Systematic Review of Guidelines for the Management of Asymptomatic and Symptomatic Carotid Stenosis

Anne L. Abbott, PhD, MBBS, FRACP; Kosmas I. Paraskevas, MD, PhD; Stavros K. Kakkos, MD, PhD; Jonathan Golledge, MB, BChir, BA, MA, MChir; Hans-Henning Eckstein, MD, PhD; Larry J. Diaz-Sandoval, MD; Longxing Cao, MD, PhD; Qiang Fu, MD, PhD; Tissa Wijeratne, MD, FRACP; Thomas W. Leung, MD; Miguel Montero-Baker, MD; Byung-Chul Lee, MD, PhD; Sabine Pircher, BNutrDiet, MPH; Marije Bosch, PhD; Martine Dennekamp, PhD, MSc; Peter Ringleb, MD, PhD

Background and Purpose—We systematically compared and appraised contemporary guidelines on management of asymptomatic and symptomatic carotid artery stenosis.

Methods—We systematically searched for guideline recommendations on carotid endarterectomy (CEA) or carotid angioplasty/stenting (CAS) published in any language between January 1, 2008, and January 28, 2015. Only the latest guideline per writing group was selected. Each guideline was analyzed independently by 2 to 6 authors to determine clinical scenarios covered, recommendations given, and scientific evidence used.

Results—Thirty-four eligible guidelines were identified from 23 different regions/countries in 6 languages. Of 28 guidelines with asymptomatic carotid artery stenosis procedural recommendations, 24 (86%) endorsed CEA (recommended it should or may be provided) for ≈50% to 99% average-surgical-risk asymptomatic carotid artery stenosis, 17 (61%) endorsed CAS, 8 (29%) opposed CAS, and 1 (4%) endorsed medical treatment alone. For asymptomatic carotid artery stenosis patients considered high-CEA-risk because of comorbidities, vascular anatomy, or undefined reasons, CAS was endorsed in 13 guidelines (46%). Thirty-one of 33 guidelines (94%) with symptomatic carotid artery stenosis procedural recommendations endorsed CEA for patients with ≈50% to 99% average-CEA-risk symptomatic carotid artery stenosis, 19 (58%) endorsed CAS and 9 (27%) opposed CAS. For high-CEA-risk symptomatic carotid artery stenosis because of comorbidities, vascular anatomy, or undefined reasons, CAS was endorsed in 27 guidelines (82%). Guideline procedural recommendations were based only on results of trials in which patients were randomized 12 to 34 years ago, rarely reflected medical treatment improvements and often understated potential CAS hazards. Qualifying terminology summarizing recommendations or evidence lacked standardization, impeding guideline interpretation, and comparison.

Conclusions—This systematic review has identified many opportunities to modernize and otherwise improve carotid stenosis management guidelines. (***Stroke*. 2015;46:3288-3301. DOI: 10.1161/STROKEAHA.115.003390.**)

Key Words: carotid endarterectomy ■ carotid guideline ■ carotid stenosis ■ carotid stenting ■ stroke prevention

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From the Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine (A.L.A, M.D.), Department of Surgery, Central Clinical School (M.B.), Monash University, Melbourne, Victoria, Australia; Neurology Department, The Alfred Hospital, Prahran, Victoria, Australia (A.L.A.); Department of Cardiovascular Sciences, St. George'sVascular Institute, St George's Hospital, London, United Kingdom (K.I.P.); Department of Vascular Surgery, University of Patras, Patras, Greece (S.K.K.); Queensland Research Centre for Peripheral Vascular Disease, College of Medicine and Dentistry, James Cook University, Townsville, Queensland, Australia (J.G.); Department of Vascular and Endovascular Surgery, The Townsville Hospital, Townsville, Queensland, Australia (J.G.); Department for Vascular and Endovascular Surgery, Klinikum Rechts der Isar, Technical University Munich, Munich, Germany (H.-H.E.); Department of Medicine, Michigan State University, Metro Health Hospital, Grand Rapids, MI (L.J.D.-S.); Cardiology Department, Xiamen Cardiovascular Hospital, Xiamen, Fujian, China (L.C.); Center for Cardiology Intervention Treatment, Department of Cardiology, Zhujiang Hospital, Southern Medical University, Guangzhou, Guangdong, China (Q.F.); Stroke Unit, Department of Neurology, Western Hospital, University of Melbourne, Footscray, Melbourne, Victoria, Australia (T.W.); Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, China (T.W.L.); Department of Vascular Surgery, University of Arizona and Pima Vascular Group, Tucson (M.M.-B.); Department of Neurology, Hallym Neurological Institute, Hallym University, Sacred Heart Hospital, Seoul, South Korea (B.-C.L.); Centre for Health and Social Research, Faculty of Health Sciences, Australian Catholic University, Melbourne, Victoria, Australia (S.P.); and Department of Neurology, University Hospital Heidelberg, Heidelberg, Germany (P.R.).

Correspondence to Anne L. Abbott, PhD, MBBS, FRACP, Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Monash University, 99 Commercial Rd, Melbourne, Victoria 3008, Australia. E-mail Anne.L.Abbott@gmail.com

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Moderate and severe (50%–99%) carotid artery stenosis is an important public health issue. This condition affects ≈10% of the general population by their 8th decade, and it causes ≈10% of all strokes.[1] For many years, procedural management has been commonly recommended for stroke prevention. However, important relatively recent discoveries should improve treatment decisions for patients with carotid stenosis. These include:

1. The 60% to 80% fall in stroke risk associated with asymptomatic carotid stenosis (ACS) with medical treatment alone (encouraging a healthy lifestyle and appropriate medication) since the start of the randomized trials of medical treatment alone versus additional carotid endarterectomy (CEA).[2–6] This improved stroke prevention efficacy also has implications for better outcomes for patients with symptomatic carotid stenosis (SCS) given medical treatment, with or without additional CEA.[7]
2. Stroke risk stratification studies of patients with ACS showing that transcranial embolus detection,[8] degree of stenosis,[9] plaque echolucency,[10] and asymptomatic progression[11] are not sufficiently powerful individually to identify asymptomatic patients likely to benefit from carotid procedures. Combinations of markers are most likely to provide clinically meaningful stroke risk stratification.[9]
3. Falls in the risk of stroke or death associated with CEA for patients with ACS or SCS.[12–14]
4. The significantly higher overall risk of stroke or death associated with carotid angioplasty/stenting (CAS) than with CEA.[7]

This systematic review of contemporary international guidelines was performed to compare and appraise recommendations for the management of patients with ACS and SCS (including accessibility, organization, clarity, and consistency) and the evidence used in making these recommendations.

Methods

Guideline Searches

Guidelines with recommendations on the use of CEA or CAS or both patients with ACS or SCS or both were sought systematically using popular search engines, bibliographies, and author professional networks. PubMed and ISI Web of Knowledge were searched independently and synchronously by 2 authors on September 9, 2013 (A.L.A., K.I.P.). PubMed was searched using *carotid guideline* and then *stroke guideline* in the title, yielding 91 references after duplicate removal. ISI Web of Knowledge was searched using *carotid and guideline* and then *stroke and guideline* in the title, yielding 422 references after removal of duplicates, abstracts, reference materials, letters, corrections, meetings, news, and case reports. Wider searches using the words carotid or stroke and guideline in any PubMed field or the ISI Web of Knowledge topic field yielded thousands of results, beyond our scope. In addition, PubMed was searched on December 13, 2013 (S.K.K.) using *carotid* as a keyword with *guideline* and *consensus development* as filters yielding 148 references. Relevant guidelines were then independently identified using titles, abstracts, and full articles. Several search updates were performed using these methods (A.L.A., K.I.P., J.G., S.K.K., P.R.) until January 28, 2015, to identify new or updated guidelines.

Guideline Inclusion Criteria

We included all guideline recommendations for routine practice use of CEA and CAS published from January 1, 2008, to January 28, 2015. A guideline was considered a set of latest recommendations covering CEA or CAS, or both for ACS or SCS, or both based on evidence appraisal and consensus from a single writing group, even if such recommendations were published separately. No guideline was excluded because of language. When a guideline document was not available in English, translation was undertaken by at least 2 authors. However, when guidelines were available in English and another language, the English translation was used in preference. When guidelines were published in abbreviated and full-length versions, the full-length version was scrutinized when required information was not given in the abbreviated version. Guidelines on acute stroke treatment (such as carotid procedures and thrombolysis) or medical treatment alone were excluded.

Guideline Analysis

Each guideline was independently reviewed by at least 2 authors using predetermined questions on guideline identifying information, treatment recommendations, research evidence used, and qualifying terms (such as level of evidence or grade of recommendation) used by some groups to summarize the nature of their recommendations and the evidence used in making them. Each guideline was reviewed by at least 1 author not affiliated with that guideline. Each guideline was checked for completeness in defining ACS and SCS (the target populations) with respect to the degree of stenosis, method of quantifying stenosis (North American Symptomatic Carotid Endarterectomy Trial [NASCET], European Carotid Surgery Trial [ECST], or other[15]), and the timing and territory/laterality of any previous clinically defined strokes or transient ischemic attacks (TIA). Subcategories of patients with ACS or SCS were differentiated when possible.

The nature of recommendations was classified as the treatment: (1) should be provided, (2) may be provided (it may be provided or should/may be considered), or (3) should not be provided in routine practice using our interpretation of the guideline authors' comments. Similarly, when the nature of the research evidence used to make recommendations was characterized (its relevance, quality, and reliability), we classified author comments as meaning the evidence was (1) excellent, (2) reasonable, or (3) poor. We also checked for the provision of corresponding procedural standards, which indicated patients should have an overall stroke prevention benefit (specifically, the 30-day periprocedural rate of clinically defined stroke or death from the relevant randomized trials). Each guideline was searched for evidence from the authors that any recommendations may be limited. When differences occurred in interpretation among our authors, consensus was reached by revisiting the relevant guideline and discussion.

Results

During the process of this systematic analysis, 6 eligible guidelines were replaced by updates from the same writing group on the same clinical scenario(s).[16–22]

Included Guidelines

We identified 34 guidelines meeting the inclusion criteria. These were sets of recommendations on CEA or CAS, or both for ACS or SCS, or both published between January 1, 2008, and January 28, 2015, in 41 separate documents from 23 different regions/countries (including 2 representing Europe and 5 the United States). They were written by 32 different groups in 6 languages (English, Chinese, Korean, Spanish, Dutch, and German).[23–63] One group (American Heart Association/American Stroke Association) published a guideline on carotid stenosis for men and women together[60,61] and a separate one for women only,[62] both were included. Also included was an American Heart Association/American Stroke Association guideline published as part of a larger group.[41] Three guideline documents came in full-length and abbreviated forms.[23,24,44,45,55,56] All except 5 guideline documents were available in English. Two were only available in Chinese,[30,31]

1 (the full-length form) was only available in German,[55] 1 was only available in Dutch,[29] and 1 only in Spanish.[39] Eighteen of 41 guideline documents (44%) were not found from the search-engine enquiries and only via bibliographies and author professional networks.[23–26,28–30,33,36,38,42,43,46,47,52,54,55,57]

For 12 guidelines (35%), at least 1 separately published document was required for full interpretation (range, 1–3 extra documents per guideline).[32–34,36,40,43–48,53,55,56,62] A total of 11 different supplementary documents were required; 5 provided definitions of qualifying terms summarizing treatment recommendations and the evidence used,[64–68] and 6 were other guidelines to which readers were referred for treatment recommendations.[19,20,41,69–71] Each guideline was independently reviewed by an average of 4 authors (range, 2–6). Each author reviewed an average of 8 guidelines (range, 1–30). Twenty-eight of 34 guidelines had procedural recommendations for ACS (3 with CAS recommendations only[23–26,40,43] and 1 with CEA recommendations only).[54] All except 1[60] of the 34 guidelines had procedural recommendations for SCS (2 with CAS recommendations only).[40,43]

Definitions of ACS

Only 2 of 28 (7%) guidelines with procedural recommendations on ACS completely defined ACS according to degree of stenosis, method of determining degree of stenosis, and timing and territory of any previous stroke or TIA.[48,55,56] Even then, in 1 case, the timing of any previous stroke or TIA (<6 months) was deduced from the definition of SCS.[48] Three guidelines contained no definition of ACS.[23–26,40,52] Among the remaining 23 guidelines, degree of stenosis was always specified and 1 distinct cutoff value was given (producing 2 stenosis ranges) for determining procedural use. This value/range was >50%, 50% to 99%, >60%, ≥60%, 60% to 99%, >70%, ≥70%, 70% to 99%, >80%, ≥80%, or 80% to 99% in different guidelines. Four guidelines used different ranges of stenosis severity according to different recommended imaging techniques or procedures or the same treatment recommendations, sometimes in different parts of their guideline.[30,41,46,47,59] In 2 guidelines, there were no recommendations for ACS of 50% to 60% or 69%, yet there were recommendations for higher and lower degrees of ACS.[35,41]

Where the method of measuring ACS was indicated, it was by the NASCET method in all cases.[27,32,33,36–38,41,48,55,56,58–60] Timing of any previous stroke or TIA was specified in only 4 guidelines (14%), requiring the complete absence of such events in the past[63] or absence only in the previous 3[37] or 6 months.[28,55,56,63] However, the territory or laterality of such events was specified in only 3 guidelines (11%).[28,37,55,56]

Definitions of SCS

SCS generally referred to patients with previous stroke or nondisabling stroke or TIA, or a combination of these terms. Only 4 of 33 guidelines (12%) with procedural recommendations on SCS completely defined SCS according to degree of stenosis, method of determining stenosis, and timing and territory of any previous stroke or TIA.[37,41,48,59] All guidelines at least partly defined SCS, including the degree of stenosis. In 6 guidelines, there was 1 distinct cutoff value (producing 2 stenosis ranges) for determining procedural use. This value/range was ≥50%, 50% to 99%, or ≥70% in different guidelines[23–26,40,43–45,52,63] or moderate or severe SCS.[49] Elsewhere stenosis severity was divided into 3 stenosis ranges with respect to procedural recommendations: <50% for mild/no stenosis; >50%, 50% to 69%, or 50% to 70% for moderate; and ≥70% or 70% to 99% for severe SCS.[27–39,41,42,46–48,50,51,53–59,61,62] All 33 guidelines with procedural recommendations for SCS covered the moderate and severe ranges, except one which just covered the severe range (>70%)[40] and another that covered the moderate (50%–69%) range only if defined by conventional angiography.[41]

Where the method of measuring SCS was indicated (17 guidelines), it was by the NASCET method[27,28,33,34,36–38,40,41,46–49,52,55,56,58,59] or by the NASCET or ECST method.[23–26] Timing of any previous stroke or TIA was specified in only 16 (48%) guidelines, indicating a stroke or TIA within the previous 3[37,54,58] or 6 months.[28–32,41,48,50,51,55–57,59,61,62] Elsewhere, timing was only described as in the very recent past[35] or recent past.[38] The territory or laterality of such events was specified in 17 guidelines (52%).[28,31,33,34,36–38,41,42,48–51,53,59,61–63]

Clinical Scenarios Covered

Guidelines most often gave recommendations on the use of CEA and or CAS in relation to average-CEA-risk ACS or SCS. However, average-CEA-risk was usually inferred rather than explicitly stated and was not generally defined. According to the European Society for Vascular Surgery guidelines,[32] average-CEA-risk refers to patients who would fulfill the inclusion criteria for the randomized trials of medical treatment alone versus additional CEA[72–78] and, therefore, high-CEA-risk refers to those who would not meet these criteria. Two guidelines[41,46,47] cited the Stenting and Angioplasty With Protection in Patients at High Risk for Endarterectomy Trial (SAPPHIRE)[79] for defining high-CEA-risk clinical scenarios.

Twenty-nine guidelines included specific recommendations for the use of CAS for patients with high-CEA-risk ACS[28,31,32,35–38,41,43–47,55–58,62,63] or SCS,[27,28,31–36,38–42,44–56,58,61–63] or both. In 12 of these, high-CEA-risk was not further characterized.[36–39,42,48,49,54–57,62,63] In the other 17 guidelines, the cause of high-CEA-risk was characterized as being because of only reasons related to vascular anatomy and in others as being because of vascular anatomy or medical comorbidities. Nine of these guidelines gave no specific examples of high-CEA-risk scenarios[42–45,48,49,54,57,63] or referred to other guidelines.[62] Where given, examples of high-CEA-risk because of vascular anatomy were contralateral recurrent laryngeal nerve palsy, cranial nerve injury, previous neck dissection or irradiation, high or low carotid bifurcation, inaccessible lesion because of obesity, intracranial extension, restenosis after CEA, tracheostomy, severe neck arthritis, contralateral carotid occlusion, tandem lesion, fibromuscular dysplasia, pseudoaneurysm, and Takayasu's arteritis.[28,31–33,36,38,40,41,44–47,50–53,55,56,58,61] Examples of high-CEA-risk because of medical comorbidities were age >80 years, New York Heart Association class III or IV heart failure, cardiac ejection fraction <30%, class III or IV angina, left main or multivessel coronary artery disease, severe uncorrectable coronary artery disease, myocardial infarction (MI) within 4 weeks, need for cardiac surgery within 30 days, severe lung disease and obesity.[33,40,41,44–47,50,51,58,61] Characterization

of high-CEA-risk generally applied to both ACS and SCS. Stenosis severity referred to with CAS recommendations for high-CEA-risk ACS or SCS was not usually specified and inferred from CEA recommendations.

Treatment Recommendations

Where indicated, procedural recommendations were derived from results of randomized trials of medical treatment alone versus additional CEA,[72–78,80,81] randomized trials of CEA versus CAS,[79,82–87] and sometimes CAS registries (such as Charisma[88] and Caress[89]). In 1 guideline,[52] a meta-analysis of stroke risk with medical treatment alone[2] and a cost effectiveness analysis[90] were used to substantiate a nonprocedural approach to ACS.

Management of Moderate or Severe Carotid Stenosis

ACS: Average-CEA-Risk

CEA Recommendations

Of 25 guidelines with CEA recommendations for patients with moderate or severe ACS (≈50%–99% by NASCET criteria), 24 (96%) endorsed CEA for average-CEA-risk patients by either recommending that it should be provided (7 guidelines)[27,32,35,37,46,47,58,59] or that it may be provided (17 guidelines).[28–31,33,36,38,41,44,45,48,50,51,54–57,60,62,63] In 6 guidelines, CEA endorsement for average-CEA-risk ACS was limited to patient subgroups: men with >80% stenosis,[27] life expectancy >3 to 5 years,[27,30,37,38,44,45,48,50,51,55,56,59,63] men <75 years,[29,32,37,50,51] younger fitter women,[32] high-medical-risk patients (not defined),[35] high-medical-risk because of progression of ACS,[37,50,51] embolic signals on transcranial Doppler, history of contralateral TIAs, or silent ipsilateral cerebral infarction.[50,51] Other guideline authors indicated patient factors that should be considered (such as life expectancy, age, sex comorbidities, or patient preferences) without specifying how these factors should direct treatment decisions.[33,36,41,54,57] Others endorsed CEA for selected patients with moderate or severe average-CEA-risk ACS without defining selected.[62,63] Only 1 guideline (4%) advised that CEA (or CAS) should not be provided, endorsing medical treatment alone for average-CEA-risk ACS patients unless part of a randomized trial.[52] However, in the background text (rather than in recommendation summaries), it was added that CEA may be considered in exceptional circumstances, such as patients not tolerant of hypertension treatment because of symptomatic hypoperfusion.[52] In 1 guideline, CEA recommendations for ACS were inconsistent or unclear (Table 1).[29]

CAS Recommendations

Of 27 guidelines with CAS recommendations for moderate or severe ACS, CAS was endorsed for average-CEA-risk patients in 17 (63%) by recommending that it should be provided (2 guidelines)[30,59] or it may be provided (15 guidelines).[23–26,29,32,38,41,43–48,50,51,55–58,60,62] In 4 of these guidelines, CAS endorsement was limited to particular subgroups of patients with average-CEA-risk ACS: men <75 years±with an expected survival >5 years[29,50,51] or highly selected patients (not defined).[41,60] In 3 guidelines, endorsement of CAS was inconsistent or unclear,[29,32,58] One guideline recommended CAS for average-CEA-risk ACS when CEA was not available.[43] In 8 other guidelines (30%), CAS was explicitly not recommended for average CEA-risk-ACS, advising it should not be performed routinely.[27,28,31,33,35–37,40]

Medical Treatment Alone Recommendations

Only 1 guideline (4%) advised medical treatment alone for patients with ACS with some qualification, as mentioned above.[52]

ACS: High-CEA-Risk

CAS Recommendations

Of 27 guidelines with CAS recommendations for moderate or severe ACS, 2 (7%) gave CAS recommendations specifically for patients considered high-CEA-risk because of vascular anatomy, and both recommended it may be provided.[28,43] Nine guidelines (30%) gave CAS recommendations for patients with ACS considered high-CEA-risk because of vascular anatomy or medical comorbidities.[32,33,38,40,41,44–47,58,62] Seven of these (26%) endorsed CAS by stating that it should be provided (2 guidelines)[46,47,58] or that it may be provided (5 guidelines).[32,33,38,41,62] In 1 of these 7 guidelines, CAS endorsement was provided in one part[46] and not in another[47] and in 3 it was provided only in the background text (rather than in recommendation summaries)[33,62] or only via reference to other guidelines.[62] One guideline advised against CAS for high-CEA risk ACS because of vascular anatomy and medical comorbidities.[40] High-CEA-risk ACS was not subcategorized or further defined in 4 (15%) guidelines, and all 4 of them endorsed CAS by recommending it may be provided.[37,55–57,63]

Medical Treatment Alone Recommendations

In one guideline, medical treatment alone was endorsed as a possible alternative option to CAS in high-CEA-risk ACS patients,[58] and in another only for those considered extremely high-CEA-risk because of multiple comorbidities.[32] Only 1 guideline endorsed medical treatment alone by advising that it may be provided.[44,45] Twelve of 28 guidelines (43%) with procedural recommendations for ACS contained no specific treatment recommendations for high-CEA-risk ACS.[23–27,29–31,35,36,48,50–52,59,60]

SCS: Average-CEA-Risk

CEA Recommendations

All 31 guidelines with CEA recommendations for SCS endorsed CEA for patients with severe (≈70%–99% by NASCET) average-CEA-risk SCS by recommending that it should be provided (28 guidelines)[23–27,30–39,41,42,44–48,50–59,61–63] or may be provided (3 guidelines).[28,29,49] All 31 guidelines also endorsed CEA for patients with moderate (≈50%–69% by NASCET) average-CEA-risk SCS by recommending that it should be provided (14 guidelines)[23–26,31,37–39,41,42,44,45,52,53,58,61–63] or it may be provided (17 guidelines).[27–30,32–36,46–51,54–57,59] Some guidelines, particularly on moderate (in contrast to severe) average-CEA-risk SCS, specified patient conditions for providing CEA (only men[29] or life expectancy >5 years[30] or old age, men, men >75 years, recent symptoms, hemispheric/nonocular symptoms, vascular risk factors, nondiabetics, and ulcerated plaque).[35,37,39,50,51,55,56,58] Others indicated patient factors to consider (age, sex, timing/territory/severity of symptoms, and comorbidities) without specifying how these should direct treatment decisions.[33,36,38,46,47,53,57,61,62] Others endorsed CEA for selected patients with moderate average-CEA-risk SCS without defining selected (Table 2).[34,42,48]

CAS Recommendations

Nineteen of 33 guidelines (58%) with CAS recommendations for SCS endorsed CAS for severe (≈70%–99% by NASCET) average-CEA-risk SCS by recommending that it should be provided (6 guidelines)[30,41,42,48,61,62] or that it may be provided (13

Table 1. Specific Guideline Recommendations for Moderate or Severe Asymptomatic Carotid Stenosis*†

Recommendation	Average CEA Risk‡	High-CEA-Risk: Anatomy Only	High-CEA-Risk: Anatomy or Comorbidities	High-CEA-Risk: Not Defined
CEA: yes	7 (28%)[27,32,35,37,46,47,58,59]	0	0	0
CEA: maybe	17 (68%)[28–31,33,36,38,41,44, 45,48,50,51,54–57,60,62,63]	0	0	0
CAS: yes	2 (7%)[30,59]	0	2 (7%)[46,47,58]	0
CAS: maybe	15 (56%)[23–26,29,32,38,41,43–48,50,51,55–58,60,62]	2 (7%)[28,43]	5 (19%)[32,33,38,41,62]	4 (15%)[37,55–57,63]
CAS: no	8 (30%)[27,28,31,33,35–37,40]	0	1 (4%)[40]	0
MT alone: yes	1 (4%)[52]§	0	1 (4%)[44,45]	0
MT alone: maybe	0	0	2 (7%)[32,58]	0

Approximately 50% to 99% stenosis by North American Symptomatic Carotid Endarterectomy Trial criteria; data from 28 guidelines with any procedural recommendations for asymptomatic carotid stenosis, including 25 on CEA and 27 on CAS. Denominators for the percentages are 25 for CEA recommendations, 27 for CAS recommendations and 28 for MT recommendations. CAS indicates carotid angioplasty/stenting; CEA, carotid endarterectomy; and MT, medical treatment.

*Yes, the treatment should be provided routinely; maybe, the treatment may be provided routinely (it may be provided or should/may be considered); and no, the treatment should not be provided routinely.

†Endorsements were limited to patient subgroups in some cases (see text).

‡Includes 3 guidelines with inconsistent/unclear CEA or CAS endorsement.[29,32,58]

§Includes endorsement of CEA in exceptional circumstances in background text.[52]

guidelines).[23–26,29,38–40,43–47,50,51,53,55–57,59] One guideline endorsed CAS in such patients only if aged <70 years and if revascularization was appropriate.[40] In 1 guideline, CAS endorsement was provided only in the background text (rather than recommendation summaries) and via referral to other guidelines.[62] CAS was specifically not recommended (advising it should not be provided) for patients with average-CEA-risk severe SCS in 9 guidelines (27%).[27,28,32,33,35–37,58,63] In 1 of these, this recommendation was made only for patients aged >75 years.[63]

Eighteen of 33 guidelines (55%) with CAS recommendations for SCS endorsed CAS for moderate (≈50%–69% by NASCET) average-CEA-risk SCS by recommending that it should be provided (3 guidelines)[30,41,42] or that it may be provided (15 guidelines)[23–26,29,38,39,43–48,50,51,53,55–57,59,61,62] CAS was specifically not recommended (advising that it should not be provided) for patients with average-CEA-risk moderate SCS in 8 of 33 (24%) guidelines.[27,28,32,33,35–37,58] In 2 guidelines, CAS endorsement for average-CEA-risk, severe SCS was inconsistent or unclear.[29,58] Three guidelines recommended CAS for average-CEA-risk SCS when CEA was not available.[42,43,53]

Medical Treatment Alone Recommendations

No guidelines contained endorsements of medical treatment alone in patients with moderate or severe average-CEA-risk SCS.

SCS: High-CEA-Risk

CAS Recommendations

Of 33 guidelines with CAS recommendations for SCS, 10 (30%) provided specific CAS recommendations for patients with moderate or severe (≈50%–99% NASCET) SCS considered high-CEA-risk according to vascular anatomy.[27,28,31,32,34,35,52,53,55,56,61] CAS was endorsed in all 10 by stating that it should be provided (4 guidelines)[27,32,34,35] or it

Table 2. Specific Guideline Recommendations for Moderate or Severe Symptomatic Carotid Stenosis*†

Recommendation	Average-CEA-Risk 70%–99% NASCET‡	Average-CEA-Risk 50%–69% NASCET‡	High-CEA-Risk Anatomy Only 50%–99%	High-CEA-Risk: Anatomy or Comorbidities 50%–99%	High-CEA-Risk: Not Defined 50%–99%
CEA: yes	28 (90%)[23–27,30–39,41,42,44–48,50–59,61–63]	14 (45%)[23–26,31,37–39,41,42,44,45 52,53,58,61–63]	0	0	0
CEA: maybe	3 (10%)[28,29,49]	17 (55%)[27–30,32–36,46–51,54–57,59]	0	0	0
CAS: yes	6 (18%)[30,41,42,48, 61,62]	3 (1%)[30,41,42]	4 (14%)[27,32, 34,35]	3 (10%)[44–47,58]	1 (3%)[39]
CAS: maybe	13 (39%)[23–26,29,38–40, 43–47,50,51,53,55–57,59]	15 (45%)[23–26,29, 38,39,43–48,50,51,53, 55–57,59,61,62]	6 (18%)[28,31,52,53,55,56,61]	4 (12%)[33,40,41,50, 51]	9 (27%)[36–38,42,48,49,54,62,63]
CAS: no	9 (27%)[27,28,32,33, 35–37,58,63]	8 (24%)[27,28,32,33, 35–37,58]	0	0	0
MT alone: yes	0	0	0	0	0
MT alone: maybe	0	0	0	2 (6%)[44,45,58]	0

Data from 33 guidelines with any procedural recommendations for symptomatic carotid stenosis, including 31 on CEA and 33 on CAS. Denominators for the percentages are 31 for CEA recommendations and 33 for CAS and MT recommendations. CAS indicates carotid angioplasty/stenting; CEA, carotid endarterectomy; MT, medical treatment; and NASCET, North American Symptomatic Carotid Endarterectomy Trial.

*Yes, the treatment should be provided routinely; maybe, the treatment may be provided routinely (it may be provided or should/may be considered); and no, the treatment should not be provided routinely.

†Endorsements were limited to subgroups in some cases (see text).

‡Three guidelines with inconsistent/unclear CAS endorsement.[29,32,58]

may be provided (6 guidelines).[28,31,52,53,55,56,61] Seven guidelines (21%) provided CAS recommendations for patients with moderate or severe SCS considered high-CEA risk because of vascular anatomy or medical comorbidities.[33,40,41,44–47,50,51,58] All 7 endorsed CAS by stating that it should be provided (3 guidelines)[44–47,58] or it may be provided (4 guidelines).[33,40,41,50,51] In 10 of 33 (30%) guidelines, high-CEA-risk was not subcategorized or further defined.[36–39,42,48,49,54,62,63] All 10 endorsed CAS by stating that it should be provided[39] or it may be provided.[36–38,42,48,49,54,62,63] Sometimes recommendations were provided only in the background text[33,36,62] and sometimes also only via other guidelines.[62]

Medical Treatment Alone Recommendations

Medical treatment alone for high-CEA-risk SCS because of vascular anatomy or medical comorbidities was not endorsed in any guideline although the possibility was mentioned as an alternative option in 2.[44,45,58] Six of 33 guidelines (18%) with procedural recommendations for SCS contained no specific treatment recommendations for high-CEA-risk SCS.[23–26,29,30,43,57,59]

Recommendations for Management of Mild Carotid Stenosis

Most guidelines indicated that CEA or CAS were not recommended for mild ACS (<50%–70% by NASCET) or SCS (<50% by NASCET) by not including procedural recommendations or explicitly stating that these procedures should not be done or that medical treatment alone was indicated. However, procedural endorsements for mild ACS were found in 3 guidelines, which stated that CEA or CAS was indicated in extraordinary circumstances (not defined)[41] or that CEA or CAS may be considered if examination indicated the plaque was unstable.[30,46,47] Procedural endorsements for mild SCS were found in 2 guidelines stating that CEA or CAS was indicated in extraordinary circumstances (not defined)[41] or CEA or CAS may be considered.[46,47]

Procedural Standards

Asymptomatic Carotid Stenosis

Of 28 guidelines with procedural recommendations for ACS, none included a fully defined procedural standard from which patients should expect an overall stroke prevention benefit. Using results from relevant randomized trials, this would be a 30-day periprocedural rate of stroke or death of <3%.[72–75,80] Four guidelines gave no procedural standard at all.[23–26,40,46,47,52] However, in 1 case, this was appropriate as this was a CAS-only guideline and CAS was not recommended for ACS.[40] Twenty-four guidelines included only a partial standard by not specifying the 30-day periprocedural period, sometimes with additional omissions. Where specified, the maximum complication rate was ≤3%[27–33,35–38,44,45,48,50,51,54–60,62,63] or low.[41] However, it was <6% in 1 guideline, where the CAS standards for ACS and SCS were not differentiated.[43] Referred to complications were generally stroke (of any type or localization) or death.[28–30,32,35,44,45,48,58,59] However, 2 guidelines referred to stroke, death, or MI.[41,60] In 12 guidelines (43%), the complications referred to were not fully specified because terms like morbidity were used.[27,31,33,36–38,50,51,54–57,62,63] In 3 guidelines, CEA endorsement was conditional on a documented CEA complication rate,[38,59] in 1 by a stroke physician or neurologist.[37]

Where CAS was endorsed for ACS patients considered high-CEA-risk, specific procedural CAS standards were not usually given. Where CAS standards were explicitly given, they were the same as for CEA in 9 cases[29,30,44,45,48,50,51,55–58,63] and higher in 1.[32]

Symptomatic Carotid Stenosis

Of 33 guidelines with procedural recommendations for moderate or severe SCS, only 1 included a fully defined CEA standard from which patients should expect an overall stroke prevention benefit.[58] This standard comprised a 30-day peri-CEA rate of stroke or death of <6%,[58] as expected from the relevant randomized trials.[76–78,81] Twelve guidelines gave no CEA standard at all for either moderate or severe SCS[23–26,28,29,44–49,52,53,59] or for moderate SCS only.[38,57] The remaining 20 included a partial standard by not specifying the 30-day perioperative period, sometimes with additional omissions. Where specified, the maximum CEA complication rate was <6%[27,30–35,37,38,41,42,50,51,54–58,61–63] or <7%[39] for severe average-CEA-risk SCS and <3%,[27,31,33–35,37] <6%,[30,32,41,42,50,51,54–56,58,61–63] or <7%[39] for moderate average-CEA-risk SCS, generally referring to stroke only or stroke or death. However, in 9 guidelines, the complications referred to were not fully specified because terms such as morbidity were used.[33,36–38,42,50,51,61–63] In 3 guidelines, CEA endorsement was conditional on a documented CEA complication rate by a stroke physician or neurologist[37] or the surgeon's participation in an audit.[28,34,52]

Where CAS was endorsed for patients with moderate or severe high-CEA-risk SCS, specific procedural CAS standards were not usually given. Where CAS standards were explicitly given, they were the same as CEA in 8 cases,[30,35,38,41,55–57,61] higher in 1[32] and lower (<5%) in another.[63] All except 4[30,31,46,47,49] of 33 guidelines (88%) included a recommendation that CEA (or CAS) should be performed as soon as possible or within 2 weeks of symptoms (as long as there were no contraindications).

General and Periprocedural Medical Treatment

Recommendations on general and periprocedural medical treatment often appeared only in guideline background text, rather than in summaries with procedural recommendations and were not always clearly applicable to patients with carotid stenosis. Evidence for medical treatment was often ranked lower in quality or reliability than for procedures. Of 28 guidelines with procedural recommendations for ACS, 19 (68%) contained endorsements of general medical treatment of vascular risk factors, whether a procedure was done. Depth of coverage consisted of no further detail[37,46,47] to endorsing management of hypertension, lipids, smoking addiction, diabetes mellitus or other risk factors with/without antiplatelet therapy advice and with/without treatment targets.[27,30–32,35,38,41,44,45,48,50,51,54–57,59,60,62,63] Fourteen guidelines (50%) specifically endorsed peri-CEA medical management, including no further detail[48] or endorsing aspirin[27,28,35,44–47,54–56,59,60,62,63] sometimes with additional statin or antihypertensive medication.[32,37] Nine (32%) specifically endorsed peri-CAS medical management, including no further

detail[23–26] or endorsing aspirin and clopidogrel,[30,32,43,48,55,56,59] sometimes with additional endorsement of statins or antihypertensive medication.[41,44,45]

Thirty of 33 guidelines (91%) containing procedural recommendations for patients with SCS contained endorsements of general medical treatment, including no further detail[31,37] or covering similar aspects as for ACS[23–30,32–36,38,41–49,52–57,59,61–63] or just antiplatelet therapy.[50,51] Sixteen guidelines (48%) specifically endorsed peri-CEA medical treatment for SCS, including no further detail[48] or endorsing aspirin,[27,28,31,34,35,46,47,53,54,62] sometimes with additional statin or antihypertensive medication.[32,37,41,44,45,55,56,59] Sixteen guidelines (48%) specifically endorsed peri-CAS medical treatment, including no further detail[23–26] or endorsing clopidogrel (usually with aspirin),[27,30–32,34,35,43,48,53,54,57] sometimes with additional statin or antihypertensive medication.[41,44,45,55,56]

Terminology Summarizing Recommendations Made and Evidence Used

In all except 6[23–26,29,30,37,42,52] of the 34 included guidelines, systems of qualifying terms were used to summarize the nature of recommendations provided (treatment should be provided, may be provided, or should not be provided) or the nature of the evidence used in making recommendations (excellent, reasonable, or poor). In 1 guideline, such a system was used only for conclusions, rather than recommendations.[29] In 3 cases,[27,34,35] strength of recommendations was summarized without indicating whether a procedure was recommended or not (after Brainin et al,[64] sometimes with transcription errors). Where such systems were used, qualifying terms were only partially defined within the guideline in 5 cases[33,36,44,45,53,55,56] although reference(s) containing full definition were provided. In 3 guidelines, these terms were not defined and no reference was provided[39,40,43] although a definition was independently found in 1 case (Table 3).[40,65]

In most cases, qualifying terms were used to summarize the nature of evidence used (27 guidelines) with only 10 guidelines[38,40,44–48,55,56,59–62] using such terms to summarize the nature of recommendations. In several instances, the full procedural recommendation was at odds with qualifying terminology summarizing it because of inconsistency or lack of clarity[27,34,35,38,39,43–45,55,56,61] In this analysis, preference was given to the full procedural recommendation. In 14 guidelines, 2 systems of qualifying terms were used and both referred to the nature of evidence used, with 1 system being a summary of the other.[27,28,31,33–36,40,49,50,53,54,57,58] As can be seen from Table 3, there was no standardized use of qualifying terms across guidelines. Different guidelines used different words, letters, numbers, and other symbols to summarize their recommendations or evidence used. In addition, it was common across guidelines for the same words, letters, numbers, and other symbols to summarize recommendations or evidence used. Systems of qualifying terms varied from most complex[29,55,56] to relatively simple[38,41,48,59–62] The nature (reliability) of evidence used in making recommendations was almost always in proportion to the extent that randomized trial data had been used, usually with nothing else taken into consideration.

Acknowledgment of Possible Guideline Limitations

Results of randomized trials of CEA versus medical treatment alone[72–78] underpinned recommendations and procedural standards in all guidelines, although in 4 guidelines, this is uncertain because references were omitted.[23–26,30,57,63] Randomized trials of CEA versus CAS and CAS registries were also common evidence sources. However, these had no medical treatment only arm, and their relevance, therefore, was also solely supported by the same randomized trials of CEA versus medical treatment alone.[72–78] Only 12 guidelines (35%) included mention of documented falls in stroke risk with medical treatment alone since the 1980s in patients with ACS, sometimes indicating that recommending CEA or CAS may no longer be valid. However, except for 1 guideline,[52] such comments were generally brief, appearing only in the background text (not recommendation summaries) and did not change historic procedural recommendations or standards for

Table 3. Qualifying Terminology for Recommendations Made or Evidence Used (Data From 26 Guidelines*†)

Aspect Summarized	No. of Guidelines	Terms Used	Associated Symbols Used
Nature of recommendation (treatment should be, may be, or should not be provided)	10	Class[38,41,48,59–62]	Upper or lower case letters[38,41,46–48,59–62]
		Grade[44,45]	Numbers[44–47]
		Grade of recommendation[55,56]	Roman numerals[38,41,48,59–62]
			Arrows[55,56]
Nature of evidence used in making recommendation (excellent, reasonable, or poor)	27	Class[27,31,34,35,53]	Upper, lower, or upper and lower case letters[27,28,31–36,38, 40,41,44–51,53,54,57–63]
		Levels of recommendation[27]	
		Grade[28,32,49–51,54,58]	Numbers[31,49–51,55,56,58]
		Level of evidence[28,31,38, 44,45,48–51,53–58]	Roman numerals[27,28,33–36,40,46, 47,53,54,57]
		Level[33–36,40,41,46,47,59–62]	Plus and minus signs[28, 31,49,58]
		NHMRC grade[33,36,40]	Arrows[55,56]
		Grade of recommendation[57]	
		Evidence level[63]	

NHMRC indicates National Health and Medical Research Council of Australia.

*Qualifying terminology were used in 2 guidelines; however, the definitions could not be found.[39,43]

†Fourteen guidelines used 2 recommendation qualifying systems, both meaning nature of evidence used.[27,28,31,33–36,40,49,50,53,54,57,58]

ACS.[33,36,37,41,44,45,48,50,51,55–57,59,60] We found only 1 guideline[55,56] clearly casting doubt on the validity of historic procedural recommendations and standards for patients with SCS because of improvements in medical treatment. These authors called for new randomized trials.[55,56,91]

Guidelines Replaced by Updates

Six eligible guidelines[16–22] (published in 7 separate documents) were each independently analyzed by an average of 4 authors and later replaced by updated guidelines from the same writing group on the same clinical scenario(s).[36,57,58,60,61,63] The updates included no significant differences with respect to treatment recommendations or procedural standards except for the addition of CEA endorsements for ACS, slightly weaker CEA endorsement and more specific CEA standards for SCS from New Zealand,[16,36] stronger endorsements of CAS for ACS and high-CEA-risk SCS and more specific CEA standards for SCS from Italy,[17,58] slightly weaker CEA endorsements for ACS and more specific CEA and CAS standards for SCS from Korea,[18,57] omission of CAS standards for high-CEA-risk SCS from 1 American group,[19,61] and stronger endorsements of CAS for moderate, noninvasively identified average-CEA-risk SCS from another.[19,60]

Discussion

The primary goal of a medical guideline is to use research (the evidence base) to produce an easily accessible tool that helps clinicians chose the treatment strategy that maximizes an individual's chance of achieving the best outcome in routine practice. Guidelines should summarize what is known from research and what is not. To our knowledge, this is the first systematic review of all identifiable contemporary international guidelines of carotid stenosis management. We have found many weaknesses in the accessibility and organization of these guidelines and a procedurally biased representation of the relevant evidence base. Such problems work against maximizing a patient's chance of stroke prevention and need addressing in all future guidelines.

Guideline Accessibility

Nearly half (44%) of the 34 guidelines, we identified were not found in our PubMed or ISI Web of Knowledge searches and were only available via the professional affiliations of particular authors. We do not know how many guidelines we missed because of this limited accessibility. To encourage utility and accountability, all guidelines should be easily identified and freely available to professionals and the public from popular search engines. Furthermore, it is unreasonable to expect clinicians or others to sort hundreds or thousands of references to find relevant guidelines. Inclusion of guideline in the document title would assist. Nonspecific guideline name terms, such as national, should be replaced by the country, region or group of origin. Guidelines should be scientifically peer reviewed, independently of industry interests before publication. All involved and their sources of income should be included. Updated guidelines are justified only when patient outcomes are likely to be improved and changes from previous versions should be summarized.

Organization, Clarity, and Consistency

Guidelines need to be completely self-contained, including complete definitions of target populations and treatments, clear and consistent recommendations on all relevant treatment strategies and treatment standards, brief summaries of research justifying recommendations (including references) and indicate guideline limitations. This required information should come directly from the evidence base, which will ensure accuracy and standardization. However, this systematic review has revealed that such fundamentals of good guideline organization were often missing. For instance, in 12 guidelines (35%), we identified at least one other separately published document was required to understand the nature of recommendations made.[32–34,36,40,43–48,53,55,56,62] On occasion, this information was not locatable.[39,43] In some guidelines, all references were omitted, making interpretation difficult.[23–26,30,57,63]

Moreover, most guidelines (93% on ACS and 88% on SCS) omitted complete definitions of the target populations for their recommendations. These definitions, with respect to guideline procedural endorsements, must match those of patients who had a procedural benefit over medical treatment alone in the relevant randomized trials.[72–78,80,81] Asymptomatic in these trials largely meant free of any ipsilateral clinically recognized stroke or TIA[1,72–75] and symptomatic meant a history of ipsilateral clinically recognized nondisabling stroke or TIA within the past 3 or 6 months.[76–78] However, it was only patients with life expectancy of >3 to 5 years and the following characteristics who clearly achieved a statistically significant CEA benefit in these trials.[72–78,80,81,92]

1. Asymptomatic men <75 to 79 years with >60% (NASCET) stenosis.
2. Symptomatic women with 70% to 99% (NASCET) stenosis randomized within 2 weeks of their last ischemic event.
3. Symptomatic men with 50% to 69% (NASCET) randomized within 2 weeks of their last ischemic event or
4. Symptomatic men with 70% to 99% stenosis (NASCET) and without near-occlusion randomized within 12 weeks or longer from their last ischemic event.

In NASCET and ECST the overall median delay from randomization to surgery was 6 days.[92]

These patient subgroups (if they also satisfy the average-CEA-risk trial entry criteria[32,72–78,80,81]) are easily defined and should be the target populations of guideline procedural endorsements.

However, this statement assumes that results of the randomized trials of medical treatment alone versus additional CEA are relevant to current routine practice and that CAS results matched those of CEA in later randomized trials (see below). Furthermore, in most guidelines, definitions of average and high-CEA-risk were omitted or procedural recommendations were not clearly distinguished, leaving readers unsure. Also usually omitted was explanation of the lack of randomized trial data backing a procedural approach over medical treatment alone for patients considered high-risk from CEA because of medical comorbidities. Current guidelines endorse

procedures for just about any patient with carotid stenosis, which is clearly not justified by the evidence base.

At least 11 different ranges in stenosis severity are used in current guidelines to indicate whether CEA or CAS are being recommended for patients with ACS, sometimes differing according to imaging technique, procedure recommended, or part of the guideline.[30,41,46,47,59] There is no scientific basis for such variability. Furthermore, ACS and SCS are parts of a disease spectrum and should be covered in a single guideline document, along with all relevant treatment options. However, to avoid confusion, recommendations for these 2 risk-disparate groups should never be mixed. A notable example of the consequences of combining these patient groups was endorsement of a 6% periprocedural complication rate for ACS.[43]

We found underinclusion of medical treatment recommendations. Specific recommendations on general medical treatment for ACS were included in only 19 of 28 guidelines (68%) and for peri-CEA or peri-CAS medical treatment in 14 (50%) and 9 (32%) cases, respectively. Inclusion was also incomplete for SCS with specific recommendations for general medical treatment found in 29 guidelines (88%) and for peri-CEA or peri-CAS medical treatment in 16 cases (48%), respectively. Furthermore, medical treatment recommendations were often separated from procedural recommendations and omitted from summaries. Summaries matter most because they are the most likely to be read. In addition, when medical treatment recommendations were included, they were usually incomplete.

Many examples of organizational inconsistencies leading to difficulty comprehending recommendations exist. These could be avoided by clearly distinguishing comments on the evidence base from recommendations, stating recommendations for a particular clinical scenario once (not in multiple places)[46,47] and including all procedural[33,36,52,62] and other recommendations in summaries, not just background text or referring to other guidelines. Furthermore, recommendations should be simple, using literal meanings, to avoid ambiguity. For example, should be considered does not mean should be done.

Recommendations and evidence evaluation should be consistent with any summarizing terminology. We found several examples where this did not occur with respect to procedures.[27,34,35,38,39,43–45,55,56,61] Improvement will come from simpler systems of qualifying terminology. We propose 3 categories to summarize the nature of recommendations to indicate a treatment should be provided, may be provided, or should not be provided, indicating any conditions or limitations to research settings.[93] We propose separate categories to summarize the nature (quality and current relevance) of the evidence used for recommendations (excellent, reasonable, or poor). Similar categorization is currently used in some guidelines.[38,41,48,59–62] However, such categorization needs to be based on much more than use of randomized trial results (see below) and should be internationally standardized.[94]

Gaps in current knowledge remain. These should be indicated as they relate to recommendations and treatment standards, preferably with suggestions on how to address them. There is also always room for improvement in patient outcomes and better ways to ensure that trial results are at least as good in routine practice. We found discussion of these issues rudimentary or omitted in most current guidelines on carotid stenosis management, particularly with respect to symptomatic patients.

Representation of the Evidence Base

Variability Across Guidelines

Others have reported significant procedural recommendation variability across prominent international guidelines on carotid stenosis, despite the same evidence base.[95] Such variability can be largely explained by errors or procedural bias.[94,96] For instance, the importance of administering any medical treatment, whether patients have a carotid procedure, was omitted in 32% of guidelines for ACS and 12% for SCS. Any specific peri-CEA or peri-CAS medical treatment recommendations were omitted in 50% and 68%, respectively, of ACS guidelines with somewhat better coverage for SCS.

There was also marked variability across guidelines in CAS recommendations. For instance, CAS was endorsed for average-CEA-risk patients with ACS in 17 of 27 applicable guidelines (63%) and for average-CEA-risk SCS in 19 of 33 (58%), whereas 8 of 27 (30%) and 9 of 33 (27%), respectively, specifically stated that CAS should not be used routinely. This reflects error or bias in scientific interpretation. Overall, CAS has been associated with approximately twice as many strokes or deaths as CEA.[7,97] Particularly vulnerable are those with symptoms within the previous week[98] (those most likely to benefit from CEA), women,[99,100] and those >70 years, whereas a statistically significant CAS benefit over CEA has not been demonstrated for those <70 years.[97,101]

Furthermore, this excess CAS risk of stroke or death is not compensated[97] by a higher 30-day periprocedural risk of clinically defined MI with CEA (seen in some trials[41]). In randomized trials of CEA versus CAS, where the number of both periprocedural outcomes were reported, overall strokes were 4.5× more common (250 versus 56) than MI,[7,79,82–86,94,102] whereas death from any cause was ≈1.5× more common with CAS (31 versus 20 deaths). Therefore, even in recent, rigorous randomized trials, CAS caused more stroke, death, and MI than CEA. Current scientific evidence demonstrates that CAS should not be represented as a similar alternative to CEA.[103] Furthermore, the excess CAS disability caused by strokes should not be confused with (or distracted by) other causes of disability as patients survive 1 to 5 years after a carotid procedure.[94,104]

Similarities Across Guidelines

Of more concern than guideline variability was what they have in common. Guideline procedural endorsements and standards for CEA and CAS were always ultimately derived from trials of CEA versus medical treatment alone in which patients were randomized 12 to 34 years ago.[72–78,92,105] These early trials also underpin the use of the results of randomized trials of CEA versus CAS and CAS registries in substantiating guideline recommendations.[79,82–89] However, substantial improvements in the stroke prevention efficacy of medical treatment have occurred over the past 2 to 3 decades.[2–6] These have not yet

affected guideline recommendations or procedural standards, except possibly for 1 case with respect to ACS.[52]

Ipsilateral stroke rates are now so low (≈0.5% per year)[3,106–109] in ACS patients given medical treatment alone that overall, CEA, or CAS are more likely to cause harm or be relatively safe but ineffective.[110] There is no current evidence that these procedures benefit any subgroup of patients with ACS. This serious deficiency was not portrayed in any contemporary guideline we identified, possibly with the exception of 1 case.[52] Also missing are inclusions of discoveries that transcranial embolus detection,[8] degree of stenosis,[9] plaque echolucency,[10] and asymptomatic progression[11] are not powerful enough individually to identify asymptomatic patients likely to benefit from carotid procedures (even in the context of relatively less effective historical medical treatment). Combinations of risk markers offer the best hope of clinically meaningful risk stratification.[9] Also missing (except in 1 case)[55,56] are the implications of improved outcomes and better procedural standards in patients with SCS because of improvements in medical treatment.[7] Missing are observations of the reduced stroke or death risk associated with CEA in patients with ACS and SCS.[12–14,110] All guidelines we identified contained recommendations based only on outcomes of patients randomized 12 to 34 years ago, rather than better outcomes measured more recently in routine practice or other trials.[2–6,12–14]

In addition, entrenched across guidelines was strong bias in what constitutes quality and relevant evidence in making routine practice treatment decisions. Too much confidence is placed in randomization alone, rather than whether treatments compared are contemporary, all reasonable treatments are compared, whether randomized trial methods and results are replicated in routine practice, or whether a randomized trial is the best way to answer a particular clinical question.[94,96,111] For instance, if it is found from multiple, reliable, and independent sources that stroke rates are sufficiently low with medical treatment alone, randomized trials of CEA or CAS become unnecessary or even unethical.

Conclusions

This systematic review of contemporary carotid stenosis management guidelines has documented weaknesses in accessibility, organization, clarity, and consistency of recommendations and weaknesses in representation of available scientific evidence. All current guideline procedural endorsements of CEA and CAS are still based only on trials of CEA versus medical treatment alone in which patients were randomized 12 to 34 years ago.[72–78,92,105] Furthermore, there was underutilization of evidence on medical treatment, advances in medical treatment, stroke risk stratification for ACS, and evidence from nonrandomized trials (including routine practice). There was often under-representation of the hazards of CAS. These weaknesses encourage the use of costly carotid procedures,[112,113] which, for many patients, are currently more likely to harm than help. There is a need for new guidelines that address these problems in the interests of patients and health professionals. There is a need for improved access, standardization, and accurate representation of all available research results[114] (including reevaluation of how randomized and nonrandomized trial evidence is handled) and fair representation of all relevant specialties, independent researchers, and patient advocate groups.

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