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The Impact of Gender on In-hospital Outcomes after Carotid Endarterectomy or Stenting

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WHAT THIS PAPER ADDS

- Controversial results regarding the benefit of carotid artery stenting (CAS) vs. endarterectomy (CEA) have challenged the management of carotid artery disease in women.
- Our paper analyses the impact of gender on the in-hospital outcomes after both carotid interventions in New York State population.
- The results favour CEA for symptomatic women and show similar outcomes for CEA and CAS in asymptomatic women and in men regardless of symptomatology.

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ABSTRACT

Aim: We sought to better define the impact of sex on 'in-hospital outcomes' after carotid endarterectomy (CEA) or stenting (CAS).
Methods: Hospital discharge databases for all carotid interventions obtained from the New York State (NYS) Department of Health, Statewide Planning and Research Cooperative System between 2000 and 2009 (29,917 women, 39,771 men) were analysed. Mortality, stroke and composite event (stroke/death) were compared between procedures after matching of patients by propensity score. Acute myocardial infarction (AMI) was our secondary 'end' point.
Results: More than 90% of patients in both sexes were asymptomatic (27,439 women and 36,295 men). Compared to men, asymptomatic women experienced more strokes after CEA (women: 1.38%, men: 1.16%, $P = 0.03$) and higher AMI rates after both procedures (CEA; women: 0.75%, men: 0.51%, $P = 0.0009$, CAS; women: 0.96%, men: 0.28%, $P = 0.01$). Between procedures, symptomatic women undergoing CAS showed higher rates of mortality (CAS: 4.19%, CEA: 0.47%, $P = 0.01$) and combined (stroke/mortality) events (CAS: 12.09%, CEA: 6.05%, $P = 0.02$). In all other cohorts, no statistically significant difference was found between the procedures.
Conclusions: Compared to CEA, CAS led to inferior in-hospital outcomes only in symptomatic women in the last decade in NYS. Men and asymptomatic women showed comparable outcomes after both procedures, whereas asymptomatic females were more prone to AMI after both interventions. These sex-associated differences should be taken into account for the treatment of carotid artery disease.

Endovascular treatment of carotid artery disease has been suggested as a potentially safe and less-invasive therapeutic alternative to carotid endarterectomy (CEA).[1] However, the merit of using carotid artery angioplasty and stenting (CAS) has been questioned in specific subgroups of patients.[2,3] The role of gender in the selection of the most effective carotid intervention remains a matter of debate. Earlier reports comparing CEA or CAS failed either to analyse the influence of gender or to show a clear benefit for men or women.[4]

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Large trials that confirmed effectiveness of CEA in asymptomatic (VA Cooperative Trial, ACAS (Asymptomatic Carotid Atherosclerosis Study) and ACST (Asymptomatic Carotid Surgery Trial))[5–7] and symptomatic patients (MRC European Carotid Surgery Trial (ECST) and North American Symptomatic Carotid Endarterectomy Trial (NASCET))[8,9] showed marginal or decreased long-term benefit in women with at least 2-fold increase in the peri-operative complication rate as compared to men. Regarding endovascular therapy, the SAPPHIRE (Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy) trial established long-term equivalency of CAS compared to CEA, but did not look at the effect of sex on outcome.[10] Carotid stenting trialists' collaboration (CSTC) conducted a formal meta-analysis of EVA-3S (Endarterectomy Versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis),[11] SPACE (Stent-Protected Angioplasty vs. Carotid Endarterectomy)[3] and ICSS (International Carotid Stenting Study)[12] trials (symptomatic patients);[2] they found that gender did not play a role in CAS- or CEA- stroke and combined stroke and death rates. In the CREST trial, on the other hand, both men and women had higher rates of peri-procedural stroke after CAS and only men had a lower rate of peri-procedural myocardial infarction (MI) after endovascular treatment.[13]

The discrepancy between the CREST trial and the CSTC meta-analysis continues to fuel the debate. The difference in MI risk may, in part, be due to underreporting in the studies analysed by meta-analysis, as ascertainment of this outcome was routinely required only in CREST (Carotid Revascularization Endarterectomy vs. Stenting Trial).[13] Thus, to further inform the debate, we conducted a retrospective observational population-based study to determine the impact of sex on the outcomes of both carotid interventions by reviewing the New York State (NYS) experience.

Patients and Methods

Data sources

The study used publicly available hospital discharge data sets obtained from the NYS Department of Health, Statewide Planning and Research Cooperative System (SPARCS) between 2000 and 2009 including a total of 10 years. This is a comprehensive data reporting system established in 1979 as a result of cooperation between the health-care industry and the government and was, initially, created to collect information on discharges from all hospitals in NYS. These databases currently collect patient level details of patient characteristics (age, race and gender), diagnoses and procedures, services and charges for every hospital discharge, ambulatory surgery discharge and emergency department admission with approximately 100% coverage of in- or outpatient data. NYS-administrative data sets contain a 'present on admission' (POA) flag for each diagnosis. This was used to separate pre-existing co-morbidities from complications that occurred during hospitalisation.[14] The POA flag is important in measuring the provided health-care quality and in receiving appropriate reimbursement for services rendered.[15]

Patient cohort

Patients undergoing carotid revascularisation were identified using the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) procedure codes. For CAS procedures, the ICD-9-CM code was 00.63 and for CEA procedures 38.12 in the primary- or secondary position. Hospitalisations for endovascular repair of endocranial vessels (39.72) or carotid dissections (443.21) were excluded. To prevent any bias from neurological deficits that may have arisen from concomitant surgical procedures, we excluded patients with concomitant major interventions (e.g., cardiac surgery) during the same hospitalisation. Patients were stratified by gender: 'males' and 'females' and further stratified by symptomatology: symptomatic and asymptomatic.

Definition of symptomatology and co-morbidities

'Symptomatic presentation' was defined if the admitting or primary diagnosis codes were for neurological symptoms that were POA. The process of selection of symptomatic patients and symptomatic codes has been described elsewhere.[14] 'Asymptomatic patients' were defined as those without these POA-flagged diagnoses.

Co-morbidities

A modified *Elixhauser* coding algorithm was used to define baseline co-morbidities according to specifications of Quan et al.[16] Only POA diagnoses were included as co-morbidities. The codes for all co-morbidities have been described elsewhere.[14]

Study design

This is a retrospective cohort study with 'primary endpoints' of in-hospital mortality, postoperative stroke and the composite end point of stroke or death. Acute MI was our 'secondary endpoint'.

Definition of end points

'Postoperative stroke' was defined if a discharge had the ICD-9-CM code for postoperative stroke (997.02) or if any of the following diagnoses codes were not present on admission and were observed and documented during hospitalisation: hemiplegia (342.90), intracerebral haemorrhage (431), cerebral embolism with infarction (434.11), cerebral artery occlusion with infarction (434.91), aphasia (784.3), surgical complications from central nervous system (997.01), acute cerebrovascular insufficiency (437.1), cerebral vascular accident (436) and retinal arterial occlusions (362.30–34 and 362.84). Transient cerebral ischaemia (435.8 and 435.9) was excluded. 'Acute MI' was defined if a discharge had the code '410' in any position.

Statistical analysis

Statistical analysis was performed using the SAS software (SAS Institute Inc, Cary, NC, USA). Confidence intervals for rates were calculated using normal approximation to the binomial distribution. Propensity scores were used to match cohort and create eight balanced groups for comparative analysis (males vs. females for each procedure and *CAS* vs. *CEA* for each sex). In the respective logistic regression analysis, gender or procedures were set as dependent variables, while independent variables were patients' demographics, co-morbidities and hospital annual volume in CAS and CEA reflecting operators' experience and learning curve (Table 1). The cut point for the hospital volume was 17 CAS procedures and 33 CEA procedures.[14] The fit of logistic regression model was assessed through the concordance index[17] and calibration through the Hosmer–Lemeshow test. Female and male hospitalisations were matched 1:1 using individual propensity scores by the greedy match algorithm.[18] We calculated the standardised ratio to assess the matching between cohorts. Differences between matched pairs were evaluated using the paired *t*-test for continuous variables and the McNemar test was performed for binary data. Statistical significance was confirmed by values of $P < 0.05$.

Table 1
Patients' characteristics and comorbidities on admission in 69,688 females and males undergoing either carotid endarterectomy or stenting in New York State between 2000 and 2009.

Parameter	Females N = 29,917	Males N = 39,771	*P*-value
Symptomatic	2478(8.3%)	3476(8.7%)	0.03
Mean age, *years*	71.8	71.2	<0.0001
Race			
White	25,250(84.4%)	34,124(85.8%)	<0.0001
Black	1286(4.3%)	955(2.4%)	
Cardiac comorbidities			<0.0001
Arterial Hypertension	22,258(74.4%)	28,078(70.6%)	0.95
Congestive heart failure	1855(6.2%)	2466(6.2%)	<0.0001
Cardiac arrhythmias	2663(8.9%)	5051(12.7%)	<0.0001
Valvular disease	2214(7.4%)	2386(6.0%)	<0.0001
Coronary artery disease	10,052(33.6%)	11,778(44.7%)	
Pulmonary comorbidities			0.31
Emphysema	509(1.7%)	636(1.6%)	<0.0001
Other pulmonary	5086(17%)	5567(14%)	0.70
Neurological disorders	449(1.5%)	597(1.5%)	0.12
Diabetes mellitus	8437(28.7%)	11,414(28.7%)	0.0002
Dyslipidemia	13,522(45.2%)	17,420(43.8%)	<0.0001
Obesity	1047(3.5%)	915(2.3%)	<0.0001
Renal failure	987(3.3%)	1551(3.9%)	0.67
Dialysis	90(0.3%)	119(0.3%)	<0.0001
Neck cancer	90(0.3%)	239(0.6%)	0.02
Metastatic cancer	60(0.2%)	80(0.2%)	

Results

Between 2000 and 2009, we identified 69,688 hospitalisations in NYS for carotid intervention (CEA or CAS). Among these hospitalisations, 29,917 (43%) were for women and 39,771 (57%) for men. Table 1 presents the analysed co-morbid conditions. The frequency of emergent procedures (defined by emergent admission type (code 1) in the in the SPARCS database) in the two cohorts was identical (5623 females (18.8%) vs. 7486 males (18.8%)).

Use of CAS and CEA procedure by gender and symptomatology

Within females, 27,843 patients (93%) underwent CEA and 2074 (7%) CAS. The same proportion was found within men; 36,445 (92%) patients underwent CEA and 3326 (8%) CAS. With reference to symptomatology, only 8% of women (2478 patients) and 9% of men (3476 patients) were symptomatic. More specifically, in the female cohort, 12% (250 patients) of all CAS and 8% (2228 patients) of all CEA were performed in symptomatic patients. Similarly in men, 12% (387 patients) of all CAS and 9% (3089 patients) of all CEA procedures were performed for symptomatic disease. The mean time for the performance of CAS or CEA in symptomatic patients was the 4th day after hospitalisation, while the mean length of stay (LOS) amounted to 8 days (median LOS: 5 days) for CEA and 7 days (median LOS: 5 days) for CAS in symptomatic cohorts.

Trends in per capita hospitalisations for each gender with respect to symptomatology and carotid procedure are illustrated in Fig. 1. The proportion of carotid interventions in asymptomatic women slightly decreased during the study period, whereas it remained stable for symptomatic women. The same trends were observed in asymptomatic and symptomatic male counterparts respectively.

Comparison of outcomes of CAS vs. CEA depending on sex and symptomatology

Comparison of outcomes was done for matched groups. Within 27,439 asymptomatic females (1824 CAS/25,615 CEA), we matched

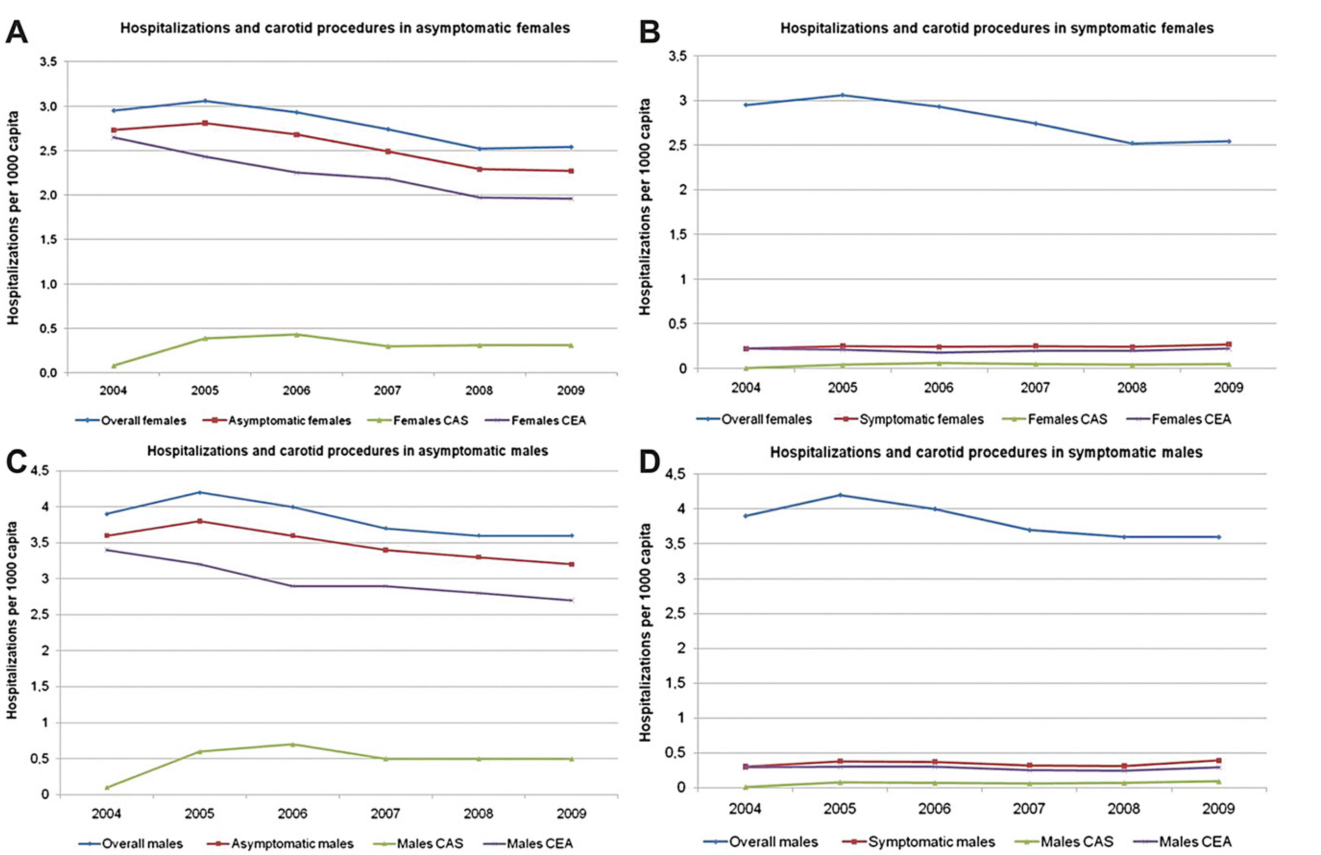

Figure 1. Proportions per 1000 capita hospitalisations show the trends of hospitalisations and carotid procedures for (A) Asymptomatic females (B) Symptomatic females (C) Asymptomatic males and (D) Symptomatic males in NYS (Note: Before October 2004, no dedicated ICD-9-CM procedural code for CAS existed).

Table 2
Primary and *secondary endpoints* comparing carotid artery stenting (CAS) vs. – endarterectomy (CEA) between propensity-matched *asymptomatic* cohorts for each gender.

Asymptomatic females			
Endpoints	CAS (*N* = 1754)	CEA (*N* = 1754)	*P*
Primary			
In-hospital mortality	0.68% (95%CI:0.30–1.07)	0.29% (95%CI:0.04–0.53)	0.09
Stroke	2.17% (95%CI:1.15–2.85)	1.77% (95%CI:1.15–2.38)	0.39
Stroke/death	2.57% (95%CI:1.82–3.31)	1.94% (95%CI:1.29–2.54)	0.20
Secondary			
Acute myocardial infarction	0.79% (95%CI:0.38–1.21)	0.74% (95%CI: 0.34–1.14)	0.85
Median–Mean length of stay (days)	1/3.0 (2.7–3.3)	2/3.8 (3.5–4.2)	<0.001
Asymptomatic males			
Endpoints	CAS (*N* = 2792)	CEA (*N* = 2792)	*P*
Primary			
In-hospital mortality	0.71% (95%CI:0.40–1.03)	0.50% (95%CI:0.24–0.76)	0.30
Stroke	2.11% (95%CI:1.58–2.65)	1.61% (95%CI:1.14–2.08)	0.17
Stroke/death	2.54% (95%CI:1.96–3.13)	1.89% (95%CI:1.39–2.40)	0.10
Secondary			
Acute myocardial infarction	0.43% (95%CI:0.19–0.67)	0.57% (95%CI: 0.29–0.85)	0.45
Median-Mean length of stay (days)	1/2.6 (2.4–2.8)	1/3.2 (2.9–3.5)	<0.001

1754 CAS (96%) and 1754 CEA (7%), respectively (4% sample reduction (SR) for the smallest group). In 2478 symptomatic females (250 CAS/2228 CEA), 215 CAS (86%) and 215 CEA (10%) were matched (SR: 14%). In 36,295 asymptomatic males (2939 CAS/33,356 CEA), we matched 2792 CAS (95%) with 2792 CEA (8%) (SR: 5%). Finally, in 3476 symptomatic males (387 CAS/3089 CEA), 341 CAS (88%) with 341 CEA (11%) were matched (SR: 12%). Tables 2 and 3 present the numeric results of the primary and secondary end points as well as the median and mean LOS for asymptomatic and symptomatic patients, respectively.

Summing up, CAS was comparable to CEA in asymptomatic patients and symptomatic men for each primary end point. In symptomatic women, CAS was inferior to CEA with considerably high rates of mortality (CAS: 4.19% vs. CEA: 0.47%, $P = 0.01$) and composite events (CAS: 12.09% vs. CEA: 6.05%%, $P = 0.02$), Regarding acute MI, both procedures were comparable, irrespective of sex or symptomatology.

Table 3
Primary and *secondary endpoints* comparing carotid artery stenting (CAS) vs. – endarterectomy (CEA) between propensity-matched *symptomatic* cohorts for each gender.

Symptomatic females			
Endpoints	CAS (*N* = 215)	CEA (*N* = 215)	*P*
Primary			
In-hospital mortality	4.19% (95%CI:1.49–6.20)	0.47% (95%CI:-0.45–1.38)	0.01
Stroke	9.30% (95%CI:5.39–13.22)	5.58% (95%CI:2.49–8.67)	0.12
Stroke/Death	12.09% (95%CI:7.70–16.49)	6.05% (95%CI:2.83–9.26)	0.02
Secondary			
Acute myocardial infarction	1.40% (95%CI:–0.19–2.98)	1.86% (95%CI: 0.04–3.68)	0.71
Median–Mean length of stay (days)	6/7.8 (6.8–8.8)	5/7.1 (6.2–7.9)	0.57
Symptomatic males			
Endpoints	CAS (*N* = 341)	CEA (*N* = 341)	
Primary			
In-hospital mortality	2.05% (95%CI:0.54–3.57)	1. 17% (95%CI:0.02–2.32)	0.37
Stroke	5.87% (95%CI:3.36–8.37)	4.40% (95%CI:2.21–6.59)	0.40
Stroke/Death	7.04% (95%CI:4.31–9.77)	4.99% (95%CI:2.66–7.30)	0.27
Secondary			
Acute myocardial infarction	1.76% (95%CI:0.36–3.16)	1.17% (95%CI: 0.02–2.30)	0.53
Median–Mean length of stay (days)	5/7.3 (6.3–8.2)	5/6.9 (6.1–7.7)	0.58

Comparison of outcomes in females vs. males for each carotid procedure in asymptomatic and symptomatic groups

Within 4763 CAS for asymptomatic patients (2939 men/1824 women), 1773 men (60%) with 1773 women (97%) were matched (SR: 3%). In 637 CAS for symptomatic sexes (387 men/250 women), we matched 233 men (60%) and 233 women (93%) (SR: 7%). Regarding CEA for asymptomatic patients, within 58 971 patients (33 356 men/25 615 women), we matched 24 251 men (73%) with 24 251 women (95%) (SR: 5%). In 5317 symptomatic CEA recipients (3089 men/2228 women), 2164 men (70%) and 2164 women (97%) were matched (SR: 3%). Tables 4 and 5 summarise the numeric results of the primary and secondary end points as well as the mean and median LOS for asymptomatic and symptomatic patients, respectively.

We observed no significant differences between sexes (asymptomatic or symptomatic) undergoing CAS for all primary end points. On the other hand, CEA led to higher rates of stroke in asymptomatic women (women: 1.38% vs. men: 1.16%, $P = 0.03$), while there was no sex-related difference in symptomatic patients.

Table 4
Primary and *secondary endpoints* comparing *asymptomatic* females vs. males between propensity-matched cohorts for each procedure.

Carotid artery stenting			
Endpoints	Asymptomatic females (*N* = 1773)	Asymptomatic males (*N* = 1773)	*P*
Primary			
In-hospital mortality	0.79% (95%CI:0.38–1.20)	0.79% (95%CI:0.38–1.20)	1.00
Stroke	2.14% (95%CI:1.47–2.82)	1.97% (95%CI:1.33–2.62)	0.73
Stroke/death	2.65% (95%CI:1.90–3.40)	2.43% (95%CI:1.71–3.14)	0.67
Secondary			
Acute myocardial infarction	0.96% (95%CI:0.50–1.41)	0.28% (95%CI: 0.03–0.53)	0.01
Median–Mean length of stay (days)	1/3.1 (2.8–3.4)	1/2.7 (2.4–3.0)	<0.0001
Carotid endarterectomy			
Endpoints	Asymptomatic females (*N* = 24,521)	Asymptomatic males (*N* = 24,521)	*P*
Primary			
In-hospital mortality	0.47% (95%CI:0.39–0.56)	0.48% (95%CI:0.38–0.55)	0.95
Stroke	1.38% (95%CI:1.24–1.53)	1.16% (95%CI:1.02–1.29)	0.03
Stroke/death	1.65% (95%CI:1.49–1.81)	1.65% (95%CI:1.49–1.81)	0.06
Secondary			
Acute myocardial infarction	0.75% (95%CI:0.64–0.85)	0.51% (95%CI:0.42–0.60)	0.0009
Median–Mean length of stay (days)	1/3.1 (3.0–3.2)	1/2.8 (2.7–2.8)	<0.0001

Table 5
Primary and *secondary endpoints* comparing *symptomatic* females vs. males between propensity-matched cohorts for each procedure.

Carotid artery stenting			
Endpoints	Symptomatic females ($N = 233$)	Symptomatic males ($N = 233$)	*P*
Primary			
In-hospital mortality	4.29% (95%CI:1.67-6. 91)	3.86% (95%CI:1.37–6.36)	0.83
Stroke	8.15% (95%CI:4.61–11.69)	5.58% (95%CI:2.61–8.55)	0.29
Stroke/death	10. 73% (95%CI:6.73–14.73)	8.58% (95%CI:4.96–12.21)	0.46
Secondary			
Acute myocardial infarction	1.72% (95%CI:0.04–3.40)	2.58% (95%CI: 0.53–4.62)	0.53
Median–Mean length of stay (days)	6/8.0 (7.1–9.0)	5/8.1 (6.8–9.3)	0.40

Carotid endarterectomy			
Endpoints	Symptomatic females ($N = 2184$)	Symptomatic males ($N = 2184$)	*P*
Primary			
In-hospital mortality	0.74% (95%CI:0.38–1.10)	1.06% (95%CI:0.63–1.50)	0.25
Stroke	4.02% (95%CI:3.19–4.85)	3.60% (95%CI:2.82–4.39)	0.48
Stroke/death	4.44% (95%CI:3.57–5.30)	4.11% (95%CI:3.28–4.95)	0.60
Secondary			
Acute myocardial infarction	1.29% (95%CI:0.82–1.77)	0.97% (95%CI: 0.56–1.38)	0.32
Median–Mean length of stay (days)	5/7.1 (6.8–7.5)	5/6.7 (6.4–7.1)	0.006

Finally, when we compared the post-procedural rate for MI between different sexes and procedure cohorts, asymptomatic women compared to asymptomatic men had statistically significant higher MI rates after CAS (women: 0.96% vs. men: 0.28%, $P = 0.01$) or CEA (women: 0.75% vs. men: 0.51%, $P = 0.0009$). In symptomatic patients, MI rates were statistically comparable between sexes after either procedure.

Discussion

In our study, CAS and CEA showed comparable outcomes in asymptomatic men and women and in symptomatic men. However, in symptomatic women, CAS showed clearly inferior outcomes in mortality and composite events, with remarkably high rates of combined stroke and death (12.09%). In fact, female CAS recipients were the cohort most prone to adverse events in NYS during the last decade with a twofold increase of stroke/death rates compared to CEA recipients. Moreover, the stroke rates in symptomatic women undergoing CAS, despite statistical insignificance compared to CEA, were numerically quite higher compared to the stroke rate after CEA (CAS: 9.30% vs. CEA: 5.58%). Additional comorbidities or worse overall condition of the symptomatic patients could possibly explain the high mortality rates, and this is also reflected in the considerably longer LOS in symptomatic cohorts (6–9 days). However, the delayed performance of the procedures after the beginning of the hospitalisation (mean time: 4th day) could also explain the lengthy LOS in symptomatic cohorts.[14] Of note, only 39% of the CAS procedures and 38% of the CEA procedures were done in symptomatic patients on the first day of hospitalisation in this database.

Historical large CEA-randomised trials were not designed for sex-subgroup analysis. Most of the information concerning women was derived from either post hoc-analysis or trials, where there was an underrepresentation of women.[13] For instance, initially NASCET and ECST did not report any sex-subgroup analysis.[8,9] In symptomatic women, 30-day stroke and death rates with CEA reached 7.6% in NASCET and 11.1% in ECST.[8,9] In symptomatic men, NASCET showed a 5.9% 30-day stroke and mortality rate, whereas ECST reported 6.4%.[8,9] For asymptomatic patients, ACAS and ACST reported the same 30-day composite stroke/death rates for men and women (3.6%) and either no difference or marginal difference in the 5-year benefit for reduction of stroke risk after CEA. However, as emphasised before, these gender-related results are difficult to interpret due to significant design limitations.[5,6] In any case, women had higher perioperative adverse events (i.e., stroke and combined stroke and death) rates than men.

When it comes to carotid stent trials, the impact of sex on the procedural outcomes is not well identified.[10,19] A meta-analysis of EVA-3S, SPACE and ICSS trials, conducted to better define gender-associated differences in symptomatic cohorts, had results similar to ours: surgical risk for the composite event of stroke or death was higher in women than in men (6.9% vs. 5.4%), whereas the risks of stenting were unaffected by gender (women: 8.5% vs. men: 9.0%).[2] In our study, which analysed only in-hospital outcomes, asymptomatic women did worse only after CEA, and symptomatic women had equivalent immediate outcomes after CEA and CAS as compared to men. This marginal difference or no difference in immediate outcomes between men and women after carotid procedures is quite different from what was historically indicated by large-scale trials but agrees with the results of CSTC meta-analysis.[2] More importantly, our data agree with findings from the CREST trial derived from the analysis of the female cohort. Indeed, the CREST trial, although it did not show any gender-related difference, in separate analysis focussed on 832 enrolled women, CEA was superior to CAS in symptomatic women (as in our study) based on lower rates of peri-procedural stroke (CAS: 7.5% vs. CEA: 2.7%, $P = 0.03$) or the composite stroke, MI or death (CAS: 9.2% vs. CEA: 4.0%, $P = 0.03$).[13] In addition, similar to our observations, asymptomatic women in the CREST trial showed comparable rates of stroke (CAS: 3.3% vs. CEA: 1.6%, $P = 0.28$) and composite events of stroke or death (CAS: 3.3% vs. CEA: 1.6%, $P = 0.28$).[13]

In the existing literature, a number of risk factors (vessel diameter, plaque composition, sensitivity for anti-platelet therapy, sex hormones, etc.) have been suggested as potential mechanisms for the different outcomes between men and women after CEA.[20] In theory, women should also do well after CAS or at least should not have worse outcomes than men based on the following considerations: The literature suggests that in women the atherosclerotic plaque is relatively stable, female carotid arteries are higher-velocity vessels with increased outflow/inflow ratio and women tend to have relatively localised lesions compared to men.[20–23] Such factors are usually associated with favourable immediate and long-term outcomes after CAS. On the other hand though, women tend to have atherosclerotic plaque mainly distributed in the common carotid as opposed to the proximal internal carotid artery, which is usually seen in men.[4] This may cause challenges when the lesions are traversed during CAS especially in symptomatic patients who have unstable and friable plaque. In fact, symptomatic women had significantly larger particles captured by the cerebral protection device during CAS compared to asymptomatic suggesting higher embolic potential in symptomatic women compared to their asymptomatic counterparts during stenting.[22]

A notable finding in our study was that 92% of the carotid procedures (63,734 out of 69,688 patients) were performed in asymptomatic patients. Interestingly, the same trend was shown for the US national use of carotid procedures in a recent publication from the Nationwide Inpatient Sample (NIS) by Rockman et al., although in this study the definition of symptomatic patients was not well described, as POA flags for each diagnosis (they are not part of the NIS database) were missing.[24,25] Similar results were found in the analysis of the peri-procedural outcomes after carotid interventions in the NIS for the year 2005 by McPhee et al.[26] All these databases reflect real-world medical practice as compared to databases from randomised controlled trials that usually include tertiary care and university centres only, and these findings probably suggest that medical practice in the community is rather different from that in large centres.

Rockman et al.[24] also reported comparable rates of peri-procedural stroke for both carotid interventions for symptomatic and asymptomatic patients. Similar to our findings, they reported a 2-fold increase in stroke in symptomatic women undergoing CAS compared to those who had CEA (6.2% vs. 3.4%, $P = 0.1$). In contrast to what we found, in this study, asymptomatic women experienced significantly higher stroke rates after CAS (2.1%) than CEA (0.9%, $P < 0.001$).[24] This discrepancy may be attributed to the fact that their analyses were performed in unmatched populations and therefore their CAS population could be overall sicker than the CEA cohort and consequently more prone to inferior outcomes.

Another finding in our study is asymptomatic women had higher MI rates after CEA (women: 0.75% vs. men: 0.51%, $P = 0.0009$) or CAS (women: 0.96% vs. men: 0.28%, $P = 0.01$). Interestingly, the CREST trial, which is the only large trial that assessed sex differences in MI rates, failed to show a gender-related difference.[13] However, it did show equivalent rate of peri-procedural MI in women regardless of carotid procedure (CAS or CEA). There is ample evidence in the literature that coronary disease in women is often underdiagnosed and undertreated and women are less likely than men to be optimised with adequate anti-platelet agents, statins and b-blockade.[27,28,29] Suboptimal optimisations and recognition of their coronary risks in women may explain the higher rate of cardiac complication when compared to men and lack of cardiac benefit after CAS when compared to CEA. However, MI does not seem to be a key driver in the adverse outcomes in mainly asymptomatic patients.[13]

Our study has limitations. As with all studies of administrative data sets, there is a potential for coding errors. The comparison of two different procedures, however, reduces the impact of such errors, assuming that frequency of coding errors is similar in both groups.[14] Another limitation of administrative databases is the lack of clinical data, that is, it is impossible to determine the severity of complications such as transient ischaemic attack (TIA) or stroke. Because there are no patient identifiers in the SPARCS database, longitudinal follow-up was not possible, and for this reason we could not assess long-term freedom from restenosis, stroke prevention or survival. We could not study the re-admission rates since each admission to the hospital counts as a separate encounter and cannot be related to a previous one as re-admission. The reported in-hospital mortality or stroke rates are not equivalent to 30-day peri-procedural event rates. In this context, the interval between index event and type of revascularisation could not be assessed and the analysis performed might underestimate the event rate especially in the CAS cohort. We used propensity score to create balanced and comparable cohorts for analysis. However, propensity score-based analysis compared to randomisation can only adjust for observed covariates and not for unobserved.[14] In any case, propensity score matching only reduces the bias, but does not eliminate it. Besides, the relative paucity for symptomatic patients remains a limitation as well. Thus, the absence of statistically significant differences regarding symptomatic cohorts despite the clear trend for more adverse events after CAS may be due to type II error. In this database, we were unable to assess or match patients who were treated for restenosis after previous CEA or CAS, contralateral occlusion, hostile neck or high bifurcation. Protection devices and anti-platelet therapy could not be matched between the cohorts as well. Age was used as a continuous variable and all patients in the matched cohorts were between 70 and 72 years old. Despite all these limitations, administrative data sets are advantageous by measuring how a specific therapeutic intervention fares in the community at large centres and provide cohorts of sufficient size allowing comparison between sexes and symptomatic and asymptomatic patients that is not easily attainable in randomised studies.

Conclusions

In the last decade in NYS, more than 90% of patients of both sexes underwent CAS or CEA due to asymptomatic carotid artery disease. CEA showed a clear superiority to CAS regarding the *in-hospital* outcomes in symptomatic women. However, CAS was not inferior to CEA in all other cohorts (men regardless symptomatology and asymptomatic women). CEA and CAS demonstrated comparable rates of MI in all cohorts and asymptomatic females were more prone to MI than males after both procedures. This study suggests that CAS is not a reasonable treatment option in symptomatic women with carotid artery disease and reinforces the notion that sex should be taken into account when different carotid procedures are being considered in different symptom-related settings.

Conflicts of Interest/Funding

None.

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