

Short Summaries of Papers on FACTCATCS website

1. **Medical (Nonsurgical) Intervention Alone is Now Best for Prevention of Stroke Associated with Asymptomatic Severe Carotid Stenosis: Results of a Systematic Review and Analysis.**
Abbott, AL. *Stroke*. 2009;40:e573-583.

PUBLICATION SUMMARY (prepared by AL Abbott, January, 2016)

RESEARCH OVERVIEW

This was an analysis of all published studies to 2009 which included measurement of the average annual rate of same-sided stroke with or without transient ischaemic attack (TIA) in patients with moderate and severe (50-99%) symptom-free (asymptomatic) carotid stenosis given only medical treatment. Medical treatment here refers to encouragement of healthy lifestyle habits and use of medication to reduce stroke risk factors, including high blood pressure (hypertension), smoking and high blood cholesterol (hyperlipidaemia). These patients did not have carotid surgery or stenting for the studied carotid artery. The included studies were limited to only those with sound and comparable research methods. The search yielded only 11 suitable studies from an examination of hundreds of publications. The analysis included a total of 3724 patients from a mixture of randomized and nonrandomized studies. Most patients were identified from their personal hospital contact. Approximately 61% were male and the average age of the patients was approximately 66 years at study entry. The average duration of monitoring these patients varied among studies from 1.9 to 4.5 years. The average annual rate of stroke (plus/minus TIA) from each included study was plotted by the study's publication year.

MAJOR FINDINGS

- i. The average annual rates of same-sided stroke and any stroke (involving any brain territory) with or without TIA in patients given medical treatment alone fell significantly (by about 60%) since the first quality measurements were published in the mid-1980s. The average annual rate of stroke, same-sided to the studied carotid artery, was about 2.5% in the mid-1980s and only about 1% by 2007.
- ii. On average, patients in these studies were getting older over time despite their falling stroke rates.
- iii. Definitions of hypertension, high cholesterol and diabetes changed between the early 1980s and 2007 to become more sensitive, such that patients were likely to be treated earlier in more recent years.

SIGNIFICANCE

This research confirmed correct the preliminary finding, and first known published alert, regarding a major fall in stroke risk in patients with asymptomatic carotid stenosis using medical treatment alone which was published in 2007 by Abbott et al, *IJS*, 2007. This fall in stroke risk in asymptomatic patients has been independently confirmed (Naylor, 2009, Raman et al 2012). Therefore, past randomised trials of CEA versus medical treatment alone (or early versus delayed CEA) are outdated. Also outdated are randomised trials of CEA versus CAS because they rely on the assumption medical treatment has not changed in the last 20-30 years.

Available scientific research now indicates that asymptomatic patients should now receive current best medical treatment alone given this fall in stroke risk, other complications of carotid surgery and stenting (such as heart attack, bleeding and cranial nerve damage), the usual lack of measurement of such procedural complications in every-day practice and because patients with high enough risk of same-sided stroke (despite current best medical treatment) who overall benefit from carotid procedures have not yet been identified. There are also implications for improved prevention of stroke and other complications of arterial disease (atherosclerosis) in patients with symptomatic

carotid stenosis (stenosis and same-sided stroke or TIA). Further, best medical prevention of stroke is fundamentally the same as best prevention of all complications of arterial disease. Therefore, these research findings indicate better outcomes for all patients at risk of any complication of arterial disease.

RESEARCH FUNDING

Dr Abbott received a part-time salary from the National Health and Medical Research Council (NHMRC) of Australia to perform and publish this analysis.

INDEPENDENT FACULTY MEMBER COMMENT: nil at the time of posting

2. **Abbott, A. L., K. I. Paraskevas, S. K. Kakkos, J. Golledge, H. H. Eckstein, L. J. Diaz-Sandoval, L. Cao, Q. Fu, T. Wijeratne, T. W. Leung, M. Montero-Baker, B. C. Lee, S. Pircher, M. Bosch, M. Dennekamp and P. Ringleb. Systematic Review of Guidelines for the Management of Asymptomatic and Symptomatic Carotid Stenosis. *Stroke*.2015;46(11): 3288-3301.**

PUBLICATION SUMMARY (prepared by AL Abbott, January, 2016)

RESEARCH OVERVIEW

This was an analysis of all guideline recommendations published between January 2008 and January 2015 we could identify regarding routine carotid surgery (carotid endarterectomy, CEA) and/or carotid stenting (CAS) in patients with asymptomatic (ACS) and/or symptomatic carotid stenosis (SCS). The aims were to examine the extent to which all available scientific research on optimising patient outcomes was utilised and to assess recommendation clarity. Only the latest guideline published by a particular writing group was included and all relevant languages were accommodated. We used predefined questions to determine how often CEA or CAS and medical treatment were recommended and the scientific research used to support such recommendations. Each guideline was independently analysed by at least two authors, most of whom were multilingual.

MAJOR FINDINGS

- i. 34 eligible guidelines were identified. These originated from 23 different countries or regions and were written in six different languages (English, German, Chinese, Korean, Dutch and Spanish).
- ii. Most often treatment recommendations were given with respect to patients considered at average-surgical (CEA) risk, like patients selected in past randomised trials of medical treatment alone versus additional CEA (ACAS, ECST, NASCET and the Veterans Affairs trials) or early vs delayed CEA (ACST). Some guidelines also gave recommendations for patients considered high-CEA risk due to their anatomy or co-existing medical conditions (such as severe heart or lung disease).
- iii. Definitions of asymptomatic and symptomatic carotid stenosis varied and were often incomplete-omitting details on the degree of stenosis referred to, how to measure the stenosis and the timing and territory of any previous stroke or TIA.
- iv. For patients considered at average-surgical risk, CEA was endorsed (recommended it should or may be performed) in 100% of guidelines for ACS patients and 100% of guidelines regarding SCS patients. This is despite overall evidence now indicating medical treatment alone is now best for ACS patients while modern research to determine a surgical benefit for SCS patients is required.
- v. For patients considered at average-surgical risk, CAS was recommended in %guidelines for ACS patients and %guidelines regarding SCS patients. This is despite overall randomised trial and registry evidence indicating that CAS is more likely to cause stroke or death than CEA or medical treatment alone in such patients. The excess risk of stroke or death caused by CAS is not compensated by a slightly higher risk of heart attack associated with CEA in some past randomised trials. This last point was usually omitted.
- vi. For patients considered at high-surgical risk, CAS was endorsed by % of guidelines for ACS patients and % of guidelines regarding SCS. This is despite no evidence of benefit over CEA or medical treatment alone and the limited life expectancy of many such patients.
- vii. Definitions of the 30-day rate of stroke and death which would infer an overall benefit from CEA or CAS over medical treatment alone (assuming the past randomised trials ACAS, ACST, ECST, NASCET and the Veterans Trials were still relevant) were often incomplete.

viii. All endorsements of CEA and CAS were based on outdated (20-30 year old) comparisons of medical treatment alone versus additional CEA (from the past randomised trials ACAS, ACST, ECST, NASCET and the Veterans Trials) and so lacked current scientific validity.

ix. Recommendations regarding best medical treatment were often omitted, whether or not patients underwent CEA or CAS. Improvements in medical treatment since randomised trials of CEA versus medical treatment alone were rarely mentioned and impacted on guideline recommendations in only one case (regarding ACS patients in the guideline from the UK Royal College of Physicians).

x. Terminology used to summarise recommendations, or the evidence used to make them, were not standardised across guidelines, making interpretation and comparison difficult.

xi. Many guidelines were identified only via the personal professional networks of the authors, not via popular search engines. This obstructs public access to guidelines.

SIGNIFICANCE

This research has demonstrated how contemporary international guidelines over encourage the use of risky and expensive procedures which in many cases are, overall, more likely to harm than help patients. There were also many fundamental organisational problems and in many instances very limited public access to guidelines. These issues should be addressed in all future guidelines on carotid stenosis management. This research also indicates the need for modern research to inform patient management decisions, including that each centre measure and publish its own key outcomes such as the 30-day rate of stroke and death following CEA or other carotid procedures.

RESEARCH FUNDING

Dr Abbott received a part-time salary from the Bupa Health Foundation of Australia to perform and publish this analysis.

INDEPENDENT FACULTY MEMBER COMMENT (posted by)

REPLY FROM THE PUBLICATION AUTHOR (Dr AL Abbott)

