiologists, the "cardiological technique" to treat carotid artery stenoses was preferred, namely the use

of guiding catheters and 0.014-inch guidewires with continuous pressure monitoring, as described by Satler et al.¹⁸

Statistical Analysis

The patient population is described by absolute numbers and percentages. Medians and quartiles or means with SD were computed as appropriate. Categorical variables were compared between sex by the χ^2 test, and crude odds ratios with 95% confidence intervals were computed for the event rates. Age and other metrical variables were compared by the Mann-Whitney test. To take the significant difference in age between men and women into account, age-adjusted *P* values for patient and interventional characteristics were calculated by the Wald test of logistic regression, including the respective variable together with age as a linear term. The Cochran-Armitage test was used to analyze temporal trends in the proportion of women over the years. Factors influencing the combined clinical endpoint of all in-hospital death and all strokes were analyzed in a logistic regression model, and the corresponding adjusted odds ratios with confidence limits were computed. In addition sex, age (per 10-year increase), symptomatic stenosis, use of an embolic protection device, and the side intervened upon were included in the model. The discrimination of the model was assessed by the C statistic. *P* values ≤ 0.05 were considered significant. All *P* values are results of 2-tailed tests. The tests were performed using the SAS statistical package, version 9.1 (SAS Institute Inc, Cary, NC).

Results

From July 1996 to May 2009, 5130 patients underwent 5186 interventions at 35 hospitals and were enrolled into the prospective ALKK CAS Registry.

Proportion of Women

Of the 5130 patients, 1443 were women (28.1%) and 3687 were men (71.9%). The proportion of women enrolled into the CAS registry ranges from 17.7% at the beginning in 1996 to 31.9% in 2008, but remained stable at between 24% and 31% over the last years. Therefore, no significant differences in the ratio of female patients undergoing CAS could be determined between 1996 and May 2009 (*P* = 0.15). The

Figure 1. The proportion of women undergoing CAS over the time of enrollment. Abbreviations: CAS, carotid artery stenting.

Figure 2. The age distribution of patients undergoing CAS subdivided by sex. Abbreviations: CAS, carotid artery stenting.

ratio of enrollment of women into the registry ranges from 17.7% at the beginning in 1996 to 31.9% in 2008 (Figure 1).

Patient and Interventional Characteristics

The age distribution of CAS patients showed important differences between women and men. The median age in women was 73 years (range, 67–78 y), whereas it was only 70 years (range, 65–76 y) in men (*P* < 0.001) (Figure 2).

Men had significantly more often a history of coronary artery disease, MI, previous percutaneous coronary intervention, or coronary artery bypass graft and peripheral arterial disease (all *P* < 0.001). The prevalence of heart failure, severe chronic obstructive pulmonary disease and smoking was significantly higher in men (heart failure, *P* = 0.034; chronic obstructive pulmonary disease, *P* = 0.045; smoking, *P* < 0.001), which persisted after age-adjusting of the data (Table 1).

Women more often had symptomatic carotid stenosis than men (*P* = 0.03). After adjustment for age differences, there remained a trend toward a higher prevalence of symptomatic stenoses in women (*P* = 0.06).

The use of embolic protection devices such as filters and distal or proximal occlusion systems was also similar in men and women (*P* = 0.55). No differences were found in peri-interventional anticoagulation between women and men (Table 1).

Clinical Events

No significant differences between women and men were found regarding in-hospital events such as death, major or minor stroke, TIA, amaurosis fugax, intracranial bleeding, or MI (Table 2). Referring to the combined endpoint of all nonfatal strokes and all death, no difference between male and female CAS patients could be determined either (Table 2).

The 30-day events also showed no significant differences in the occurrence of MI, all-cause death, or in the combined endpoint of “nonfatal strokes and all-cause death” between women and men (Table 2). In the logistic regression model, there was a trend toward a lower occurrence of nonfatal strokes and all death in women compared with men, although this trend did not reach statistical significance (*P* = 0.068) (Table 3).

Table 1. Baseline Characteristics, Concomitant Diseases, Carotid Lesion, and Interventional Characteristics

Patients	Women, n = 1443, 28.1%	Men, n = 3687, 71.9%	P Value	Age-Adjusted P Value
Age, y ^a	73 (67–79)	70 (65–76)	<0.01	
Symptomatic carotid stenosis	582/1215 (47.9%)	1387/3130 (44.3%)	0.03	0.06
Type of ipsilateral symptoms (in symptomatic patients)				
Amaurosis fugax	84/562 (14.9%)	255/1339 (19.0%)	0.03	0.15
TIA	277/562 (49.3%)	589/1339 (44.0%)	0.03	0.06
Minor stroke	86/562 (15.3%)	236/1339 (17.6%)	0.22	0.14
Major stroke	140/562 (24.9%)	347/1339 (25.9%)	0.65	0.59
Prior carotid artery surgery	105/1415 (7.4%)	270/3611 (7.5%)	0.95	0.98
Prior carotid artery dilation	81/1127 (7.2%)	235/2855 (8.2%)	0.27	0.28
Prior ipsilateral carotid artery intervention	83/1422 (5.8%)	195/3639 (5.4%)	0.50	0.37
Concomitant diseases				
CHD	813/1419 (57.3%)	2560/3636 (70.4%)	<0.01	<0.01
Prior MI	255/1422 (17.9%)	1106/3647 (30.3%)	<0.01	<0.01
PAD	279/1411 (19.8%)	1019/3606 (28.3%)	<0.01	<0.01
HF (≥NYHA class III) ^b	70/1132 (6.2%)	233/2856 (8.2%)	0.03	0.03
AF ^b	113/1137 (9.9%)	281/2895 (9.7%)	0.82	0.57
COPD ^b	40/1138 (3.5%)	144/2892 (5.0%)	0.04	0.03
Arterial HT ^b	1067/1149 (92.9%)	2672/2921 (91.5%)	0.14	0.34
DM ^b	412/1140 (36.1%)	975/2889 (33.7%)	0.15	0.13
Hypercholesterolemia ^b	953/1146 (83.2%)	2447/2903 (84.3%)	0.38	0.74
Current smoker ^b	209/1132 (18.5%)	924/2863 (32.3%)	<0.01	<0.01
Interventions	Women, n = 1462, 28.2%	Men, n = 3724, 71.8%		
Location of target stenosis				
Right carotid artery	690/1401 (49.3%)	1817/3618 (50.2%)	0.54	0.67
Bilateral intervention	14/1401 (1.0%)	40/3618 (1.1%)	0.74	0.70
Lesion characteristics				
Restenosis after surgery or dilation ^b	67/1137 (5.9%)	156/2894 (5.4%)	0.53	0.42
Visible thrombus	74/1416 (5.2%)	264/3628 (7.3%)	<0.01	<0.01
Ulcer	243/1416 (17.2%)	896/3628 (24.7%)	<0.01	<0.01
Severe calcification	377/1416 (26.6%)	795/3628 (21.9%)	<0.01	<0.01
Length >10 mm	461/1416 (32.6%)	1377/3628 (38.0%)	<0.01	<0.01
Bifurcation involved	439/1416 (31.0%)	927/3628 (25.6%)	<0.01	<0.01
% stenosis before intervention ^a	90 (80–90)	90 (80–90)	<0.01	<0.01
Interventional characteristics				
Intervention completed	1404/1462 (96.0%)	3634/3724 (97.6%)	<0.01	0.02
Maximal balloon diameter, mm	5.2 ± 0.9	5.3 ± 0.9	<0.01	<0.01
Maximal balloon pressure, mm Hg	12.0 (9.0–14.0)	12.0 (8.0–14.0)	0.30	0.18

Table 1. *Continued*

Interventions	Women, n = 1462, 28.2%	Men, n = 3724, 71.8%		
Stent implantation	1365/1401 (97.4%)	3545/3618 (98.0%)	0.23	0.25
Stent length, mm ^a	30 (30–40)	30 (30–40)	0.02	0.02
Use of EPD	1092/1378 (79.2%)	2848/3560 (80.0%)	0.55	0.40
% stenosis after intervention ^a	1 (0–10)	1 (0–10)	0.53	0.17
Duration of procedure, min ^a	40 (30–57)	40 (30–55)	0.07	0.20
LMWH	14/1112 (1.3%)	57/2857 (2.0%)	0.12	0.10
Unfractionated heparin	1082/1116 (97.0%)	2746/2870 (95.7%)	0.06	0.04
GP IIb/IIIa antagonists	25/1112 (2.2%)	92/2853 (3.2%)	0.10	0.11
ASA	1082/1116 (97.0%)	2764/2870 (96.3%)	0.32	0.28
Clopidogrel	1074/1115 (96.3%)	2743/2871 (95.5%)	0.27	0.24

Abbreviations: AF, atrial fibrillation; ASA, aspirin; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; EPD, embolic protection device; GP, glycoprotein; HF, heart failure; HT, hypertension; LMWH, low molecular weight heparin; MI, myocardial infarction; NYHA, New York Heart Association; PAD, peripheral arterial disease; TIA, transient ischemic attack. ^aMedian and quartiles. ^bData available only in a subset of patients.

We separately analyzed the risk for death or stroke in patients age >70 years and according to the patient's symptomatic status. In addition, we did not find a significantly different outcome of patients age >70 years regarding in-hospital or 30-day events between women and men undergoing CAS in clinical practice today (Table 2). However, we found a general increase in in-hospital and 30-day events in the elderly population undergoing CAS. Patients with symptomatic carotid artery stenosis also showed higher rates of death or stroke compared with asymptomatic patients (Table 2).

Discussion

Proportion of Women Undergoing Carotid Artery Stenting

Our data showed that less than one-third (28.1%) of all patients undergoing CAS for severe carotid artery stenosis in Germany were female. The proportion of women seemed to be almost stable, within a range from 24% to 31% over the last 10 years of enrollment into the CAS Registry of the ALKK. This is in accordance with data from the PRO-CAS registry, which is another German, prospective, multicenter registry for CAS, reporting a ratio of 29.2% of female patients in their registry.

Characteristics of Women vs Men Undergoing Carotid Artery Stenting

Our analysis showed the majority of patients undergoing CAS in German clinical routine to be between 60 and 90 years of age, with a mean age of 71 years. A relevant proportion of patients in advanced age (at least octogenarians) undergoing CAS were seen in daily routine (19% of women vs 12% of men), which conciliates well with data from the Pro-CAS Registry showing a mean age of CAS patients of 70 years with 13% of their patients being at least 80 years of age. Patient age >80 years was an exclusion criterion in the CREST trial until March 2004; therefore, the data of

these 2 comparable German registries cannot be compared with the CREST trial in a direct manner. Nevertheless, the mean age of patients in the CREST trial was 70 years and the baseline variables of this trial also showed 72% of women and 73.6% of men had already passed an age limit of 65 years while undergoing CAS.

Outcome in Women vs Men Undergoing Carotid Artery Stenting

Our results show that sex differences neither affect the outcome of patients undergoing CAS in clinical practice today, nor are they associated with an increased rate of periprocedural complications. Regarding subgroup analyses such as elderly patients age >70 years, symptomatic or asymptomatic patients, we did not find any significant differences in the outcome between women and men undergoing CAS in clinical practice. As described previously, elderly patients undergoing CAS carry a higher risk for stroke or death compared with younger patients in general. In addition, symptomatic patients showed higher rates of death or stroke compared with patients with asymptomatic carotid stenoses, which corresponds with previous reports from randomized trials or registry data regarding this topic.

This comparable risk for women and men undergoing CAS in our registry is in good accordance with data from the PRO-CAS registry.¹⁵ In their statistical subgroup analysis, sex also was not an independent predictor of peri-interventional stroke or death.¹⁵ Theiss et al reported a periprocedural stroke or death rate in 3.5% of men and 3.0% of women undergoing CAS ($P = 0.42$), which corresponds nicely to our peri-interventional death or stroke rates of 3.4% in women and 3.0% in men treated with CAS ($P = 0.47$) in a comparable population in clinical practice. In addition, several randomized clinical trials (SPACE, CREST, International Carotid Stenting Study [ICSS]) comparing CAS to CEA also did not show a significant impact of sex on the outcome of patients undergoing CAS.^{10,14,20}

Table 2. Hospital Medication, In-Hospital, and 30-Day Events for All Patients Enrolled, for Women and Men Age >70 Years, and According to Their Symptomatic Status

Patients	Women, n = 1443, 28.1%	Men, n = 3687, 71.9%	P Value	OR (95% CI)
Hospital medication				
ASA	1347/1413 (95.3%)	3463/3612 (95.9%)	0.39	
Ticlopidine/clopidogrel	1280/1334 (96.0%)	3301/3401 (97.1%)	0.05	
Phenprocoumon	62/1390 (4.5%)	173/3550 (4.9%)	0.54	
Statins ^a	943/1119 (84.3%)	2389/2843 (84.0%)	0.85	
ACEI ^a	646/1120 (57.7%)	1680/2829 (59.4%)	0.33	
β-Blockers ^a	688/1121 (61.4%)	1784/2837 (62.9%)	0.38	
In-hospital events				
Ipsilateral TIA	39/1388 (2.8%)	91/3535 (2.6%)	0.64	1.09 (0.75–1.60)
Ipsilateral stroke	29/1390 (2.1%)	90/3537 (2.5%)	0.35	0.82 (0.53–1.25)
Minor stroke	14/1390 (1.0%)	56/3537 (1.6%)	0.12	0.63 (0.35–1.14)
Major stroke	23/1390 (1.7%)	58/3537 (1.6%)	0.97	1.01 (0.62–1.64)
Ipsilateral stroke/TIA/amaurosis fugax	65/1390 (4.7%)	192/3537 (5.4%)	0.29	0.85 (0.64–1.14)
Any ischemic event contralateral	14/1390 (1.0%)	38/3537 (1.1%)	0.84	0.94 (0.51–1.73)
MI	1/1434 (0.1%)	1/3658 (0.0%)	0.48	2.55 (0.16–40.83)
Death	7/1443 (0.5%)	18/3687 (0.5%)	0.99	0.99 (0.41–2.38)
All nonfatal strokes and all death	42/1398 (3.0%)	121/3551 (3.4%)	0.47	0.88 (0.61–1.25)
Local vascular complications	30/1115 (2.7%)	45/2772 (1.6%)	0.03	1.68 (1.05–2.67)
30-day events				
MI	0/870 (0%)	4/2240 (0.2%)	0.58	
Death	13/967 (1.3%)	32/2535 (0.4%)	0.85	1.07 (0.56–2.04)
All nonfatal strokes and all death	31/882 (3.5%)	109/2273 (4.8%)	0.12	0.72 (0.48–1.09)
	Women Age >70 Years, n = 934, 32.0%	Men Age >70 Years, n = 1988, 68.0%	P Value	OR (95% CI)
In-hospital events				
Death	7/934 (0.7%)	13/1988 (0.7%)	0.77	1.15 (0.46–2.88)
All nonfatal strokes and all death	36/902 (4.0%)	82/1903 (4.3%)	0.70	0.92 (0.62–1.38)
30-day events				
Death	13/595 (2.2%)	21/1336 (1.6%)	0.34	1.40 (0.70–2.81)
All nonfatal strokes and all death	29/539 (5.4%)	71/1205 (5.9%)	0.67	0.91 (0.58–1.42)
Symptomatic Patients	Women, n = 774, 29.8%	Men, n = 1823, 70.2%	P Value	OR (95% CI)
In-hospital events				
Death	6/774 (0.8%)	10/1823 (0.5%)	0.50	1.42 (0.51–3.91)
All nonfatal strokes and all death	27/746 (3.6%)	76/1749 (4.3%)	0.40	0.83 (0.53–1.29)
30-day events				
Death	11/482 (2.3%)	14/1190 (1.2%)	0.09	1.96 (0.88–4.35)

Table 2. Continued

	Women, n = 1443, 28.1%	Men, n = 3687, 71.9%	P Value	OR (95% CI)
All nonfatal strokes and all death	22/436 (5.0%)	62/1030 (6.0%)	0.46	0.83 (0.50–1.37)
Asymptomatic Patients	Women, n = 553, 26.0%	Men, n = 1572, 74.0%	P Value	OR (95% CI)
In-hospital events				
Death	1/553 (0.2%)	7/1572 (0.4%)	0.38	0.41 (0.05–3.30)
All nonfatal strokes and all death	10/537 (1.9%)	38/1517 (2.5%)	0.40	0.74 (0.37–1.49)
30-day events				
Death	1/418 (0.2%)	16/1165 (1.4%)	0.05	0.17 (0.02–1.30)
All nonfatal strokes and all death	8/412 (1.9%)	44/1150 (3.8%)	0.07	0.50 (0.23–1.07)

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ASA, aspirin; CI, confidence interval; MI, myocardial infarction; OR, odds ratio; TIA, transient ischemic attack. ^aData available only in a subset of patients.

Table 3. Multivariable Model of Risk Factors for Death or Stroke Over All Patients Enrolled

	Wald's χ^2	Adjusted OR ($\pm 95\%$ CI)	P Value
Age (per decade)	21.51	1.70 (1.36–2.14)	<0.001
EPD	16.70	0.43 (0.29–0.65)	<0.001
Left carotid artery	3.73	1.42 (0.99–2.03)	0.054
Female sex	3.33	0.68 (0.45–1.03)	0.068
Symptomatic stenosis	1.27	1.24 (0.86–1.78)	0.260

Abbreviations: CI, confidence interval; EPD, embolic protection device; OR, odds ratio. The C statistic for this analysis was 0.68.

A meta-analysis of individual patient data recently performed by the Carotid Stenting Trialists Collaboration, taken from the randomized trials ICSS, EVA-3S, and SPACE, comparing short-term outcome after CAS vs endarterectomy for symptomatic carotid stenosis, did not show a significant impact of sex on the outcome of patients undergoing each therapy.²¹ In contrast to the trials mentioned above, the EVA-3S trial showed a significantly worse outcome of men undergoing CAS compared with women, which was mainly caused by a lower risk of stroke or death in men undergoing CEA compared with women. Thus, an increased risk for stroke or death in women undergoing CEA seems to graduate the overall risk in women in comparison with CAS in the EVA-3S trial.¹²

To be able to terminally define the indications for CAS, and find eligible patients who will have a low risk for periprocedural complications, it is necessary to evaluate further data from ongoing randomized clinical trials comparing state-of-the-art procedures for CAS.

Study Limitations

There are some important limitations of this work. Because the CAS Registry of the ALKK is an observational study, it is not possible to fully control for the selection of patients. However, sex cannot be randomized. Therefore, this analysis suffers from the limitations faced by all

registries and it is not possible to draw definitive conclusions for the mechanism responsible for differences in short-term outcome in patients undergoing CAS.

Until 2008, 30-day follow-up data were retrospectively achieved in only 61.5% and then calculated by using the Kaplan-Meier method, which is a limitation of this analysis. Therefore, we predominantly can only report on the short-term outcome of patients undergoing CAS in clinical practice today. Nevertheless, there is no relevant difference in the proportions of women and men having a complete 30-day follow-up, which makes a bias of the results by this limitation unlikely in our opinion.

We believe that the setup of the CAS registry of the ALKK, including an enrollment of all performed CAS procedures at 1 site, the large number of interventions, prospective monitoring of the data, and the central and independent data evaluation, is a relatively solid basis for the performed analysis.

Conclusion

In summary, the data of the German CAS Registry of the ALKK do not show a significant impact of patient sex on the results and the outcome of patients undergoing CAS for severe carotid artery stenoses. Furthermore, there was no significant difference in the primary endpoint of death or stroke between women and men in the registry regarding subgroup analyses, such as patient age >70 years or the symptomatic status of a patient. The proportion of women who underwent CAS in Germany over the last 10 years was approximately 30% of all patients.

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