

Introduction

About 11% of all strokes are due to thromboembolism from a previously asymptomatic carotid stenosis of more than 50%, which is also an independent predictor of vascular events in patients with already clinically manifesting arterial disease or type 2 diabetes without a history of cerebrovascular ischemia. Although substantial improvements in medical therapy have attributed to decreased rates of stroke, it might ultimately need revascularization. Recent studies have shown significant benefit in reducing stroke and death in patients treated with CEA and CAS. We aimed to review and analyze the most recent studies comparing short- and long-term complications of CEA and CAS in asymptomatic patients with carotid stenosis.

Methods

Two recent major clinical trials involving asymptomatic carotid stenosis (i.e. ACT I and CREST) were included. Outcome measures included in the analysis were: stroke, myocardial infarction (MI), and death or stroke, both individually and as a composite outcome as defined in the trials. Methodological quality was assessed using the Cochrane Collaboration’s tool for assessing risk of bias. A meta-analysis was performed on comparable outcomes at the same time-points using RevMan ver 5.3 software. Risk ratios (RRs) with 95 % confidence interval (CI)s were calculated using the Mantel-Haenszel method with fixed-effect models. Heterogeneity was assessed by I2 and Cochran Q tests.

Results

ACT I showed a lower methodological quality, having a higher risk of attrition bias and failing to report blinding of outcome assessment. There was no significant difference in the composite outcome of death, stroke (ipsilateral or contralateral, major or minor), or MI during the periprocedural period (p=0.70). No heterogeneity was observed in the analyses (I2= 0). During the periprocedural period, CAS had a significantly higher rate of stroke alone than CEA (p=0.05), and trend towards higher stroke or death than CEA (p=0.07). In the postprocedural period, the two treatments did not have different rates for the composite of death, stroke or MI at 5 years.

Conclusions

Both CREST and ACT I individually failed to show any differences between CEA and CAS in asymptomatic patients (CREST was not powered to determine such a difference in asymptomatic patients a priori). However, their combined meta-analysis demonstrates a higher risk of periprocedural stroke after CAS than CEA in asymptomatic extracranial ICA stenosis. It is unclear whether further evolution in endovascular techniques may change this, and whether any intervention is superior to medical therapy in asymptomatic carotid stenosis.

Learning Objectives

Current trials (such as CREST-2) are underway to determine whether any intervention is warranted in asymptomatic carotid stenosis. Until then, patients selected for intervention should preferentially undergo CEA rather than CAS due to a lower risk of periprocedural stroke.

References

- 1.Donnan GA, Fisher M, Macleod M, Davis SM. Stroke. Lancet 2008;371:1612-1623.
- 2.Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics--2015 update: a report from the American Heart Association. Circulation 2015;131:17.
- 3.Strong K, Mathers C, Bonita R. Preventing stroke: saving lives around the world. Lancet Neurol 2007;6:182-187.
- 4.Naylor AR. Why is the management of asymptomatic carotid disease so controversial? Surgeon 2015;13:34-43.
- 5.Goessens BM, Visseren FL, Kappelle LJ, Algra A, van der Graaf Y. Asymptomatic carotid artery stenosis and the risk of new vascular events in patients with manifest arterial disease: the SMART study. Stroke 2007;38:1470-1475.
- 6.Huang JF, Meschia JF. Interventions for Extracranial Carotid Artery Stenosis: An Update. Current treatment options in cardiovascular medicine 2016;18:34.
- 7.Rosenfield K, Matsumura JS, Chaturvedi S, et al. Randomized Trial of Stent versus Surgery for Asymptomatic Carotid Stenosis. N Engl J Med 2016.
- 8.Brott TG, Hobson RW, 2nd, Howard G, et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis. N Engl J Med 2010;363:11-23.
- 9.Brott TG, Howard G, Roubin GS, et al. Long-Term Results of Stenting versus Endarterectomy for Carotid-Artery Stenosis. N Engl J Med 2016.
- 10.Barnett HJ, Pelz DM, Lownie SP. Reflections by contrarians on the post-CREST evaluation of carotid stenting for stroke prevention. Int J Stroke 2010;5:455-456.

Figure 1. Forrest plot for risk ratios of endpoints in 30 days, between patients undergoing CEA and CAS

Study or Subgroup	Endarterectomy Events	Endarterectomy Total	Stent Events	Stent Total	Weight	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI	Z Score	P-value
ACT I	9	348	35	1072	45.1%	0.70 [0.38, 1.63]			
CREST I	21	587	21	594	54.9%	1.01 [0.56, 1.83]			
Total (95% CI)	30	935	56	1666	100.0%	0.91 [0.58, 1.44]			

Heterogeneity: Chi²= 0.26, df= 1 (P= 0.61); I²= 0%
Test for overall effect: Z= 0.39 (P= 0.70)

Figure 2. Forrest plot for risk ratios of the composite of death, stroke, or MI in 30 days, between patients undergoing CEA and CAS

Study or Subgroup	Endarterectomy Events	Endarterectomy Total	Stent Events	Stent Total	Weight	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI	Z Score	P-value
ACT I	9	348	35	1072	45.1%	0.70 [0.38, 1.63]			
CREST I	21	587	21	594	54.9%	1.01 [0.56, 1.83]			
Total (95% CI)	30	935	56	1666	100.0%	0.91 [0.58, 1.44]			

Heterogeneity: Chi²= 0.26, df= 1 (P= 0.61); I²= 0%
Test for overall effect: Z= 0.39 (P= 0.70)

Figure 3. Forrest plot for risk ratios of the composite of death, stroke, or MI in 5 years, between patients undergoing CEA and CAS

Study or Subgroup	Endarterectomy Events	Endarterectomy Total	Stent Events	Stent Total	Weight	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI	Z Score	P-value
ACT I	12	348	41	1072	25.2%	0.90 [0.48, 1.70]			
CREST I	53	587	60	594	74.8%	0.89 [0.63, 1.27]			
Total (95% CI)	65	935	101	1666	100.0%	0.90 [0.66, 1.22]			

Heterogeneity: Chi²= 0.00, df= 1 (P= 0.98); I²= 0%
Test for overall effect: Z= 0.70 (P= 0.48)

Figure 4. Methodological quality of the studies reviewed

Study	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
CREST 1	+	+	-	+	+	+	
ACT I	+	+	-	+	+	+	