2022 MID-ATLANTIC CONFERENCE

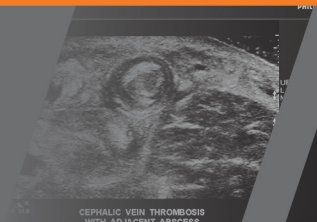
10th ANNUAL CURRENT CONCEPTS IN

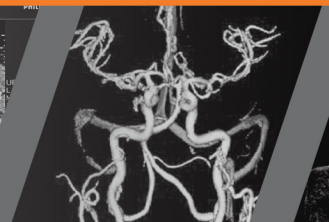
VASCULAR THERAPIES

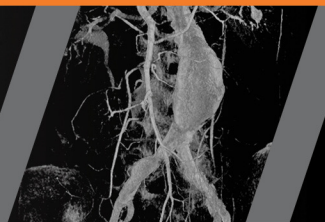
2022

Hilton Virginia Beach Oceanfront
Virginia Beach, Virginia

APRIL 28-30







Sentara Vascular Specialists

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Women and Carotid Disease

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Sentara Vascular Specialists

April 30th, 2022

Carotid Disease

- Prevalence in US
  - High grade asymptomatic 0.1-3%
  - General Stroke/TIA 0.5-6%
    - 8%-15% attributed to extracranial carotid disease
  - Higher Prevalence with increasing age

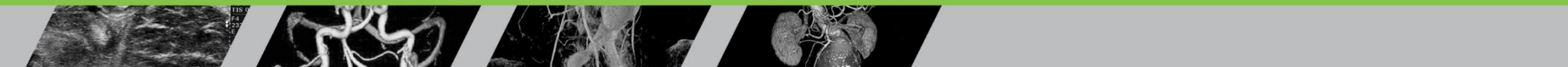
Ref 1

Carotid Disease

Table 1. Estimated Prevalence of Increased Carotid Intima-Media Thickness, Carotid Plaque, and Carotid Stenosis in Subjects, by Sex (Table view)

	Men (30–79 y)	Women (30–79 y)
Increased carotid intima-media thickness	32.1% (20.2–46.7)	23.2% (13.7–35.9)
Carotid plaque	25.2% (16.1–36.7)	17.1% (10.4–26.5)
Carotid stenosis	1.8% (1.3–2.6)	1.2% (0.8–1.6)

Ref 2



Carotid Disease

- Gender
  - ♂ > strokes each year, possibly secondary to longer life span
  - Growing disparity: stroke rate tripled in the last decade in ♂ ages 35-54
  - ♂ worse outcomes after ischemic stroke: disability and higher mortality
  - Risk factors and their effects on stroke different in the genders: HTN

Ref 3

Carotid Disease

- Suspect multifactorial etiology to the gender stroke outcome differences
  - Disease pathology, biological: hormones, ischemic response
  - Access to care
  - Provider bias
  - Socioeconomic status
  - Behavioral: call for ambulance
  - Clinical manifestations: nonconventional stroke symptoms

Ref 3-8

Trial Data

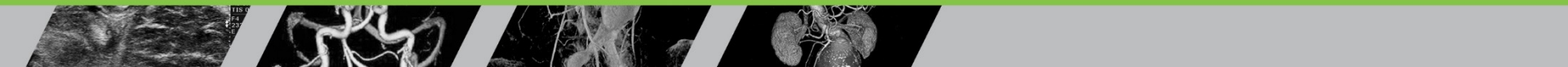
- Underrepresentation in most clinical trials
  - Most seminal trials did not analyze data by sex: NASCET, ECST
- Trial Data with a significant number of ♂ that reported results by sex
  - Asymptomatic
  - Symptomatic

Ref 9

Asymptomatic Trial Data♂

- ACAS and ACST-1
  - Less robust benefit of CEA over BMT in ♂: 5 year ARR of stroke 4.1% vs 8.2%
  - Higher perioperative complication rate 3.6% vs 1.7%
- CREST gender comparison of CEA patients
  - No significant gender difference noted in either risk of perioperative stroke (~2%) stroke/death (~2%) or 4 year risk of stroke/death (~5%), even when stratified by symptoms
- ACST-2
  - No prognostic relevance to gender in treatment effects of CAS or CEA

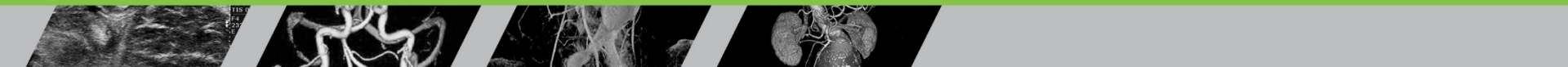
Ref 10-14



Asymptomatic Trial Data♁

Women were underrepresented in trials of CEA for asymptomatic carotid disease

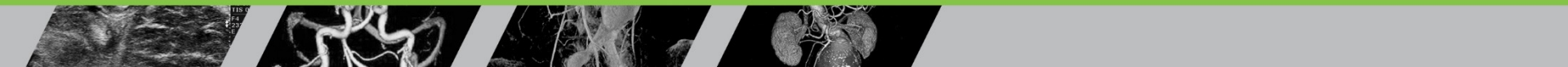
Possibly a decreased efficacy in stroke prevention in women when compared to men



Symptomatic Trial Data♁

- Pooled NASCET/ECST data
  - Higher 30 day risk of perioperative stroke/death 8.7% vs 6.8%
  - Less benefit of CEA: 5 year ARR of periop stroke/death 2.8% vs 11%
- Pooled NASCET and ACE data
  - Increased risk of death within 30 days of surgery 2.3% vs 0.8%
  - >70% stenosis, CEA 5 year ARR of stroke no difference 15-17%
- CREST
  - No significant gender diff in perioperative stroke or death (2-3%) or 4 year risk of stroke/death (6%) with CEA

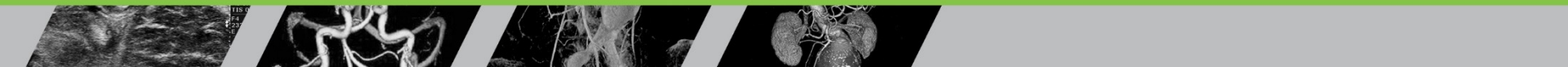
Ref 15-16



Symptomatic Trial Data♁

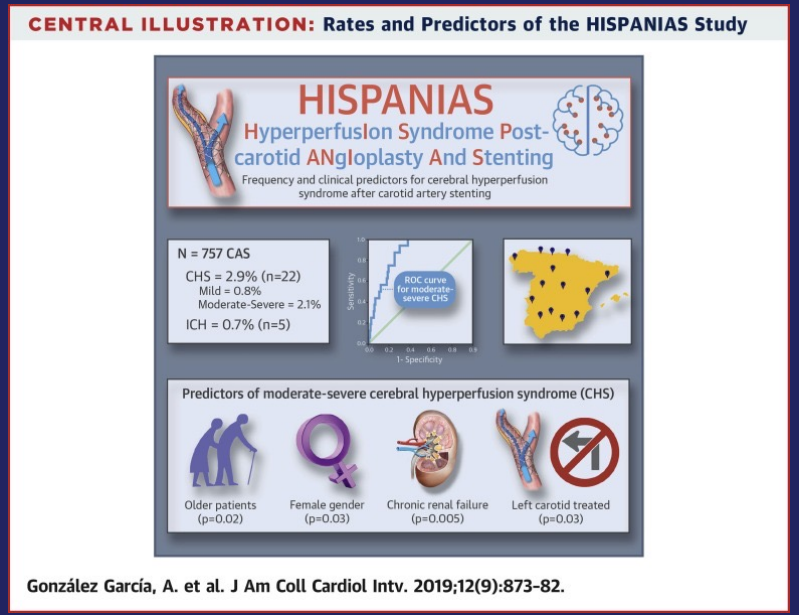
Women were underrepresented in trials of CEA for symptomatic disease

Possibly the benefit of surgery in stroke prevention was greater in men than in women



Outcomes after CEA

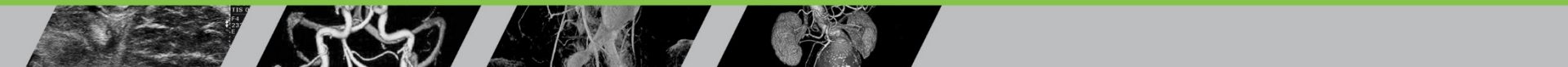
- Recent institutional/database studies significantly more ♂ than the older RCT
  - Wide range of outcomes
    - No significant gender differences (most of the studies reviewed)
    - Some show higher perioperative stroke rate
    - Suggestion that♂gender is an independent predictor of cerebral hyperperfusion syndrome following CEA



Ref 10,17-19

Outcomes after CEA

Nontrial data including large institutional, registry, and database analyses demonstrate mixed results; however, many studies demonstrated equivalent perioperative results following CEA in women and men, in contrast to some clinical trial results



Specific sex-related considerations

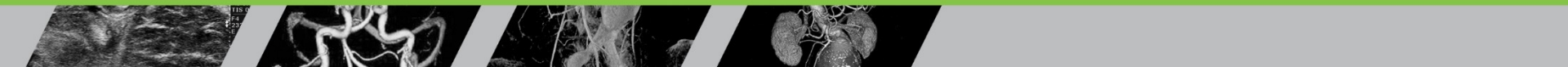
- Hypothesis for increased perioperative complications
  - Smaller size
    - Technical errors, thrombosis
  - Less compliance
  - Differences in anatomic features

Table 2. Characteristics of Carotid Artery Features and Plaque in Both Sexes (Table view)

Women	Men
Smaller artery size[54]	
Larger ICA than ECA with higher outflow areas[54]	Presence of maximum stenosis distal to the ICA bulb[54]
Higher prevalence of recurrent carotid artery stenosis[54]	Higher prevalence of intraplaque hemorrhage[56]
Higher mean ICA/CCA velocity ratio[54]	Increased presence of calcium[56]
Increased presence of ECA stenosis[54]	Increased presence of lipid-rich necrotic core combined with intraplaque hemorrhage[56]
Increased presence of smooth muscle cells with decreased protease activity[55]	

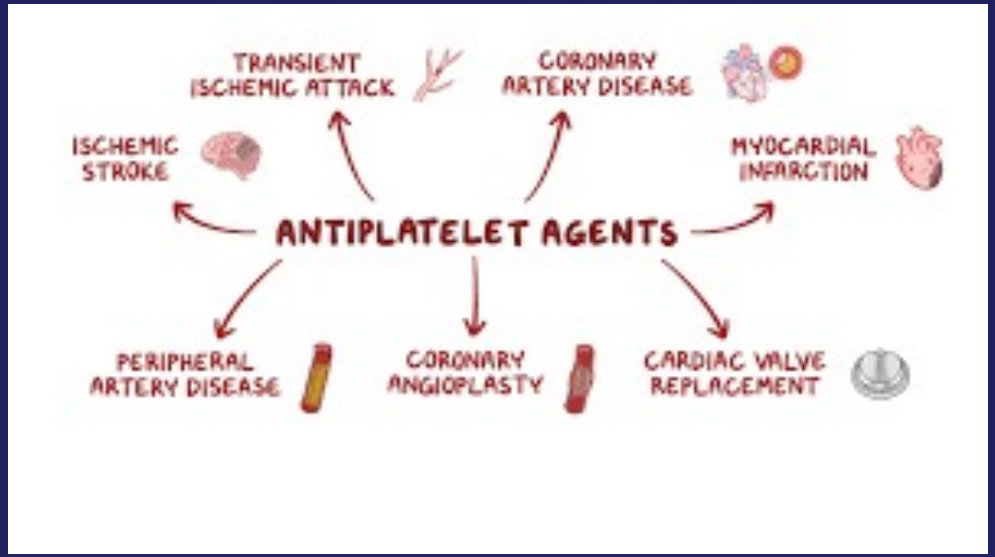
CCA indicates common carotid artery; ECA, external carotid artery; and ICA, internal carotid artery.

Ref 2, 20



Specific sex-related considerations

- Patch use recommended
- In symptomatic ♁patients, surgery within 2 weeks of symptoms may be more critical
- ♁sex might predispose to recurrent carotid artery stenosis
- Sensitivity to antiplatelet therapy may be different

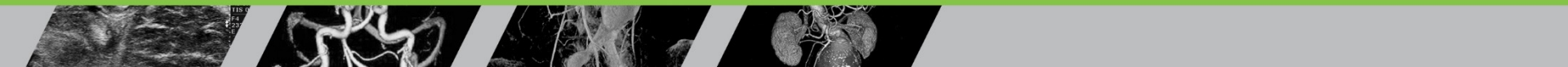


Ref 20-25

Transfemoral CAS and TCAR

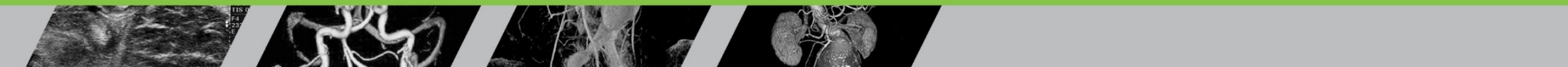
- Mixed results
  - No gender differences
  - Increased risk of stroke/death with TF-CAS in females
    - Smaller arteries
    - Absence of periop antiplatelet/statin
    - Hypotension postop
- Outcomes for TCAR compared to CEA – limited data
  - No significant gender differences in stroke and stroke/death

Ref 26-28



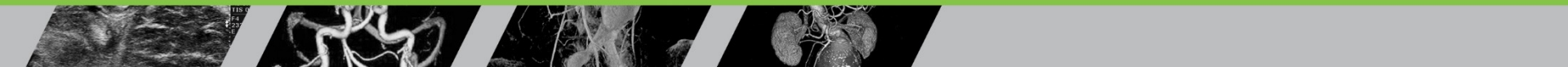
Transfemoral CAS and TCAR

Trial and nontrial data provided mixed results on the outcome of TF-CAS in women as compared to men. Several studies, however, demonstrate worse results with TF-CAS in women when compared to results of CEA in women. At this time, there are limited data available on the results of TCAR in women as compared to men



Choice of intervention in ♁

- Is intervention for carotid artery disease less appropriate in women especially when asymptomatic??
  - Increased periop and periprocedural stroke rate – widely varied results, newer studies do not confirm the older RCT, pervasive underrepresentation
  - Even if slightly higher, when compared to historical rates of BMT there is no data to suggest perioperative stroke rates are high enough to treat with BMT alone in severe or symptomatic carotid disease



Choice of intervention in ♁

- CEA, TF-CAS, and TCAR all good options
  - CEA, use patch or eversion, avoid primary closure
  - TCAR possibly lower stroke and death rates in both males and females
  - If TCAR not appropriate, TF-CAS can be considered if vessel size within IFU

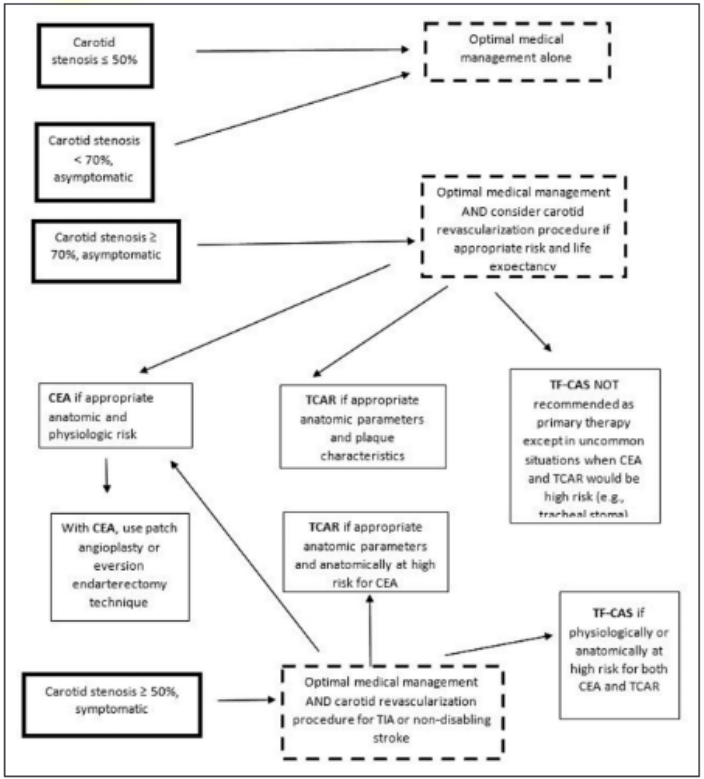
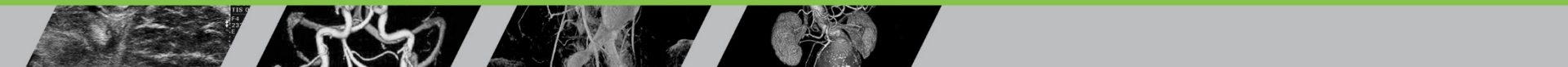


Figure 3. Algorithm for the management of carotid stenosis in women. CEA indicates carotid endarterectomy; TCAR, transcarotid artery revascularization; TF-CAS, transfemoral CAS; and TIA, transient ischemic attack.

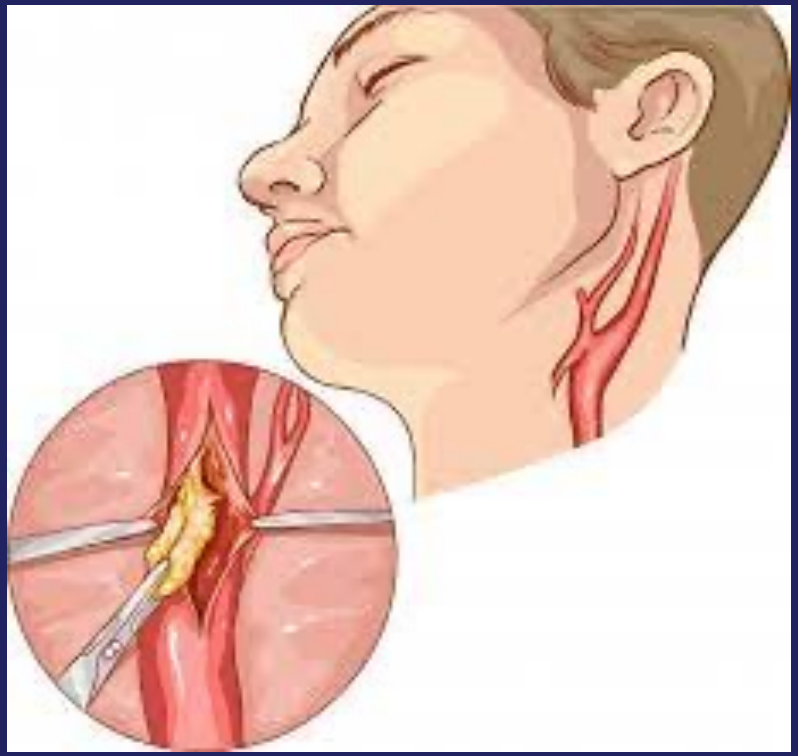


Conclusion

- Stroke and cerebrovascular disease are prevalent in women
- Biological and other gender differences exist
- Women experience worse disability and higher mortality following ischemic stroke
- The outcome of stroke in women may be worse due to many factors, including access to care and unconscious bias on the part of treating practitioners

Conclusion

- Making management recommendations is challenging given the underrepresentation of ♁in most clinical trials
- Although some data suggest that women might have worse periprocedural outcomes as compared to men following all carotid interventions, there is also an abundance of data to support a similar risk profile for carotid procedures in men and women, especially with CEA and TCAR

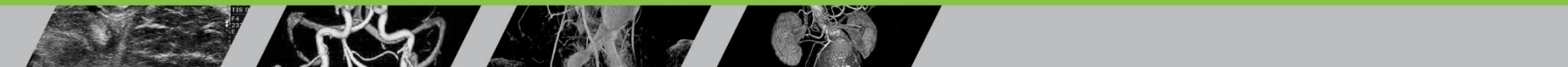


Conclusion

- Indications for carotid revascularization not gender specific
- The choice of a carotid revascularization procedure inðis not gender specific and requires careful evaluation of a particular patient's risk profile, anatomic criteria, plaque morphology, and medical comorbidities that might favor one technique over the other
- When performing carotid revascularization procedures inð, consider tailored techniques and procedures to address the small diameter of the arteries

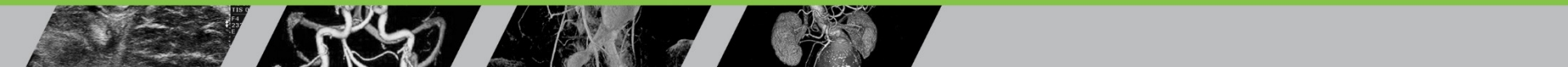
References

1. Petty GW, Brown RD, Whisnant JP, Sicks JD, O'Fallon WM, Wiebers DO. Ischemic stroke subtypes: a population-based study of incidence and risk factors. *Stroke*. 1999;30:2513–2516. doi: 10.1161/01.str.30.12.2513
2. Carotid Interventions for Women: The Hazards and Benefits Caron Rockman, Valeria Caso and Peter A. Schneider © 2022 American Heart Association, Inc.
3. Carcel C, Woodward M, Wang X, Bushnell C, Sandset EC. Sex matters in stroke: a review of recent evidence on the differences between women and men. *Front Neuroendocrinol*. 2020;59:100870. doi: 10.1016/j.yfrne.2020.100870
4. Bushnell CD, Chaturvedi S, Gage KR, Herson PS, Hurn PD, Jiménez MC, Kittner SJ, Madsen TE, McCullough LD, McDermott M, et al. Sex differences in stroke: challenges and opportunities. *J Cereb Blood Flow Metab*. 2018;38:2179–2191. doi: 10.1177/0271678X18793324
5. Cordonnier C, Sprigg N, Sandset EC, Pavlovic A, Sunnerhagen KS, Caso V, Christensen H; Women Initiative for Stroke in Europe (WISE) group. Stroke in women - from evidence to inequalities. *Nat Rev Neurol*. 2017;13:521–532. doi: 10.1038/nrneurol.2017.95 Gall SL, Donnan G, Dewey HM, Macdonell R, Sturm J, Gilligan A, Srikanth V, Thrift AG. Sex differences in presentation, severity, and management of stroke in a population-based study. *Neurology*. 2010;74:975–981. doi: 10.1212/WNL.0b013e3181d5a48f
6. Di Carlo A, Lamassa M, Baldereschi M, Pracucci G, Basile AM, Wolfe CD, Giroud M, Rudd A, Ghetti A, Inzitari D; European BIOMED Study of Stroke Care Group. Sex differences in the clinical presentation, resource use, and 3-month outcome of acute stroke in Europe: data from a Multicenter Multinational Hospital-Based Registry. *Stroke*. 2003;34:1114–1119. doi: 10.1161/01.STR.0000068410.07397.D7
7. Reeves MJ, Bushnell CD, Howard G, Gargano JW, Duncan PW, Lynch G, Khatiwoda A, Lisabeth L. Sex differences in stroke: epidemiology, clinical presentation, medical care, and outcomes. *Lancet Neurol*. 2008;7:915–926. doi: 10.1016/S1474-4422(08)70193-5



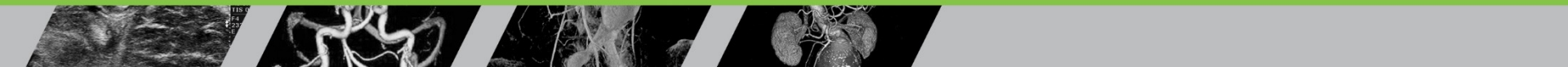
References

8. Barnett HJM, Taylor DW, Haynes RB, Sackett DL, Peerless SJ, Ferguson GG, Fox AJ, Rankin RN, Hachinski VC, Wiebers DO, et al; North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *N Engl J Med*. 1991;325:445–453. doi: 10.1056/NEJM199108153250701
9. Randomised trial of endarterectomy for recently symptomatic carotid stenosis: Final results of the MRC European Carotid Surgery Trial (ECST). *Lancet*. 1998;351:1379–1387
10. Rockman CB, Castillo J, Adelman MA, Jacobowitz GR, Gagne PJ, Lamparello PJ, Landis R, Riles TS. Carotid endarterectomy in female patients: are the concerns of the Asymptomatic Carotid Atherosclerosis Study valid? *J Vasc Surg*. 2001;33:236–240; discussion 240. doi: 10.1067/mva.2001.111804
11. Halliday A, Mansfield A, Marro J, Peto C, Peto R, Potter J, Thomas D; MRC Asymptomatic Carotid Surgery Trial (ACST) Collaborative Group. 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
12. Howard VJ, Lutsep HL, Mackey A, Demaerschalk BM, Sam AD, Gonzales NR, Sheffet AJ, Voeks JH, Meschia JF, Brott TG; CREST investigators. Influence of sex on outcomes of stenting versus endarterectomy: a subgroup analysis of the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST). *Lancet Neurol*. 2011;10:530–537. doi: 10.1016/S1474-4422(11)70080-1
13. Endarterectomy for asymptomatic carotid artery stenosis. Executive committee for the asymptomatic carotid atherosclerosis study. *JAMA*. 1995;273:1421–1428
14. Halliday A, Bulbulia R, Bonati LH, Chester J, Cradduck-Bamford A, Peto R, Pan H; ACST-2 Collaborative Group. Second asymptomatic carotid surgery trial (ACST-2): a randomised comparison of carotid artery stenting versus carotid endarterectomy. *Lancet*. 2021;398:1065–1073. doi: 10.1016/S0140-6736(21)01910-3



References

15. Rothwell PM, Eliasziw M, Gutnikov SA, Warlow CP, Barnett HJ; Carotid Endarterectomy Trialists Collaboration. Endarterectomy for symptomatic carotid stenosis in relation to clinical subgroups and timing of surgery. *Lancet*. 2004;363:915–924. doi: 10.1016/S0140-6736(04)15785-1
16. Taylor DW, Barnett HJ, Haynes RB, Ferguson GG, Sackett DL, Thorpe KE, Simard D, Silver FL, Hachinski V, Clagett GP, et al. Low-dose and high-dose acetylsalicylic acid for patients undergoing carotid endarterectomy: a randomised controlled trial. ASA and Carotid Endarterectomy (ACE) Trial Collaborators. *Lancet*. 1999;353:2179–2184. doi: 10.1016/s0140-6736(99)05388-x
17. Rockman CB, Garg K, Jacobowitz GR, Berger JS, Mussa FF, Cayne NS, Adelman MA, Maldonado TS. Outcome of carotid artery interventions among female patients, 2004 to 2005. *J Vasc Surg*. 2011;53:1457–1464. doi: 10.1016/j.jvs.2011.02.029
18. Kuy S, Dua A, Desai SS, Rossi PJ, Seabrook GR, Lewis BD, Patel B, Kuy S, Lee CJ, Subbarayan R, et al. Carotid endarterectomy national trends over a decade: does sex matter? *Ann Vasc Surg*. 2014;28:887–892. doi: 10.1016/j.avsg.2013.08.016
19. Wang GJ, Beck AW, DeMartino RR, Goodney PP, Rockman CB, Fairman RM. Insight into the cerebral hyperperfusion syndrome following carotid endarterectomy from the national Vascular Quality Initiative. *J Vasc Surg*. 2017;65:381–389.e2. doi: 10.1016/j.jvs.2016.07.122
20. Schulz UG, Rothwell PM. Sex differences in carotid bifurcation anatomy and the distribution of atherosclerotic plaque. *Stroke*. 2001;32:1525–1531. doi: 10.1161/01.str.32.7.1525
21. Rothwell PM, Eliasziw M, Gutnikov SA, Warlow CP, Barnett HJ; Carotid Endarterectomy Trialists Collaboration. Endarterectomy for symptomatic carotid stenosis in relation to clinical subgroups and timing of surgery. *Lancet*. 2004;363:915–924. doi: 10.1016/S0140-6736(04)15785-1



References

22. Reina-Gutiérrez T, Serrano-Hernando FJ, Sánchez-Hervás L, Ponce A, Vega de Ceniga M, Martín A. Recurrent carotid artery stenosis following endarterectomy: natural history and risk factors. *Eur J Vasc Endovasc Surg*. 2005;29:334–341. doi: 10.1016/j.ejvs.2004.10.007
23. Chang JB, Stein TA. Ten-year outcome after saphenous vein patch angioplasty in males and females after carotid endarterectomy. *Vasc Endovascular Surg*. 2002;36:21–27. doi: 10.1177/153857440203600105
24. Lal BK, Beach KW, Roubin GS, Lutsep HL, Moore WS, Malas MB, Chiu D, Gonzales NR, Burke JL, Rinaldi M, et al; CREST Investigators. Restenosis after carotid artery stenting and endarterectomy: a secondary analysis of CREST, a randomised controlled trial. *Lancet Neurol*. 2012;11:755–763. doi: 10.1016/S1474-4422(12)70159-X
25. Lane JS, Shekherdimian S, Moore WS. Does female gender or hormone replacement therapy affect early or late outcome after carotid endarterectomy? *J Vasc Surg*. 2003;37:568–574. doi: 10.1067/mva.2003.96
26. Vouyouka AG, Egorova NN, Sosunov EA, Moskowitz AJ, Gelijns A, Marin M, Faries PL. Analysis of Florida and New York state hospital discharges suggests that carotid stenting in symptomatic women is associated with significant increase in mortality and perioperative morbidity compared with carotid endarterectomy. *J Vasc Surg*. 2012;56:334–342. doi: 10.1016/j.jvs.2012.01.066
27. Bisdas T, Egorova N, Moskowitz AJ, Sosunov EA, Marin ML, Faries PL, Vouyouka AG. The impact of gender on in-hospital outcomes after carotid endarterectomy or stenting. *Eur J Vasc Endovasc Surg*. 2012;44:244–250. doi: 10.1016/j.ejvs.2012.06.009
28. Malas MB, Dakour-Aridi H, Kashyap VS, Eldrup-Jorgensen J, Wang GJ, Motaganahalli RL, Cronenwett JL, Schermerhorn ML. Transcarotid revascularization with dynamic flow reversal versus carotid endarterectomy in the vascular quality initiative surveillance project [published online September 15, 2020]. *Ann Surg*. 2020. doi: 10.1097/SLA.0000000000004496