Why Calls for More Routine Carotid Stenting Are Currently Inappropriate

An International, Multispecialty, Expert Review and Position Statement

Anne L. Abbott, MD, PhD, FRACP; Mark A. Adelman, MD; Andrei V. Alexandrov, MD; P. Alan Barber, PhD, MBChB, FRACP; Henry J.M. Barnett, CC, MD; Jonathan Beard, FRCS, ChM, MEd; Peter Bell, FRCS, MD, DSC, KBE; Martin Björck, MD, PhD; David Blacker, MD, FRACP; Leo H. Bonati, MD; Martin M. Brown, MD, FRCP; Clifford J. Buckley, MD, FACS; Richard P. Cambria, MD; John E. Castaldo, MD; Anthony J. Comerota, MD, FACS, RVT; E. Sander Connolly, Jr, MD; Ronald L. Dalman, MD, FACS; Alun H. Davies, MA, DM, FRCS, FHEA, FEBVS, FACPh; Hans-Henning Eckstein, MD, PhD; Rishad Faruqi, MD, FRCS (Eng), FRCS (Ed), FACS; Thomas E. Feasby, MD; Gustav Fraedrich, MD; Peter Gloviczki, MD; Graeme J. Hankey, MD, FRACP; Robert E. Harbaugh, MD, FAANS, FACS; Eitan Heldenberg, MD; Michael G. Hennerici, MD; Michael D. Hill, MD, MSc, FRCPC; Timothy J. Kleinig, PhD FRACP, MBBS (Hons), BA; Dimitri P. Mikhailidis, BSc, MSc, MD, FRSPH, FCP, FFPM, FRCP, FRCPath; Wesley S. Moore, MD; Ross Naylor, MD, FRCS; Andrew Nicolaides, MS, FRCS, PhD (Hon); Kosmas I. Paraskevas, MD, PhD; David M. Pelz, MD, FRCP; James W. Prichard, MD; Grant Purdie, MD, FRACP; Jean-Baptiste Ricco, MD, PhD; Peter A. Ringleb, MD, PhD; Thomas Riles, MD; Peter M. Rothwell, MD, PhD, FRCP, FMedSci; Peter Sandercocker, MA, DM, FRCPE, FMedSci; Henrik Sillesen, MD, DMSc; J. David Spence, BA, MBA, MD, FRCPC, FCAHS; Francesco Spinelli, MD; Jonathon Sturm, MBChB, PhD; Aaron Tan, MD, FRACP; Ankur Thapar, BSc, MBBS, MRCS; Frank J. Veith, MD; Tissa Wijeratne, MD, FRACP; Wei Zhou, MD

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From the School of Public Health and Preventive Medicine, The Alfred Centre, Monash University, Melbourne, Australia (A.L.A.); Baker IDI Heart and Diabetes Institute, Melbourne, Australia (A.L.A.); Florey Institute of Neuroscience and Mental Health, Melbourne, Australia (A.L.A.); Division of Vascular and Endovascular Surgery, New York University Langone Medical Center, New York, NY (M.A.A.); Comprehensive Stroke Center, University of Alabama Hospital, Birmingham, AL (A.V.A.); Department of Medicine, Centre for Brain Research, University of Auckland, Auckland, New Zealand (A.B.); Clinical Neurological Sciences, Division of Neurology, University of Western Ontario, London, Canada (H.J.M.B.); Sheffield Vascular Institute, Northern General Hospital, Sheffield, United Kingdom (J.B.); University of Leicester, University of Leicester Hospitals, Leicester, United Kingdom (P.B.); Department of Surgical Sciences, Vascular Surgery, Uppsala University, Uppsala, Sweden (M.B.); Neurology Department, Sir Charles Gardiner Hospital, Perth, Australia (D.B.); Department of Neurology and Stroke Unit, Hospital Universitari Basel, Basel, Switzerland (L.B.); UCL Institute of Neurology, The National Hospital, Queen Square, London, United Kingdom (M.B.); Texas A&M Health Sciences Center College of Medicine, Scott and White Health Care Systems, Central Texas Veterans Health Care System, Temple, TX (C.J.B.); Division of Vascular and Endovascular Surgery, Massachusetts General Hospital, Harvard Medical School, Boston, MA (R.P.C.); Neurology Division, USF College of Medicine, Lehigh Valley Health Network, Allentown, PA (J.E.C.); Jobst Vascular Institute, The Toledo Hospital, Toledo, OH (A.J.C.); Department of Neurological Surgery, Columbia University, New York, NY (E.S.C.); Divisions of Vascular Surgery and Cardiovascular Health (Quality and Outcomes), Stanford University, Stanford, CA (R.L.D.); Academic Section of Vascular Surgery, Department of Surgery, Imperial College School of Medicine, Charing Cross Hospital, London, United Kingdom (A.H.D.); Department for Vascular and Endovascular Surgery/Vascular Center, Klinikum rechts der Isar der Technischen Universität München, München, Germany (H.-H.E.); Stanford University, Stanford, CA (R.F.); University of California, San Francisco, CA (R.F.); Department of Vascular and Endovascular Surgery, Kaiser Permanente Medical Center, Santa Clara, CA (R.F.); Department of Clinical Neurosciences Faculty of Medicine, University of Calgary, Calgary, Canada (T.E.F.); Department of Vascular Surgery, Medical University, Innsbruck, Austria (G.F.); Division of Vascular and Endovascular Surgery, Mayo Clinic, Rochester, MN (P.G.); Neurology Department, Royal Perth Hospital, University of Western Australia, Perth, Australia (G.J.H.); Penn State Institute of the Neurosciences, Penn State University, Hershey, PA (R.E.H.); Department of Vascular Surgery, Assaf Harofeh Medical Center, Zerifin, Israel (E.H.); Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel (E.H.); Neurologische Universitätsklinik, Universitätsmedizin Mannheim, UMM; University of Heidelberg, Mannheim, Germany (M.G.H.); Department of Clinical Neurosciences, Hotchkiss Brain Institute, University of Calgary, Calgary, Canada (M.D.H.); Neurology Department, Royal Adelaide and Lyell McEwin Hospitals, Adelaide, Australia (T.J.K.); Department of Medicine, University of Adelaide, Adelaide, Australia (T.J.K.); Department of Clinical Biochemistry (Vascular Disease Prevention Clinics), Royal Free Hospital Campus, University College London Medical School, University College London, London, United Kingdom (D.P.M.); Division of Vascular Surgery, UCLA, Los Angeles, CA (W.S.M.); Vascular Surgery Group, Division of Cardiovascular Sciences, Leicester Royal Infirmary, University of Leicester, Leicester, United Kingdom (R.N.); Department of Vascular Surgery, Imperial College, London, Vascular Non-invasive Diagnostic Centre, London, United Kingdom (A.N.); Red Cross Hospital, Athens, Greece (K.I.P.); Medical Imaging and Clinical Neurological Sciences, University of Western Ontario, London, ON, Canada (D.M.P.); Neurology Department, Yale Medical School, New Haven, CT (J.W.P.); Neurology Department, The Queen Elizabeth

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To avoid misinformation from calls for more routine practice (nontrial carotid angioplasty/stenting (CAS), we need to distinguish relevant facts and patients’ best interests from all else (distractions). A recent editorial by White and Jaff is one publication which illustrates this need particularly well. First, these authors are correct in reminding us that the responsibility of physicians is to provide best patient care, putting aside personal interest. This is inherent in any profession. However, misconception, bias, and conflict of interest exist. Therefore, healthcare payment organizations, such as the US Center for Medicare and Medicaid Services are important gatekeepers to facilitate patient access to interventions that are likely to help them, as opposed to all others.

It is also true that CAS and carotid endarterectomy (CEA) result in better outcomes when patients are carefully selected and skilled operators perform the procedures in experienced centers. We would add that key indicators (such as 30-day periprocedural stroke/death rates) must be accurately measured in routine (real-world) practice, particularly as stroke and death rates here may be unacceptably higher than in trials. Therefore, it is most appropriate, as suggested by White and Jaff, that coverage for carotid procedures be dependent on facility accreditation and audited measurement of key standards indicators in all practices performing these procedures. This is a priority issue.

White and Jaff also correctly state “a major change in evidence based stroke prevention strategies will require clinical trial data.” These authors are calling for extended US Center for Medicare and Medicaid Services funding for CAS beyond the current indication of high surgical risk symptomatic patients to include asymptomatic and low/average surgical risk symptomatic patients. For CAS, there is a substantial body of data from randomized trials (including the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST)), meta-analyses, and routine practice. Most of these data relate to low/average risk symptomatic patients and demonstrate that, for these patients, even in the best academic centers, CAS is consistently associated with significantly higher rates of stroke or death (during or after the periprocedural period) compared with CEA. It is incorrect that CREST “failed to show a difference in overall stroke rate between CAS and CEA” as stated by White and Jaff. In CREST, for average surgical risk symptomatic patients, the periprocedural and death rates were 6.0% for CAS versus 3.2% for CEA (hazard ratio, 1.89; 95% confidence interval, 1.11–3.21; P=0.02). The higher periprocedural risk of stroke or death with CAS is particularly evident in the most senior patients (>68–70 years), those undergoing the procedure <7 days of incidental cerebral or retinal ischemic symptoms (when CEA has the highest stroke prevention potential), those undergoing CAS outside clinical trials, and those with certain anatomic features. No study has shown that CAS is more effective than CEA in preventing stroke. Further, most analyses show that CAS costs considerably more despite calculations derived from CREST results. No randomized trial has been adequately powered to compare the procedural and longer term risk of CAS on stroke or death in low/average risk asymptomatic patients. However, in CREST, the direction of effect was toward nearly twice the risk (periprocedural stroke/death rate was 2.5% for CAS versus 1.4% for CEA; hazard ratio, 1.88; 95% confidence interval, 0.79–4.42; P=0.15). This was consistent with the significantly higher periprocedural stroke rates seen in CREST CAS-treated symptomatic patients and nontrial CAS-treated asymptomatic patients.

Meanwhile, medical treatment for asymptomatic carotid disease has improved significantly since past randomized trials of medical treatment alone versus additional CEA. Medical treatment consists of identification of risk factors for heart and vascular disease and risk reduction using healthy lifestyles and appropriate drugs. Improvement in medical treatment is clear from robust analyses of all published comparable, quality stroke rate calculations (including from, and within, randomized surgical trials) of patients with 50% to 99% asymptomatic carotid stenosis. This knowledge is not, as claimed by White and Jaff, derived from short-cut extrapolation from coronary artery trials. Using the same standardized rate calculations, we are now seeing an average annual rate of ipsilateral stroke of 0.5% with medical treatment alone. This is about 3x lower than that of asymptomatic CREST CAS-treated patients and about half the rate of asymptomatic CREST CEA-treated patients. This low rate with medical treatment is likely to fall further with improvements in efficacy, definition, and implementation. However, recently published rate calculations indicate that, at most, only 2.5% of low/average CEA risk patients with 50% to 99% asymptomatic carotid stenosis will receive a stroke prevention benefit from CEA or CAS during their remaining average 10-year lifetime if they receive good, current medical treatment (assuming the procedural risk of stroke/death is always zero). This indicates that a one-size-fits-all procedural

Hospital, Adelaide, South Australia, Australia (G.P., A.T.); Vascular Surgery Service, University of Poitiers, Poitiers, France (J-B.R.); Department of Neurology, University Hospital Heidelberg, Germany (P.A.R.); Division of Vascular Surgery, New York University School of Medicine, New York, NY (T.R.); Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, United Kingdom (P.M.R.); Division of Clinical Neurosciences, University of Edinburgh, Western General Hospital, Edinburgh, United Kingdom (P.S.); Department of Vascular Surgery, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark (H.S.); Neurology and Clinical Pharmacology, University of Western Ontario, London, ON, Canada (J.D.S.); Stroke Prevention and Atherosclerosis Research Centre, Robarts Research Institute, London, ON, Canada (J.D.S.); Department of Cardiovascular and Thoracic Sciences, University of Messina, Messina, Italy (F.S.); Neurology Department, Gosford and Wyong Hospitals, University of Newcastle, New South Wales, Australia (I.S.); Academic Section of Vascular Surgery, Department of Surgery and Cancer, Imperial College, London, London, United Kingdom (A.T.); Division of Vascular Surgery, New York University School of Medicine, Cleveland Clinic, Lerner School of Medicine of Case Western Reserve University, Edward Hebert School of Medicine, University of The Health Sciences, New York (F.J.V.); Neurology Department, Western Hospital, Western Clinical School, University of Melbourne, Melbourne, Australia (T.W.); and Vascular and Endovascular Surgery, Stanford University, Palo Alto VA Health Care System, Stanford, CA (W.Z.).

Authors are arranged alphabetically by last name.

Bo Norrving, MD, was guest editor for this article.

Correspondence to Anne L. Abbott, MD, PhD, FRACP, School of Public Health and Preventive Medicine, The Alfred Centre, 99 Commercial Rd, Melbourne, VIC 3004, Australia. E-mail Anne.L.Abbott@gmail.com
approach for these asymptomatic patients is now unlikely to be beneficial overall. We need to be much more selective. Research is required to determine which asymptomatic subgroups now benefit from carotid procedures in addition to current optimal medical treatment.

We have found no direct information about the influence of current medical treatment in patients with low/average CEA risk symptomatic carotid stenosis. However, improving results for medically treated asymptomatic patients and procedural trial asymptomatic and symptomatic patients indicate that 6% periprocedural risk of stroke or death (the current standard) is now too high. New randomized and risk stratification studies are required using current optimal medical treatment and procedural methods. For example, improved plaque thrombus identification or embolic signal detection above and below the stenosis may help better identify carotid plaques responsible for carotid territory ischemic symptoms. Further, the best approach for patients with high surgical risk carotid stenosis remains uncertain because risk of stroke or death has not been measured with any standard of medical treatment or adequate procedural trials. However, some registries show significantly higher risks of stroke/death with CAS compared with CEA in asymptomatic and symptomatic high surgical risk patients.

Calls from other authors for more routine CAS on the grounds of lower periprocedural myocardial infarction (MI) rates compared with CEA are distracting. MI is not a measure of stroke prevention efficacy, even though it is an important procedural complication. The inclusion of periprocedural MI with stroke and death in the primary outcome measure in CREST resulted in primary outcome equivalence between CAS and CEA. However, it did not result in efficacy equivalence. In CREST, 1.1% (14/1262) of CEA patients had periprocedural clinical MI (biomarkers plus chest pain/EKG evidence) compared with 2.3% (28/1240) of CAS patients (P=0.03). However, periprocedural stroke was nearly twice as common (81/2502; 3.2%) as periprocedural clinical MI (42/2502; 1.7%) and, as mentioned above, CAS caused almost twice as many of these strokes as CEA. Further, in CREST, the mortality rate up to 4 years was equally poor for CREST patients with periprocedural stroke (20%), periprocedural clinical MI (19%), or periprocedural biomarker-positive only MI (25%). Finally, nonfatal stroke was associated with a poorer quality of life at 1 year than nonfatal MI. Therefore, MI is a measure of carotid procedural risk (not benefit) and must be considered separately from stroke risk. Moreover, in CREST, CAS-associated stroke was more troublesome for patients than CEA-associated MI.

In conclusion, current global evidence shows that, even in the best academic centers, CAS is less effective (causing more strokes) and more expensive than CEA. It is premature that some guidelines have recently added support for routine practice CAS as an alternative to CEA for asymptomatic and low/average surgical risk symptomatic patients because CAS may easily be misinterpreted by readers as being equivalent for stroke prevention and historical procedural standards were cited. CAS, for these patients, should still only be performed and paid for within well-designed, adequately powered trials. The US Center for Medicare and Medicaid Services is doing its job and setting an excellent global example. It is protecting Medicare beneficiaries from routine practice procedures, which are currently more likely to harm them and waste finite resources that could be used for their advantage. Meanwhile, we need to reassess the current routine practice role of CEA and deliver optimal current medical treatment to all who need it.

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