Transatlantic Differences in Management of Carotid Stenosis: BRIDGing the Gap in Stroke Management (BRIDGE) Project

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Abstract

Background and Purpose: Management of carotid stenosis remains controversial despite several trials evaluating carotid endarterectomy (CEA) and carotid angioplasty/stenting (CAS). We compared attitudes in the management of carotid stenosis between selected experts within Europe and North America. **Methods:** A 3-phase Delphi survey was e-mailed to select stroke experts from Europe (n = 390) and North America (n = 289). Those completing the initial survey were shown all responses after each survey round. Consensus was defined as $\geq 80\%$ agreement. **Results:** For phases 1, 2, and 3, response rates were 32%, 62%, and 73%, respectively. Overall, 100 (15%) of 679 participated in all 3 phases, 19% Europeans versus 9% North Americans ($P = .0007$). The European group reached consensus in 6 of 15 statements; The North American group reached consensus in 4 of 15. Ninety percentage of Europeans versus 70% of North Americans ($P = .017$) stated CEA is superior to CAS for symptomatic carotid stenosis. This difference was not significant in the final model (adjusted odds ratio: 3.72 [95% confidence interval: 0.95-14.5]). Sixty-nine percentage of North Americans agreed there is a stronger indication for CAS over CEA in patients younger than 65 years for symptomatic carotid stenosis, whereas 55% of Europeans ($P = .023$) disagreed. For asymptomatic carotid stenosis, when asked how likely they would recommend CAS, 62% North Americans said “sometimes” versus 60% of Europeans said “never” ($P = .06$). **Conclusion:** The majority of North American and European respondents did not consider the 2 procedures equivalent and seemed to indicate that CEA was preferred for the management of carotid stenosis. These findings need to be further explored to help establish evidence-based guidelines.

Keywords

cerebrovascular disorders, carotid artery diseases, carotid stenosis, stroke

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Introduction

Extracranial internal carotid artery atherosclerosis accounts for approximately 20% of ischemic strokes.¹ As a potentially preventable cause of stroke, its detection and management are critical. Several European and North American randomized clinical trials²⁻⁹ have compared carotid angioplasty and stenting (CAS) as an alternative to carotid endarterectomy (CEA) for both symptomatic and asymptomatic carotid stenosis, though their results and interpretation varied.¹⁰⁻¹¹

Several available trial results are viewed controversially by leading experts, and there is an ongoing international discussion.¹²⁻¹⁶ Many contributing factors make consensus elusive¹⁷; these include:

1. Differences in clinical trial methodologies in countries where the trials were conducted may have led to different results and interpretation.
2. Several international societies and associations¹⁸⁻²⁴ have published guidelines for the management of patients with carotid stenosis. Although these recommendations are based on the same randomized trials, differences in interpretation of available knowledge have often led to different, potentially conflicting recommendations.
3. Multiple medical specialists (eg, primary care physicians, interventional radiologists, cardiologists, neurologists, vascular surgeons, and neurosurgeons) are involved in treating patients with carotid stenosis, each with their own understanding and interpretation of the trials and approach with their inherent beliefs and biases on the participant.

Differences in the interpretation of clinical trial results and guidelines for the management of carotid stenosis in clinical practice have been documented in earlier survey studies.²⁵⁻²⁷

A better understanding of differences in carotid stenosis management between European and North American physicians may help to identify areas where a lack of consensus exists and may ultimately inform the development of future clinical trials.

The objective of this study was to provide an informative and comparative view of the clinical practice attitudes of North American and European physicians involved in the care of patients with carotid stenosis.

Materials and Methods

Development of the Survey Instrument

A structured survey questionnaire was developed to prompt the panelists to rate and rank a series of carotid stenosis management propositions. The survey was designed based on key factors in the management of carotid stenosis that emerged from the main carotid stenosis clinical trials. The survey was developed through multiple iterations of a group of both European and North American stroke experts, including principal

investigators of the major carotid stenosis clinical trials. The survey consisted of demographic questions followed by 18 questions addressing specific practice management. We used a 5-choice Likert-type scale²⁸ for the first 15 questions and a ranking scale (1 = most important factor affecting treatment decision up to 5 = least important factor affecting treatment decision) for the last 3 questions. We specifically tailored the survey tool to be completed in approximately 10 minutes in order to enhance response rate.

This study was ruled exempt by the institutional review board at SUNY Downstate Medical Center and a waiver of informed consent was granted (IRB#11-106).

Survey Population

With the aim to target a cohort representative of experts from North America and Europe directly involved in the management of patients with stroke, we e-mailed all members (n = 390) of the European Stroke Organisation (<http://www.eso-stroke.org/>) in the year 2011 for whom an e-mail was provided and North American vascular neurologists (n = 289) independently identified at the University of Texas at Houston Stroke Program for previous research purposes.²⁹ The list included identified academic stroke physicians at university hospitals across the United States. E-mails were collected from websites of university hospitals, directors of academic stroke programs, colleagues in the stroke field, and neurologists in charge of specific geographic consortia of stroke physicians.²⁹

The initial e-mail contained an introductory statement explaining the research purpose and the methods of the study, and that the surveys were to be conducted anonymously. Only basic demographic information was requested. There was no financial incentive offered. A weblink allowed participants to opt out of the study and to prevent any further correspondence related to the project from the study team.

Delphi Procedure

We implemented the Delphi method,³⁰ which is an anonymous, iterative tool to collect expert opinions via a series of responses and analysis techniques that include a feedback mechanism. Based on previous studies,^{31,32} we chose to survey experts over 3 rounds to acquire consensus for each group.

At each round, the questionnaire was administered to the panelists by e-mail using a web-based survey tool, *SurveyMonkey* (<https://www.surveymonkey.com/>). As per the Delphi method,³⁰ results of phase 1 were analyzed and tabulated into summary charts, graphically represented, and incorporated in phase 2 to inform respondents and to develop consensus. The same procedure was applied in phase 3.

Statistics and Data Analysis

Descriptive analysis was conducted after each survey iteration. Panelists were provided with the median score,

interquartile range of the group, and their own rating for each question from the previous questionnaire when completing phase 2 and phase 3. Fleiss κ coefficients were used to quantify agreement between panelists. General and group-specific consensus were defined a priori to be $\geq 80\%$ agreement in the response choice. χ^2 was used to determine differences between groups; P was set at $< .05$ for significance.

Logistic regression modeling was used to assess differences between regions in terms of responses whose association with region was significant at the .05 level in Table 1, controlling for age-group, main specialty and whether the respondent was affiliated with a teaching hospital. The Hosmer-Lemeshow test of goodness-of-fit data to model was applied. Adjusted odds ratios (AORs) with 95% confidence intervals (CIs) are reported. Data analyses were performed with SPSS (version 20.0; IBM, Armonk, New York) and SAS 9.3 (SAS Institute, Cary, North Carolina) software.

Results

Response Rate Across All Phases

From November 2011 to July 2012, a 3-round, e-mail Delphi survey was initially sent to a sample of 679 participants (390 Europeans and 289 North Americans). Response rates were as follows: phase 1, 218 of 679 (32% responded, 41 partial/177 complete, 11 [1.6%] opted out); phase 2 (April 2012), 136 (62%) of 218 responded (4 partial/132 complete); and phase 3 (July 2012), 100 (73%) of 136 responded (3 partial/97 complete). Overall, 100 (15%) of 679 participated in all 3 Delphi phases 19% of all Europeans versus 9% of all North Americans ($\chi^2 = 11.62$, $P = .0007$) surveyed.

Characteristics of phase 3 respondents are reported in Table 2. There were differences in age, main specialty, and a trend for differences in the type of hospital practice setting. These differences/trends were included in the final logistic regression model. The main results (overall and by region) of the phase 3 survey are reported in detail in Tables 1 and 3.

Consensus

In the final round, general consensus was achieved in 4 (22%) of 18 statements. Europeans reached consensus in 4 (22%) of 18 statements, whereas North Americans reached consensus in 2 (11%) of 18. Achievement of general and group-specific consensus is indicated in dark gray and in light gray respectively, in Tables 1 and 3.

The majority of European and North American respondents (90% vs 70%, respectively, $\chi^2 = 8.09$, $df = 2$, $P = .017$) disagreed with the statement "CAS and CEA are equivalent treatment procedures for symptomatic carotid stenosis," stating that CEA is a superior treatment. The difference was no longer significant in the final model (AOR: 3.72 [95% CI: 0.95-14.5]). European consensus was reached in phase 2 and

maintained in phase 3. No consensus was reached within the North American group.

When considering primary outcome "only stroke within 30 days of treatment," 94% of Europeans versus 82% North Americans ($\chi^2 = 8.47$, $df = 3$; $P = .037$) disagreed that CAS and CEA are equivalent treatment procedures for symptomatic carotid stenosis, and stated that CEA is a superior treatment. This difference remained significant in the final model (AOR: 12.3 [95% CI: 1.57-96.0]). General and group-specific consensus were reached.

When considering primary outcomes "stroke and death within 30 days of treatment," 96% of European versus 74% of North American respondents ($\chi^2 = 12.18$, $df = 3$; $P = .007$) disagreed that CAS and CEA are equivalent treatment procedures for symptomatic carotid stenosis and stated that CEA is a superior treatment (AOR: 8.87 [95% CI: 1.56-49.5]).

Almost two-thirds of North Americans agreed that "there is a stronger indication for CAS in patients older than 65 years old with symptomatic carotid stenosis compared to CEA." Conversely more than half of Europeans disagreed with the statement ($\chi^2 = 11.39$, $df = 4$, $P = .023$). This difference did not remain significant in the final model (AOR: 3.44 [95% CI: 0.93-12.7]).

The majority of respondents (90% of North Americans vs all Europeans) agreed that "there is a stronger indication for CEA in patients older than 65 years old with symptomatic carotid stenosis compared to CAS." General and both groups-specific consensus were reached in all 3 phases.

The majority of both groups agreed "in general, the outcome of ischemic stroke is of greater concern compared to MI in the treatment of symptomatic carotid stenosis." General consensus was reached in phase 2 and maintained in phase 3.

When asked how likely they would be to recommend CEA for asymptomatic carotid stenosis, the vast majority of both groups selected "sometimes." Conversely, when asked how likely they would be to recommend CAS for asymptomatic carotid stenosis, most of the North Americans said "sometimes" while most of the European respondents said "never."

The level of experience of the operator was rated as "the most important" or at least "a very important variable" by the vast majority of respondents from both groups in the decision to refer a patient for CAS and for CEA, respectively. General and both groups-specific consensus were reached in all 3 phases.

"CT angiography" was selected as the imaging technique most often used to grade the stenosis by more than half of the North Americans, whereas "carotid ultrasound" was the preferred imaging technique for more than half of the Europeans ($\chi^2 = 13.17$, $df = 3$, $P = .004$). The difference between groups remained significant in the final model (AOR: 0.21 [95% CI: 0.07-0.66]).

Table 3 details the variables affecting treatment decision for symptomatic carotid stenosis. "Vessel morphology (ie, level of bifurcation and tortuosity)," "patient willingness,"

Table 1. Phase-3 Delphi Survey Main Results, Overall, and by Region (North Americans vs Europeans).^a

Statement/Question	Answers	Overall	North Americans	Europeans	P
1. "In general, CAS and CEA are equivalent treatment procedures for symptomatic carotid stenosis"	Strongly agree Somewhat agree Neutral Disagree, CEA is a superior treatment Disagree CAS is a superior treatment	N = 98 0 (0%) 11 (11.2%) 4 (4.1%) 83 (84.7%) 0 (0%)	N = 27 0 (0%) 7 (25.9%) 1 (3.7%) 19 (70.4%) 0 (0%)	N = 71 0 (0%) 4 (5.6%) 3 (4.2%) 64 (90.1%) 0 (0%)	.017
2. "CAS and CEA are equivalent treatment procedures for symptomatic carotid stenosis when considering only stroke within 30 days of treatment as the primary outcome"	Strongly agree Somewhat agree Neutral Disagree, CEA is a superior treatment Disagree CAS is a superior treatment	N = 99 2 (2.0%) 6 (6.1%) 1 (1.0%) 90 (90.9%) 0 (0%)	N = 27 2 (7.4%) 2 (7.4%) 1 (3.7%) 22 (81.5%) 0 (0%)	N = 72 0 (0.0%) 4 (5.6%) 0 (0.0%) 68 (94.4%) 0 (0%)	.037
3. "CAS and CEA are equivalent treatment procedures for symptomatic carotid stenosis when considering stroke and death within 30 days of treatment as the primary outcome"	Strongly agree Somewhat agree Neutral Disagree, CEA is a superior treatment Disagree, CAS is a superior treatment	N = 99 2 (2.0%) 7 (7.1%) 1 (1.0%) 89 (89.9%) 0 (0%)	N = 27 2 (7.4%) 4 (14.8%) 1 (3.7%) 20 (74.1%) 0 (0%)	N = 72 0 (0.0%) 3 (4.2%) 0 (0.0%) 69 (95.8%) 0 (0%)	.007
4. "There is a stronger indication for CAS in younger patients (<65 years) with symptomatic carotid stenosis compared to CEA"	Strongly agree Somewhat agree Neutral Somewhat disagree Strongly disagree	N = 96 3 (3.1%) 42 (43.8%) 7 (7.3%) 33 (34.4%) 11 (11.5%)	N = 26 2 (7.7%) 16 (61.5%) 3 (11.5%) 4 (15.4%) 1 (3.8%)	N = 70 1 (1.4%) 26 (37.1%) 4 (5.7%) 29 (41.4%) 10 (14.3%)	.023
5. There is a stronger indication for CEA in older patients (>65 years) with symptomatic carotid stenosis compared to CAS.	Strongly agree Somewhat agree Neutral Somewhat disagree Strongly disagree	N = 97 63 (64.9%) 27 (27.8%) 2 (2.1%) 1 (1.0%) 4 (4.1%)	N = 26 14 (53.8%) 12 (46.2%) 0 (0.0%) 0 (0.0%) 0 (0.0%)	N = 71 49 (69.0%) 15 (21.1%) 2 (2.8%) 1 (1.4%) 4 (5.6%)	.111
6. "Consistent findings from subgroup analyses of different RCTs (and meta-analysis of individual patient data) are generalizable"	Strongly agree Somewhat agree Neutral Somewhat disagree Strongly disagree	N = 97 4 (4.1%) 73 (75.3%) 2 (2.1%) 14 (14.4%) 4 (4.1%)	N = 26 1 (3.8%) 20 (76.9%) 1 (3.8%) 2 (7.7%) 2 (7.7%)	N = 71 3 (4.2%) 53 (74.6%) 1 (1.4%) 12 (16.9%) 2 (2.8%)	.595
7. "Results from sub-group analyses of single RCTs are generalizable"	Strongly agree Somewhat agree Neutral Somewhat disagree Strongly disagree	N = 97 0 (0%) 6 (6.2%) 2 (2.1%) 40 (41.2%) 49 (50.5%)	N = 26 0 (0%) 2 (7.7%) 1 (3.8%) 9 (34.6%) 14 (53.8%)	N = 7 0 (0%) 14 (5.6%) 1 (1.4%) 31 (43.7%) 35 (49.3%)	.769
8. "In general, the outcome of ischemic stroke is of greater concern compared to MI in the treatment of symptomatic carotid stenosis"	Strongly agree Somewhat agree Neutral, they are of equal concern Somewhat disagree, MI may be of greater concern	N = 97 52 (53.6%) 33 (34.0%) 10 (10.3%) 2 (2.1%)	N = 26 19 (73.1%) 4 (15.4%) 2 (7.7%) 1 (3.8%)	N = 71 33 (46.5%) 29 (40.8%) 8 (11.3%) 1 (1.4%)	.074
9. The risk of periprocedural stroke is decreased by the use of protection devices during the CAS procedure	Strongly agree Somewhat agree Neutral Somewhat disagree Strongly disagree	N = 97 7 (7.2%) 32 (33.0%) 17 (17.5%) 29 (29.9%) 12 (12.4%)	N = 26 3 (11.5%) 11 (42.3%) 6 (23.1%) 4 (15.4%) 2 (7.7%)	N = 71 4 (5.6%) 21 (29.6%) 11 (15.5%) 25 (35.2%) 10 (14.1%)	.280

(continued)

Table 1. (continued)

Statement/Question	Answers	Overall	North Americans	Europeans	P
10. "Differences in trial protocol (eg, outcome measures, population, inclusion/exclusion criteria) in the currently published RCTs comparing CAS and CEA prevent generalizability of the results"	Strongly agree	N = 97 5 (5.2%)	N = 26 0 (0.0%)	N = 71 5 (7.0%)	.361
	Somewhat agree	54 (55.7%)	15 (57.7%)	39 (54.9%)	
	Neutral	7 (7.2%)	3 (11.5%)	4 (5.6%)	
	Somewhat disagree	27 (27.8%)	8 (30.8%)	19 (26.8%)	
	Strongly disagree	4 (4.1%)	0 (0.0%)	4 (5.6%)	
11. "How important is the level of experience of interventionalist in your decision to refer a patient for CAS?"	Most important	N = 96 45 (46.9%)	N = 26 15 (57.7%)	N = 70 30 (42.9%)	.339
	Very important	49 (51.0%)	11 (42.3%)	38 (54.3%)	
	Somewhat important	2 (2.1%)	0 (0.0%)	2 (2.9%)	
12. "How important is the level of experience of the surgeon in your decision to refer a patient for CEA?"	Most important	N = 96 31 (32.3%)	N = 26 13 (50.0%)	N = 70 18 (25.7%)	.067
	Very important	62 (64.6%)	12 (46.2%)	50 (71.4%)	
	Somewhat important	3 (3.1%)	1 (3.8%)	2 (2.9%)	
13. "Which imaging technique do you use most often to grade the stenosis?"	Carotid Ultrasound	N = 96 53 (55.2%)	N = 26 7 (26.9%)	N = 71 46 (65.7%)	.004
	Carotid MRA	5 (5.2%)	2 (7.7%)	3 (4.3%)	
	Carotid CTA	37 (38.5%)	16 (61.5%)	21 (30.0)	
	Other	1 (1.0%)	1 (3.8%)	0 (0.0%)	
14. "How likely are you to recommend CEA for asymptomatic carotid stenosis?"	Usually	N = 95 3 (3.2%)	N = 25 0 (0.0%)	N = 70 3 (4.3%)	.483
	Sometimes	77 (81.1%)	20 (80.0%)	57 (81.4%)	
	Never	15 (15.8%)	5 (20.0%)	10 (14.3%)	
15. "How likely are you to recommend CAS for asymptomatic carotid stenosis?"	Usually	N = 96 0 (0%)	N = 26 0 (0%)	N = 70 0 (0%)	.060
	Sometimes	44 (45.8%)	16 (61.5%)	28 (40.0%)	
	Never	52 (54.2%)	10 (38.5%)	42 (60.0%)	

Abbreviations: CAS, carotid artery angioplasty and stenting; CEA, carotid artery endarterectomy; CTA, computed tomography angiography; MRA, magnetic resonance imaging angiography; RCTs, randomized clinical trials.

^aGeneral and group-specific (Europeans/North Americans) consensuses were defined a priori to be $\geq 80\%$ agreement in the response choice; achievement of general and group-specific (Europeans and North Americans) consensus for each statement/question is indicated in dark gray and in light gray, respectively.

and "age" were ranked by both groups as "the most important" variables affecting treatment decision for symptomatic carotid stenosis.

Discussion

The majority of both European and North American groups did not consider the 2 treatments for symptomatic carotid stenosis to be equivalent and indicated that CEA was indeed preferred. This would suggest a need to further study the topic with scrupulous trials in the modern era to help establish evidence-based guidelines.³³

Although in the univariate analysis, the disagreement about equivalence of CEA and CAS was significantly greater in the European group, the difference did not persist in the final model. However, we found different clinical practice attitudes toward the management of both symptomatic and asymptomatic carotid stenosis management between the 2 groups. Specifically, North Americans were more likely than Europeans to suggest CAS for patients older than 65 years. Europeans were more likely to never recommend CAS for asymptomatic carotid stenosis compared to North Americans. This supports the controversy over perceived benefits of CAS

for asymptomatic carotid stenosis. Europeans were twice as likely to obtain consensus across the survey compared to the North Americans suggesting greater variability in the latter views and clinical decisions.

In general, European respondents demonstrated a consistently stronger negative attitude toward CAS compared to North Americans. Although North Americans seemed to consider CEA superior to CAS in general, Europeans seemed to consider CEA superior to CAS only for 2 specific end points: "only stroke within 30 days of treatment" and "stroke and death within 30 days of treatment." These differences may be based, in part, on weighing the relative importance of the various/combined end points in a given trial. Most stroke experts may consider stroke a more important end point for a carotid disease intervention trial than MI. Long-term follow-up data from the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST),³⁴ the Endarterectomy Versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis trial,³⁵ and the International Carotid Stenting Study trial³⁶ have shown that beyond the procedural period both procedures are equivalent in terms of prevention of ipsilateral strokes and risk of severe restenosis. These results were not published at the time of our survey.

Table 2. Characteristics of Phase 3 Respondents.

Characteristics	Total, N = 100	North Americans, N = 27 (27%)	Europeans ^a N = 73 (73%)	P
Age				
<45 years	49 (49%)	6 (22.2%)	43 (58.9%)	.001
45-65 years	46 (46%)	17 (63.0%)	29 (39.7%)	
>65 years	5 (5%)	4 (14.8%)	1 (1.4%)	
Sex				
Male	76 (76%)	20 (74.1%)	56 (76.7%)	.784
Female	34 (34%)	7 (25.9%)	17 (23.3%)	
Hospital				
Hospital for standard patient care	1 (1%)	0 (0.0%)	1 (1.4%)	.071
Hospital with specialized medical services	10 (10%)	0 (0.0%)	10 (13.7%)	
Tertiary care hospital (full service)	30 (30%)	6 (22.2%)	24 (34.9%)	
Teaching hospital	59 (59%)	21 (77.8%)	38 (52.1%)	
Main specialty				
Neurologist	32 (32%)	3 (11.1%)	29 (39.7%)	.007
Vascular neurologist	5 (5%)	24 (88.9%)	35 (47.9%)	
"Care of the elderly" physician	4 (4%)	0 (0.0%)	4 (5.5%)	
Internist or general physician	2 (2%)	0 (0.0%)	2 (2.7%)	
Other	3 (3%)	0 (0.0%)	3 (4.1%)	
Number of cases of carotid stenosis managed per month				
<1	7 (7%)	3 (11.1%)	4 (5.5%)	.658
1-4	31 (31%)	10 (37.0%)	21 (28.8%)	
5-8	38 (38%)	9 (33.3%)	29 (39.7%)	
9-12	8 (8%)	1 (3.7%)	7 (9.6%)	
>12	16 (16%)	4 (14.8%)	12 (16.4%)	

^aFive members of the European Stroke Organisation identified their place of origin and practice outside Europe (1 in Israel, 1 in Turkey, 1 in Indonesia, 1 India, and 1 in Brazil).

There are clear differences in the diagnostic imaging approach to carotid stenosis with less expensive, less invasive carotid ultrasound techniques preferred over magnetic resonance imaging angiography and computed tomography angiography by the European group. Specific reasons for this carotid imaging preference were beyond the scope of this study and were not explored.

A stepwise diagnostic evaluation would usually entail an initial carotid ultrasound for screening purposes followed by more complex and expensive imaging techniques to confirm and better characterize stenosis and vessel anatomy and to guide the more appropriate treatment strategy. The lack of consensus between groups in the initial imaging modality may need further country-specific cost-effective analyses comparing different imaging techniques to guide clinicians to a more efficient use of available resources.

Although the degree of stenosis is a major determinant of benefit from revascularization therapies, there are other clinical characteristics that influence the risks and benefits of surgery. Subgroup analyses of pooled data from the large randomized clinical trials showed the greatest benefit from CEA in men, patients aged 75 years and older, and patients randomized within 2 weeks after their last ischemic event.^{37,38}

In our survey, "age" was ranked as the most important treatment decision variable between CEA and CAS for the majority of North American and European groups over "gender," "concomitant cardiac disease," "concomitant

diabetes," and "time between symptoms and treatment." The age $\times$ treatment arm interaction from CREST⁹ may have influenced this ranking. However, there was no general (80%) consensus or country-specific consensus for any of these variables including age. Further studies could determine factors influencing decision-making. Validated, multifactorial risk stratification strategies integrating multiple high-risk features (imaging and clinical features) in a manner that is relatively simple to implement and generalizable across a wide range of practice settings are needed.

The overwhelming majority of respondents from both groups would recommend CEA "sometimes" for asymptomatic carotid stenosis; however, only North Americans would also recommend CAS "sometimes." This finding is in contrast with the current evidence of treatment strategies for asymptomatic carotid disease. In fact, in the case of asymptomatic carotid disease while trials until now have suggested some benefit from CEA in selected patients with a high risk of stroke, there is no conclusive evidence-based indication of CAS.³⁹

The CREST-2 trial⁴⁰ in North America and similarly the European Carotid Surgery Trial 2⁴¹ in Europe are ongoing multicenter, randomized-controlled trials evaluating the benefit of carotid revascularization against intensive medical management that includes antiplatelet drugs, antihypertensive agents and statins, targeted blood pressure treatment, and behavioral/lifestyle modification. Prior to these trials, carotid

Table 3. Variables Affecting Treatment Decision for Symptomatic Carotid Stenosis.^a

Variables	Answers	Total	North Americans	Europeans	P
Please number the following factors from 1 to 5 in the order of importance in your treatment decision in symptomatic carotid stenosis:	Plaque characteristic	N = 93	N = 25	N = 68	.381
	1	15 (16.1%)	4 (16.0%)	11 (16.2%)	
	2	43 (46.2%)	9 (36.0%)	34 (50.0%)	
	3	20 (21.5%)	7 (28.0%)	13 (19.1%)	
	4	1 (7.5%)	6 (4.0%)	7 (8.8%)	
Vessel morphology (ie, level of bifurcation and tortuosity)	5	8 (8.6%)	4 (16.0%)	4 (5.9%)	
		N = 93	N = 25	N = 68	.922
	1	65 (69.9%)	18 (72.0%)	47 (69.1%)	
	2	20 (21.5%)	5 (20.0%)	15 (22.1%)	
	3	6 (6.5%)	2 (8.0%)	4 (5.9%)	
Risk of nerve injury and groin hematoma	4	1 (1.1%)	0 (0.0%)	1 (1.5%)	
	5	1 (1.1%)	0 (0.0%)	1 (1.5%)	
		N = 93	N = 25	N = 68	.391
	1	4 (4.3%)	0 (0.0%)	4 (5.9%)	
	2	6 (6.5%)	3 (12.0%)	3 (4.4%)	
Risk of silent infarcts	3	6 (6.5%)	2 (8.0%)	4 (5.9%)	
	4	28 (30.1%)	9 (36.0%)	19 (27.9%)	
	5	49 (52.7%)	11 (44.0%)	38 (55.9%)	
		N = 93	N = 25	N = 68	.203
	1	2 (2.2%)	1 (4.0%)	1 (1.5%)	
Risk of restenosis	2	16 (17.2%)	6 (24.0%)	10 (14.7%)	
	3	30 (32.3%)	9 (36.0%)	21 (30.9%)	
	4	28 (30.1%)	3 (12.0%)	25 (36.8%)	
	5	17 (18.3%)	6 (24.0%)	11 (16.2%)	
		N = 93	N = 25	N = 68	.118
	1	9 (9.7%)	2 (8.0%)	7 (10.3%)	
	2	12 (12.9%)	2 (8.0%)	10 (14.7%)	
	3	30 (32.3%)	5 (20.0%)	25 (36.8%)	
	4	28 (30.1%)	12 (48.0%)	16 (23.5%)	
	5	13 (14.0%)	3 (12.0%)	10 (14.7%)	
Please number the following factors from 1 to 3 in the order of importance in your treatment decision in symptomatic carotid stenosis:	6	1 (1.1%)	1 (4.0%)	0 (0.0%)	
		N = 92	N = 25	N = 67	.349
	1	2 (2.2%)	0 (0.0%)	2 (3.0%)	
	2	8 (8.7%)	4 (16.0%)	4 (6.0%)	
	3	81 (88.0%)	21 (84.0%)	60 (89.6%)	
Patient willingness	4	0 (0.0%)	0 (0.0%)	0 (0.0%)	
	5	1 (1.1%)	0 (0.0%)	1 (1.5%)	
		N = 92	N = 25	N = 67	.088
	1	79 (85.9%)	24 (96.0%)	55 (82.1%)	
	2	13 (14.1%)	1 (4.0%)	12 (17.9%)	
Cost of treatment	3	0 (0.0%)	0 (0.0%)	0 (0.0%)	
	4	0 (0.0%)	0 (0.0%)	0 (0.0%)	
	5	0 (0.0%)	0 (0.0%)	0 (0.0%)	
		N = 97	N = 25	N = 67	.325
	1	12 (13.0%)	1 (4.0%)	11 (16.4%)	
	2	69 (75.0%)	20 (80.0%)	49 (73.1%)	
	3	10 (10.9%)	4 (16.0%)	6 (9.0%)	
	4	0 (0.0%)	0 (0.0%)	0 (0.0%)	
	5	1 (1.1%)	0 (0.0%)	1 (1.5%)	

(continued)

Table 3. (continued)

Variables	Answers	Total	North Americans	Europeans	P
Please number the following factors from 1 to 5 in the order of importance in your treatment decision in symptomatic carotid stenosis:		N = 94	N = 24	N = 70	.584
	1	3 (3.2%)	0 (0.0%)	3 (4.3%)	
	2	13 (13.8%)	3 (12.5%)	10 (14.3%)	
	3	37 (39.4%) ^a	12 (50.0%)	25 (35.7%)	
	4	23 (24.5%)	4 (16.7%)	19 (27.1%)	
	5	18 (20.8%)	5 (18.6%)	13 (19.1%)	
Age		N = 94	N = 24	N = 70	.691
	1	56 (59.6%)	15 (62.5%)	41 (58.6%)	
	2	22 (23.4%)	6 (25.0%)	16 (22.9%)	
	3	10 (10.6%)	3 (12.5%)	7 (10.0%)	
	4	5 (5.3%)	0 (0.0%)	5 (7.1%)	
	5	1 (1.1%)	0 (0.0%)	1 (1.4%)	
Concomitant cardiac disease		N = 94	N = 24	N = 70	.456
	1	19 (20.2%)	7 (29.2%)	12 (17.1%)	
	2	48 (51.1%)	11 (45.8%)	37 (52.9%)	
	3	15 (16.0%)	2 (8.3%)	13 (18.6%)	
	4	11 (11.7%)	4 (16.7%)	7 (10.0%)	
	5	1 (1.1%)	0 (0.0%)	1 (1.4%)	
Concomitant diabetes		N = 94	N = 24	N = 70	.462
	1	1 (1.1%)	0 (0.0%)	1 (1.4%)	
	2	8 (8.5%)	1 (4.2%)	7 (10.0%)	
	3	21 (22.3%)	5 (20.8%)	16 (22.9%)	
	4	41 (43.6%)	9 (37.5%)	32 (45.7%)	
	5	23 (24.5%)	9 (37.5%)	14 (20.0%)	
Time between symptoms and treatment		N = 94	N = 24	N = 70	.330
	1	13 (13.8%)	2 (8.3%)	11 (15.7%)	
	2	7 (7.4%)	3 (12.5%)	4 (5.7%)	
	3	9 (9.6%)	2 (8.3%)	7 (10.0%)	
	4	17 (18.1%)	7 (29.2%)	10 (14.3%)	
	5	48 (51.1%)	10 (41.7%)	38 (54.3%)	

^aAnswers for ranking scale: 1 = most important factor affecting treatment decision and 5 = least important factor affecting treatment decision (except a 6 in one case), with 2 through 4 rankings as intermediate.

revascularization has never been compared to optimal, modern era medical therapy—a major reason, we believe, for the need for further trials and likely, based on the results, revised guidelines.

The vast majority (greater than 70%) of both North American and European panelists thought that vessel morphology, risk of nerve injury and groin hematoma, patient willingness, cost of treatment, age, concomitant cardiac disease, level of carotid bifurcation, vessel tortuosity, and time from symptoms and treatment would influence their decision of CEA versus CAS. If these factors affect the treatment decision, all or some combination of these factors may lead both groups of respondents to recommend CAS over CEA, even in some asymptomatic patients. These factors could also potentially explain group differences in approach to applying the trial results to their patients. As we did not specifically ask how each of these factors affected their treatment decision for asymptomatic

carotid stenosis, we cannot draw further conclusions (see also limitations section).

Limitations

Several limitations of this study must be acknowledged. The overall response rate was low. Specifically, only 15% of the surveyed population participated in all 3 Delphi phases. This low response rate increases the risk of nonresponse bias. Low response rate likely results in a selection bias and affects internal validity.

Our sample may not be entirely reflective of the population of physicians involved in the management of asymptomatic or symptomatic carotid stenosis or both. Respondents consisted mainly of selected neurologists and vascular neurologists; however, physicians from other specialties may be involved in managing carotid stenosis (ie, vascular surgeons,

neurosurgeons, interventional radiologists, and cardiologists). They were not represented in our surveys, potentially limiting the generalizability of our results. The lack of sampling of other specialties affects external validity. Also, respondents' beliefs about their practices may not reflect their actual practices.

This survey was conducted in 2011 and so may not be a reflection of current practice. In the last few years, long-term follow-up data from several randomized clinical trials evaluating CAS versus CEA have been published.^{34-36,42-43} Different meta-analyses⁴⁴⁻⁴⁶ of these and prior trials found CEA to be superior to CAS for short- and long-term outcomes. Particularly, CEA was associated with a higher risk of periprocedural myocardial infarction while the risk of long-term overall stroke was significantly higher with CAS and was mostly attributed to periprocedural minor stroke. These data suggest that CEA should be offered as the first choice for both symptomatic and asymptomatic carotid stenosis at present. However, given improvements in effective medical therapy for the prevention of atherosclerotic cardiovascular and cerebrovascular disease, in particular lipid-lowering medications along with lifestyle and diet interventions, there is renewed uncertainty as to whether carotid interventions still provide meaningful net reductions in stroke risk in patients with carotid stenosis. The ongoing CREST-2 clinical trial will be addressing this specific issue.⁴⁰

In our survey, there were significant differences in the respondents' age (under 45 vs older than 45 years) and their self-identified main specialty. Europeans were significantly younger and more frequently self-identified as neurologists. In our final model, we accounted for these differences.

Other factors potentially influential in physician treatment decision-making include physician knowledge and interpretation of the trials and clinical guidelines and their implementation in their particular practice, personal experiences with the effectiveness and safety/adverse events from the procedures, values and beliefs, and individual patient characteristics (ie, age, gender, comorbidities). Biases, beliefs, systems, and uncertainty have been shown to affect acute stroke decision-making.^{47,48} Therefore, physician decision-making is complex, certainly multifactorial, and deserves to be further studied. In the absence of randomized clinical trial evidence, decision-making still depends upon knowledge of physiology and experimental medicine, interpreted in light of clinician's experiences and values.

On the other hand, this study, despite its limitations, and others^{47,48} have found that evidence from randomized clinical trials does not eliminate the interpretive aspect of physician decision-making. Although randomized clinical trials provide population-based evidence they are not necessarily tailored to the unique scenario and outcome of individual patients.^{47,48}

In the light of these considerations, risk-benefit assessment for carotid revascularization while guided by best medical evidence (multiple randomized clinical trials and meta-analyses) should be discussed with individual patients and should

be based on the inherent individual patient's variables (demographics, comorbidities individual vessel's, and plaque's characteristics), and local hospital procedural risk.

In summary, our study suggested that the majority of North American and European respondents did not consider CEA and CAS equivalent. Our data seemed to indicate that CEA was a preferred option for the management of carotid stenosis disease. Our study further suggested that differences in attitudes in carotid stenosis management between countries indeed exist. Several factors likely affect these differences (ie, different medical systems, different cultures, different interpretations of available medical evidence, demographics, and vessel/stenosis characteristics, and biases); however, they were not explored in our survey.

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References

1. Petty GW, Brown RD Jr, Whisnant JP, Sicks JD, O'Fallon WM, Wiebers DO. Ischemic stroke subtypes: a population-based study of incidence and risk factors. *Stroke*. 1999;30(12):2513-2516.
2. Endovascular versus surgical treatment in patients with carotid stenosis in the carotid and vertebral artery transluminal angioplasty study (CAVATAS): a randomised trial. *Lancet* 2001; 357(9270):1729-1737.
3. Mas JL, Chatellier G, Beyssen B, et al. Endarterectomy versus stenting in patients with symptomatic severe carotid stenosis. *N Engl J Med*. 2006;355(16):1660-1671.
4. Ederle J, Dobson J, Featherstone RL, et al; International Carotid Stenting Study investigators. Carotid artery stenting compared with endarterectomy in patients with symptomatic carotid stenosis (international carotid stenting study): an interim analysis of a randomised controlled trial. *Lancet*. 2010; 375(9719):985-997.
5. Yadav JS, Wholey MH, Kuntz RE, et al; 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*. 2004; 351(15):1493-1501.

6. Gurm HS, Yadav JS, Fayad P, et al; SAPHIRE Investigators. Long-term results of carotid stenting versus endarterectomy in high-risk patients. *N Engl J Med*. 2008;358(15):1572-1579.
7. Ringleb PA, Allenberg J, Brückmann H, et al; SPACE Collaborative Group. 30 day results from the SPACE trial of stent-protected angioplasty versus carotid endarterectomy in symptomatic patients: a randomised non-inferiority trial. *Lancet*. 2006;368(9543):1239-1247.
8. Eckstein HH, Ringleb P, Allenberg JR, et al. Results of the stent-protected angioplasty vs carotid endarterectomy (SPACE) study to treat symptomatic stenoses at 2 years: a multinational, prospective, randomised trial. *Lancet Neurol*. 2008;7(10):893-902.
9. Brott TG, Hobson RW II, Howard G, et al; CREST Investigators. Stenting versus endarterectomy for treatment of carotid-artery stenosis. *N Engl J Med*. 2010;363(1):11-23.
10. Economopoulos KP, Sergeantanis TN, Tsivgoulis G, Mariolis AD, Stefanadis C. Carotid artery stenting versus carotid endarterectomy: a comprehensive meta-analysis of short-term and long-term outcomes. *Stroke*. 2011;42(3):687-692.
11. Bangalore S, Kumar S, Wetterslev J, et al. Carotid artery stenting vs carotid endarterectomy: meta-analysis and diversity-adjusted trial sequential analysis of randomized trials. *Arch Neurol*. 2011; 68(2):172-184.
12. Makris GC, Geroulakos G, Nicolaides AN. Letter by Makris et al regarding article, "carotid artery stenting versus carotid endarterectomy: a comprehensive meta-analysis of short-term and long-term outcomes." *Stroke*. 2011;42(6):e397.
13. Hacke W, Brown MM, Mas JL. Carotid endarterectomy versus stenting: an international perspective. *Stroke*. 2006;37(2):344.
14. Hart RG, Ng KH. Stroke prevention in asymptomatic carotid artery atherosclerosis: stenosis is only part of the question, revascularization is rarely the right answer. *Pol Arch Med Wewn*. 2015, 125(5): 363-369.
15. Eastcott HH. Carotid endarterectomy: a mid-Atlantic view. *Br J Surg*. 1986;73(11):865-866.
16. Gupta R, Jovin TG, Yavargal D, Abou-Chebl A. Carotid endarterectomy vs. carotid stenting: fairly comparable or unfairly compared? *Front Neurol*. 2010;1:14.
17. Lovrencic-Huzjan A, Rundek T, Katsnelson M. Recommendations for management of patients with carotid stenosis. *Stroke Res Treat*. 2012;2012:175869.
18. European Stroke Organisation (ESO) Executive Committee and the ESO Writing Committee. Guidelines for management of ischaemic stroke and transient ischaemic attack 2008. *Cerebrovasc Dis*. 2008;25(5):457-507.
19. Tendera M, Aboyans V, Bartelink ML, et al; European Stroke Organisation; ESC Committee for Practice Guidelines. ESC guidelines on the diagnosis and treatment of peripheral artery diseases. *Eur Heart J*. 2011;32(22):2851-2906.
20. Karolinska Stroke Update Consensus Statements 2012. 1. Carotid endarterectomy versus angioplasty and stenting. www.strokeupdate.org/Cons_Carotid_session_2012.aspx. Accessed December 5, 2017.
21. NICE Interventional Procedure Guidance 388. Carotid artery stent placement for asymptomatic extracranial carotid stenosis. Guidance 388 (Issued April 2011). www.nice.org.uk/ipg388. Accessed December 5, 2017.
22. Ricotta JJ, Aburahma A, Ascher E, Eskandari M, Faries P, Lal BK; Society for Vascular Surgery. Updated society of vascular surgery guidelines of management of extracranial carotid disease. executive summary. *J Vasc Surg*. 2011;54(3):832-836.
23. Meschia JF, Bushnell C, Boden-Albala B, et al; American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; Council on Functional Genomics and Translational Biology; Council on Hypertension. Guidelines for the primary prevention of stroke. a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2014; 45(12):3754-3832.
24. Coutts SB, Wein TH, Lindsay MP, et al; Heart, and Stroke Foundation Canada Canadian Stroke Best Practices Advisory Committee. On behalf of the Heart And Stroke Foundation Canada Canadian Stroke Best Practices Advisory Committee. Canadian stroke best practice recommendations: secondary prevention of stroke guidelines, update 2014. *Int J Stroke*. 2015; 10(3):282-291.
25. Masuhr F, Busch M, Einhaupl KM. Differences in medical and surgical therapy for stroke prevention between leading experts in North America And Western Europe. *Stroke*. 1998;29(2): 339-345.
26. Malik Z, Shalhoub J, Hettige R, Davies AH. The role of endarterectomy and stenting in the management of carotid artery stenosis: a 5-year Delphi survey. *Vasc Endovascular Surg*. 2011; 45(1):15-21.
27. Chaturvedi S, Meinke JL, St Pierre E, Bertasio B. Attitudes of Canadian and U.S. neurologists regarding carotid endarterectomy for asymptomatic stenosis. *Can J Neurol Sci*. 2000;27(2): 116-119.
28. Likert R. A technique for the measurement of attitudes. *Arch Psychol*. 1932;140:1-55.
29. El Khoury R, Fisher M, Savitz SI. Current practice versus willingness to enroll in clinical trials: paradox among vascular neurologists about treatment for acute ischemic stroke. *Stroke*. 2010; 41(9):2038-2043.
30. Linstone HA, Turoff M. *The Delphi Method: Techniques and Applications*. Reading, MA: Addison-Wesley Pub. Co., Advanced Book Program; 1975.
31. Dirks M, Niessen LW, Koudstaal PJ, Franke CL, van Oostenbrugge RJ, Dippel DW; Delphi panel on indications and contraindications for intravenous thrombolysis in acute ischaemic stroke. Intravenous thrombolysis in acute ischaemic stroke: from trial exclusion criteria to clinical contraindications. an international Delphi study. *J Neurol Neurosurg Psychiatry*. 2007;78(7): 685-689.
32. Macdonald S, Lee R, Williams R, Stansby G; Delphi Carotid Stenting Consensus Panel. Towards safer carotid artery stenting: a scoring system for anatomic suitability. *Stroke*. 2009;40(5): 1698-1703.
33. Abbott AL, Adelman MA, Alexandrov AV, et al. Why calls for more routine carotid stenting are currently inappropriate: an

- international, multispecialty, expert review and position statement. *Stroke*. 2013;44(4):1186-1190.
34. Brott TG, Howard G, Roubin GS, et al; CREST Investigators. Long-term results of stenting versus endarterectomy for carotid-artery stenosis. *N Engl J Med*. 2016;374(11):1021-1031.
35. Mas JL, Arquizan C, Calvet D, et al; EVA-3S Investigators. Long-term follow-up study of endarterectomy versus angioplasty in patients with symptomatic severe carotid stenosis trial. *Stroke*. 2014;45(9):2750-2756.
36. Bonati LH, Dobson J, Featherstone RL, et al; International Carotid Stenting Study Investigators. Long-term outcomes after stenting versus endarterectomy for treatment of symptomatic carotid stenosis: the International Carotid Stenting Study (ICSS) randomised trial. *Lancet*. 2015;385(9967):529-538.
37. Rothwell PM, Eliasziw M, Gutnikov SA, Warlow CP, Barnett HJ; Carotid Endarterectomy Trialists Collaboration. Endarterectomy for symptomatic carotid stenosis in relation to clinical subgroups and timing of surgery. *Lancet*. 2004;363(9413):915-924.
38. Halliday A, Mansfield A, Marro J, et al; MRC Asymptomatic Carotid Surgery Trial (ACST) Collaborative Group. Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial. *Lancet*. 2004;363(9420):1491-1502.
39. Spence JD, Naylor AR. Endarterectomy, stenting, or neither for asymptomatic carotid-artery stenosis. *N Engl J Med*. 2016;374(11):1087-1088.
40. Howard VJ, Meschia JF, Lal BK, et al; CREST-2 study investigators. CREST-2 study investigators. Carotid revascularization and medical management for asymptomatic carotid stenosis: protocol of the CREST-2 clinical trials. *Int J Stroke*. 2017;12(7):770-778.
41. The European Carotid Surgery Trial 2 (ECST-2) (Internet). <http://s489637516.websitehome.co.uk/ECST2/protocolsummary.htm>. Accessed December 5, 2017.
42. Rosenfield K, Matsumura JS, Chaturvedi S, et al; ACT I Investigators. Randomized trial of stent versus surgery for asymptomatic carotid stenosis. *N Engl J Med*. 2016;374(11):1011-1020.
43. Brooks WH, Jones MR, Gisler P, et al. Carotid angioplasty with stenting versus endarterectomy: 10-year randomized trial in a community hospital. *JACC Cardiovasc Interv*. 2014;7(2):163-168.
44. Li Y, Yang JJ, Zhu SH, Xu B, Wang L. Long-term efficacy and safety of carotid artery stenting versus endarterectomy: a meta-analysis of randomized controlled trials. *PLoS One*. 2017;12(17):e0180804.
45. Moresoli P, Habib B, Reynier P, Secrest MH, Eisenberg MJ, Filion KB. Carotid stenting versus endarterectomy for asymptomatic carotid artery stenosis: a systematic review and meta-analysis. *Stroke*. 2017;48(8):2150-2157.
46. Sardar P, Chatterjee S, Aronow HD, et al. Carotid artery stenting versus endarterectomy for stroke prevention: a meta-analysis of clinical trials. *J Am Coll Cardiol*. 2017;69(18):2266-2275.
47. Boyko M, Iancu D, Lesiuk H, Dowlatshahi D, Shamy MCF. Decision making and the limits of evidence: a case study of acute stroke in pregnancy. *Neurohospitalist*. 2016;6(2):70-75.
48. Shamy MC, Jaigobin CS. The complexities of acute stroke decision-making: a survey of neurologists. *Neurology*. 2013;81(13):1130-1133.