Best Evidence Topic

Stroke incidence between stenting and endarterectomy for asymptomatic carotid artery stenosis

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ABSTRACT

A best evidence topic has been constructed using a described protocol. The three-part question addressed was: In patients with significant asymptomatic carotid artery stenosis (ACAS), Does Carotid artery stenting (CAS) has a peri-procedural lower Stroke rate, As compared to Carotid endarterectomy (CEA)? The outcomes assessed were the stroke rate in the two management modalities. The best evidence showed no statistically significant difference between CAS and CEA regarding the peri-procedural and the long-term non-procedural stroke incidence. However, in high-risk patients, CAS may be a better option.

1. Introduction

This BET was designed using a framework outlined by the International Journal of Surgery [1]. This format was used because a preliminary literature search suggested that the available evidence is insufficient to perform a meaningful meta-analysis. A BET provides evidence-based answers to common clinical questions using a systematic approach of reviewing the literature (see Table 1).

2. Clinical scenario

While consenting a 67-year-old man with significant asymptomatic carotid artery stenosis (60–69% NASCET criteria) for carotid endarterectomy (CEA), one of the junior doctors asked; which modality of management has long term lower stroke rates; CEA or CAS?

3. Three parts question

• [In patients with significant asymptomatic carotid artery stenosis,]
• [Which modality of treatment has lower stroke rate];
• [CAS or CEA]?

4. Search strategy

1. Embase 1974 to June 2021 using the OVID interface:
[Asymptomatic carotid artery stenosis]AND [Carotid artery stenting OR CAS] AND [Carotid endarterectomy OR CEA] AND [Stroke]

2. Medline using the PubMed interface:
[Asymptomatic carotid artery stenosis]AND [Carotid artery stenting OR CAS] AND [Carotid endarterectomy OR CEA] AND [Stroke]
The results were limited to English articles and human studies.

• Inclusion criteria: all original articles that review the stroke rate among patients with severe asymptomatic carotid artery stenosis who underwent CEA vs CAS.
• Exclusion criteria: case reports, letters to the editor, conference abstracts and systematic reviews and meta-analysis.

5. Search outcome

A total of 794 papers were found using both search engines. We excluded seven hundred sixty two essays because they were irrelevant.
Table 1
Summary of search results.

| Author et al.,  | Study type and Level of evidence | Patient group | Outcomes follow up | Key results | Additional comments |
|-----------------|----------------------------------|---------------|--------------------|-------------|---------------------|
| Halliday A et al., 2021, Lancet, UK [2]. | Randomized control trial- Level 1b | Total of 3625 patients. | *End point: 1. Cumulative peri-procedural morbidity (CVA,MI) and mortality 2. Non-Procedural stroke (5-years) | Peri-Procedural stroke *Group 1 CAS: 3.6% (61) patients. *Group 2 CEA: 2.4% (41) patients. *P value = 0.06 *Statistically Insignificant Non-Procedural stroke *Group 1 CAS: 5.2% (91) patients. *Group 2 CEA: 4.5% (79) patients. *P value = 0.33 *Statistically Insignificant | *Long term. *Multi Center. |
| Reiff T et al., 2018, International Journal of stroke, Germany [3]. | Randomized control trial- Level 1b | Total of 513 patients. | *End point: 1. Cumulative peri-procedural morbidity (CVA,MI) and mortality 2. Non-Procedural stroke | Peri-Procedural stroke *Group 1 CAS: 2.5% (5) patients. *Group 2 CEA: 2.5% (5) patients. *P value = 0.24. *Statistically Insignificant Non-Procedural stroke *Group 1 CAS: 4.1% (8) patients. *Group 2 CEA: 3.9% (8) patients. *P value = 0.25 *Statistically Insignificant | *Short term *Small sample size *Multi Centre *Included 3rd group: best medical treatment (BMT:113) *Routine cerebral MRI was not part of the study. |
| Mannheim D et al., 2017, J Cardiovasc Surg, Israel [4] | Randomized trial- Level II | Total of 136 patients. | *End point: 1. Cumulative peri-procedural morbidity (CVA,MI) and mortality 2. Non-Procedural stroke (5-years) and recurrent stenosis | Peri-Procedural stroke *Group 1 CAS: 2.9% (2) patients. *Group 2 CEA: 1.5% (1) patients. *P value = NS. Non-Procedural stroke *Group 1 CAS: 1.5% (1) patients. *Group 2 CEA: 3.9% (8) patients. *P value = 0.25. *Statistically Insignificant | *Long term. *Small sample size *Single center |
| Rosenfield K et al., 2016, NEJM, UK [5]. | Randomized control trial- Level 1b | Total of 1453 patients. | *End point: 1. Cumulative Peri-procedural morbidity (CVA,MI) and mortality 2. Non-Procedural Ipsilateral stroke (5-years) | Cumulative Peri-Procedural stroke or death *Group 1 CAS: 2.8% (30) patients. *Group 2 CEA: 1.4% (5) patients. *P value = 0.23. *Statistically Insignificant Freedom from Non-Procedural stroke *Group 1 CAS: 97.8%. *Group 2 CEA: 97.3%. *P value = 0.51. *Statistically Insignificant | *Large sample size. *Embolic protection device is used. *Patient age ≤79. *Lack of proper medical therapy *Inclusion of the peri procedural MI in the primary composite endpoint |
| Brott T G et al., 2016, N Engl J Med, UK [6]. | Randomized control trial- Level 1b | Total of 1181 patients. | End point: 1. Composite Peri-operative morbidity (CVA,MI) and mortality 2. Non-Procedural Ipsilateral stroke (10 year). | Peri-Procedural stroke *Group 1 CAS: 2.5% (15) patients. *Group 2 CEA: 1.4% (8) patients. *P value = 0.15. *Statistically Insignificant Non-Procedural stroke(4-years) *Group 1 CAS: 4.5% (24) patients. *Group 2 CEA: 2.7% (13) patients. *P value = 0.07. *Statistically Insignificant | *The post-procedural ipsilateral strokes were similar at 5 and 10 years in both groups. |
| Yadav J S et al., 2004, N Engl J Med, UK [7]. | Randomized control trial- Level 1b | Total of 237 patients with severe asymptomatic carotid stenosis | *End point: 1. Cumulative Peri-operative morbidity (CVA,MI) and mortality 2. Ipsilateral stroke (1 year). | Cumulative Peri-procedural (stroke/death/MI) *Group 1 CAS: 8.4% patients. *Group 2 CEA: 10.2% patients. *P value = 0.20. *Statistically Insignificant *Non-Procedural cumulative outcome (1-80 years) | *Small sample size *Multi center *Heterogeneous patient population (Symptomatic and asymptomatic) *Asymptomatic patients ≥80 stenosis. *Different endpoints |

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based on the titles and or the abstracts. Thirty-two full-text articles were screened and assessed for eligibility. From these, we identified six papers to provide the best evidence to answer the question.

6. Result

7. Discussion

Asymptomatic Significant carotid artery stenosis (ACAS>50%) remains a global problem (2.2%-5.2%) due to the unignorable risk of cerebrovascular events, disability, and death. ACAS is diagnosed in individuals without a history of ipsilateral ischemic stroke or TIA and without presenting focal neurologic symptoms in the last six months [8].

Despite advances in the medical management of ACAS, patients may require invasive treatment, either surgical CEA or endovascular CAS. Based on several randomized clinical trials, current guidelines recommend prophylactic CEA in patients with >70% stenosis. Given the risk of peri-operative stroke, MI, and death, CAS has been proposed as an alternative to CEA [9].

Unfortunately, Most of the trials carried out comparing CAS with CEA have produced unreliable results because of using different endpoints, different endovascular devices, variable experiences of the interventional radiologists and heterogeneous patient populations [10].

In this article, we have reviewed the best studies which compared the CEA to the CAS, considering the peri-procedural (0–30 days) and non-procedural (31 days-end of follow-up) stroke incidence.

All of the studies included were randomized controlled trials [2–7]. Three of the studies had a large sample size of more than 1000 patients [2,5,6]. All studies in our review demonstrated that the peri-procedural stroke incidence in both study groups was not statistically significant. There was no significant difference in non-procedural stroke either, the exception being the SAPPHIRE study that reported that CAS has a statistically significant lower non-procedural composite incidence of MI, stroke, and TIA than CEA [7]. This is likely to be explained by the fact that the SAPPHIRE Population had more significant co-morbidities (75.5% of patients undergoing CEA had coronary artery disease), leading to a significantly higher rate of MI in the CEA compared to the CAS group (p = 0.03) [8].

8. Clinical bottom line

According to the above articles, the best evidence shows no statistically significant difference in the peri-procedural and the long-term non-procedural stroke incidence among carotid artery stenting and carotid endarterectomy in asymptomatic carotid artery stenosis. However, in high-risk patients, carotid artery stenting may be a better option.

Ethical approval

Ethical approval was not required.

Source of funding

None.

Table 1 (continued)

| Author/date of publication/journal/country | Study type and level of evidence | Patient group | Outcomes follow up | Key results | Additional comments |
|------------------------------------------|---------------------------------|---------------|-------------------|-------------|---------------------|
|                                          |                                 |               |                   | *Group 1 CAS: 9.9%* | *Statistically Significant* |
|                                          |                                 |               |                   | *Group 2 CEA: 21.5%* | *Statistically Significant* |
|                                          |                                 |               |                   | *P Value = 0.02* | *Variety of endovascular devices used* |

Author contribution

Ahmed Abdel Rahim (AA): Conducted the literature search and wrote the paper. Mahmoud Ahmed Thabet (MT): Assisted in the literature search and Writing of paper. Ali Mahmoud Galal (AG): Editing of writing. Mohamed Ibrahim Abd-El Rahman Hammoda (MH): Assisted in writing of paper. Devender Mittapalli (DM): Assisted in the literature search and writing of paper.

Guarantor

Ahmed Abdel Rahim.

Consent

Ethics committee approval was not required as the study was review of previously done studies.

Declaration of competing interest

No conflicts of interest.

References

[1] O.A. Khan, J. Dunning, A.C. Parvaiz, R. Agha, D. Rosin, K. Mackway-Jones, Towards evidence-based medicine in surgical practice: best BETs, Int. J. Surg. 9 (8) (2011) S85–S88, https://doi.org/10.1016/j.ijsu.2011.08.001. Epub 2011 Aug 9. PMID: 21846511.

[2] A. Halliday, R. Bulbulia, L.H. Bonati, J. Chester, A. Cradduck-Bamford, R. Peto, H. Pan, A.C.S.T-2 Collaborative Group, Second asymptomatic carotid artery surgery trial (ACST-2): a randomised comparison of carotid artery stenting versus carotid endarterectomy, Lancet 398 (1005) (2021 Sep 18) 1065–1073, https://doi.org/10.1016/S0140-6736(21)01910-3. Epub 2021 Aug 29. PMID: 34469763; PMCID: PMC8473558.

[3] T. Reifl, H.H. Eckstein, U. Mansmann, O. Jansen, G. Friedrich, H. Mudra, D. Böckler, M. Rohm, H. Brückmann, E.S. Debus, J. Fisher, W. Lang, K. Mathias, E. Ringelstein, J. Schmidli, R. Stengele, R. Zahn, T. Zeller, A. Hetzel, U. Bodechtel, A. Binder, J. Glahn, W. Hacke, P.A. Ringleb, Angioplasty in asymptomatic carotid artery stenosis vs. endarterectomy compared to best medical treatment: one-year interim results of SPACE-2, Int. J. Stroke 15 (6) (2019 Mar 15), 1747493019833017, https://doi.org/10.1177/1747493019833017. Epub ahead of print. PMID: 30873912; PMCID: PMC7416333.

[4] D. Mananhein, R. Karsam, A prospective randomized trial comparing endarterectomy to stenting in severe asymptomatic carotid stenosis, J. Cardiovasc. Surg. 58 (6) (2017 Dec) 814–817, https://doi.org/10.23736/S0021-9599.16.05915-6. Epub 2016 Jun 22. PMID: 27332577.

[5] K. Rosenfeld, J.S. Matsunuma, S. Chaturvedi, T. Riles, G.M. Ansel, D.C. Metzger, L. Wechsler, M.R. Jaff, W. Gray, ACT I investigators. Randomized trial of stent versus surgery for asymptomatic carotid stenosis, N. Engl. J. Med. 374 (11) (2016 Mar 17) 1011–1020, https://doi.org/10.1056/NEJMoa1515706. Epub 2016. Feb.17. PMID: 26886419.

[6] T.G. Brott, G. Howard, G.S. Roubin, J.F. Meschia, A. Mackey, W. Brooks, W. Moore, M.D. Hill, V.A. Mantese, W.M. Clark, C.H. Timaran, D. Heck, P. Leimgruber, A.J. Sheffet, V.J. Howard, S. Chaturvedi, B.K. Lal, J.H. Voeks, R. W. Hobson 2nd, C.R.E.S.T. Investigators, Long-term results of stenting versus endarterectomy for carotid-artery stenosis, N. Engl. J. Med. 374 (11) (2016 Mar 17) 1021–1031, https://doi.org/10.1056/NEJMoa1505215. Epub 2016. Feb.18. PMID: 26890472; PMCID: PMC4874663.

[7] J.S. Yadav, M.H. Wholey, R.E. Kunz, P. Fayad, B.T. Katzen, G.J. Mushkel, T. K. Bajwa, P. Whitlow, N.E. Strickman, M.R. Jaff, J.J. Popma, D.B. Snead, D. E. Cutlip, B.G. Firth, K. Ouriel, Stenting and angioplasty with protection in patients at high risk for endarterectomy investigators. Protected carotid-artery stenting versus endarterectomy in high-risk patients, N. Engl. J. Med. 351 (15) (2004 Oct 7) 1493–1501, https://doi.org/10.1056/NEJMoa040127. PMCID:15470212.

[8] X. Bai, Y. Feng, L. Li, J. Yang, T. Wang, J. Luo, X. Wang, F. Ling, Y. Ma, L. Jiao, Treatment strategies for asymptomatic carotid artery stenosis in the era of lipid-lowering drugs: protocol for a systematic review and network meta-analysis, BMJ.
Open 10 (7) (2020 Jul 5), e035094, https://doi.org/10.1136/bmjopen-2019-035094. PMID: 32624471; PMCID: PMC7337893.

[9] G. Yuan, S. Zhou, W. Wu, Y. Zhang, J. Lei, B. Huang, Carotid artery stenting versus carotid endarterectomy for treatment of asymptomatic carotid artery stenosis, Int. Heart J. 59 (3) (2018 May 30) 550–558, https://doi.org/10.1536/ihj.17-312. Epub.2018.May.20. PMID: 29681577.

[10] K. Gaba, P.A. Ringleb, A. Halliday, Asymptomatic carotid stenosis: intervention or best medical therapy? Curr. Neurol. Neurosci. Rep. 18 (11) (2018 Sep 24) 80, https://doi.org/10.1007/s11910-018-0888-5. PMID: 30251204; PMCID: PMC5153576.