



April 17, 2009

VIA Electronic Submission

Marcel Salive, M.D.
Coverage and Analysis Group
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21224

RE: NCA for Percutaneous Transluminal Angioplasty (PTA) of the Carotid Artery Concurrent with Stenting (CAG-00085R7)

Dear Dr. Salive:

The Society for Cardiovascular Angiography and Interventions (SCAI), American College of Cardiology (ACC) and Society for Vascular Medicine (SVM) are pleased to respond to CMS' request for reconsideration of coverage for PTA of the carotid artery concurrent with stenting (CAG-000-85R7). We urge CMS to expand its coverage policy to allow patients access to a choice of treatment options that have been clinically proven beneficial, safe and effective. We request expansion of the current CMS coverage for carotid artery stenting (CAS) to be consistent with the United States Food and Drug Administration's (FDA) approved indications for carotid stent devices in *patients who are at increased perioperative risk for carotid endarterectomy (CEA) complications due to currently defined anatomic and comorbid factors¹ and who have either symptomatic carotid artery stenosis of 50-99% or asymptomatic carotid artery stenosis of $\geq 80\%$* . Our request for expanded Medicare coverage for the high surgical risk population is consistent with FDA labeling of carotid stent devices and is motivated by compelling scientific evidence that 1) revascularization with CEA prevents stroke compared to medical therapy; and 2) in more than 10,000 reported patients with high risk features (comorbid and anatomic) for CEA, revascularization with CAS has been demonstrated to be statistically significantly *non-inferior to CEA*, thereby making expansion of the current CAS coverage decision reasonable and necessary.

CAS FOR PATIENTS AT INCREASED RISK FOR CAROTID SURGERY

As you are likely aware, the vast majority of clinical trials have not stratified CAS outcomes based upon their high risk subgroup classification and thus patients with predefined medical comorbidities or adverse anatomic features that would place them in a high risk status for adverse outcomes are noted for tracking purposes rather than identification as potential exclusionary categories. For the clinical results, benefits to the entire cohort of high risk patients have been documented, particularly in recently published studies. Thus, the construct of stratifying patients at high risk for carotid surgery into separate criteria is an artificial one, not supported by clinical evidence. Indeed, under current Medicare policy, the vast majority of patients who receive carotid arterial stenting (CAS) at high risk for poor endarterectomy outcomes have been selected for CAS treatment because their physiology renders them inferior surgical candidates. Currently, about 70 percent of CAS patients have comorbid factors, and 30 percent have anatomic restrictions.

Patients with high surgical risk features (anatomic and comorbid) for CEA have been proven to have outcomes similar to CEA in a randomized controlled trial (SAPPHIRE) published in a peer reviewed journal and accepted by the FDA as evidence supporting the first CAS device approval.² Three year outcomes have confirmed the durable and beneficial results obtained in the only randomized controlled trial in this high risk subset of patients.³

Additional supporting peer-reviewed and published evidence include a meta analysis⁴, multiple pre-market⁵⁻¹² and post-market¹³⁻¹⁶ FDA mandated investigations. Additionally, a multi-specialty endorsed professional Societal document is consistent with the randomized controlled trial and has supported the benefit of CAS in high surgical risk (anatomic and comorbid features) symptomatic (>50% stenosis) and asymptomatic (>80% stenosis) patients.¹

Subsequent to CMS' publication of the October 14, 2008 memorandum (CAG-00085R6) there have been three large clinical trials published in peer-reviewed journals which are germane to this discussion. These studies support expansion of carotid stent coverage to include the FDA label indications, i.e. the full scope of high surgical risk (both anatomic and comorbid features) patients, who have symptomatic $\geq 50\%$ stenotic lesions or asymptomatic $\geq 80\%$ stenotic lesions.

POST-MARKET APPROVAL CAROTID STENT STUDIES IN HIGH SURGICAL RISK PATIENTS

SAPPHIRE WORLDWIDE: The primary objective of the Stenting and Angioplasty with Protection of Patients with High Risk for Endarterectomy World-Wide (SAPPHIRE WW) post-market approval registry trial was to evaluate 30-day outcomes after CAS performed in high surgical risk patients with CAS operators of varying experience in an array of clinical facilities, including community hospitals and high-profile centers.¹⁷ Notably, independent neurologic assessment was employed for outcomes assessment. The investigators reported 30-day safety and efficacy outcomes in 2,001 symptomatic and asymptomatic high surgical risk patients (anatomic = 716, comorbid = 918, and both = 327) treated by carotid stent operators with varying clinical experience. The overall, independently adjudicated, 30-day stroke and death rate for CAS in 2,001 high surgical risk patients was 4.0%.¹⁷

EXACT and CAPTURE-2: The results of more than 6,000 high surgical risk patients treated by CAS operators with varying levels of experience in two large prospective, multi-center, FDA mandated post-market surveillance trials (EXACT [n = 2,145]; CAPTURE-2 [n = 4,175]) were recently published demonstrating excellent outcomes.¹⁸ Both trials included independent neurologic assessment of outcomes, to reinforce the rigor for ascertaining adverse events. The overall incidence of 30-day stroke and death for 2,145 EXACT patients was 4.1% and for the 4,175 CAPTURE-2 patients was only 3.4%. Importantly, for patients that would have been comparable to patients included in the 2006 AHA published guidelines (<80 years)¹⁹, the CAS results met and exceeded the threshold recommendations for 30-day stroke and death rate for symptomatic patients ($\geq 50\%$ stenosis) at 5.3% (Benchmark for CEA $\leq 6\%$) and for asymptomatic patients ($\geq 80\%$ stenosis) it was 2.9% (Benchmark for CEA $\leq 3\%$).¹⁸

MULTISPECIALTY-SOCIETAL DOCUMENTS SUPPORTING EXPANSION OF CMS COVERAGE TO BE CONSISTENT WITH FDA LABEL INDICATIONS FOR CAROTID STENTING IN THE HIGH SURGICAL RISK PATIENT

The Bates et al. multispecialty document supports CAS as an alternative to CEA for high surgical risk patients and consistency with FDA label indications which was co-sponsored by Cardiology (ACC and SCAI), Interventional Radiology (SIR), Vascular Medicine (SVM), and Neuroradiology (ASITN). The

American Heart Association (AHA) sponsored a recently published symposium with a panel of experts regarding “Controversies in Carotid Artery Revascularization”.^{20 21} Members of the writing groups included leaders from stakeholder specialties such as Neurology, Radiology, Vascular Surgery, Vascular Medicine, and Cardiology. The Executive Committee concluded:

*for “patients with increased surgical risk for CEA due to either unfavorable anatomic characteristics or medical comorbidities, CAS offers an alternative treatment. Because it is a less invasive procedure, CAS should be considered an option for patients who are at increased risk for surgical complications of CEA”.*²⁰

The multi-specialty writing group concluded that the *preponderance* of the evidence supported expansion of the coverage decision to include the FDA-labeled indications because “CAS with embolic protection is *not inferior* to CEA in either symptomatic or asymptomatic patients at increased risk for surgical complications of CEA”.²¹

SUPPORT FOR ELDERLY AND VERY ELDERLY PATIENTS AS CANDIDATES FOR CAS

There has been published data suggesting that the very elderly (≥ 75 -80 years of age) are at increased risk from invasive procedures--not only from CEA²²⁻²⁴, but also for CAS.^{8, 18, 25, 26} However, three peer-reviewed manuscripts have been published in the past year reporting CAS with embolic protection in 389 high surgical risk patients ≥ 80 years of age.²⁷⁻²⁹ The overall 30-day stroke and death rate with independent neurological assessment in patients ≥ 80 years of age was 3.3%, 2.7%, and 0.8%.²⁷⁻²⁹ The authors emphasized the importance of operator experience and case selection to avoid CAS high risk features such as difficult aortic arch access, excessive lesion tortuosity and heavy calcification.²⁶ The published, peer-reviewed evidence does not support any age cut-off (> 80 years) for the coverage of necessary carotid revascularization, but does show that, when possible, *CAS is preferred over CEA*.

SUMMARY

In patients with predefined medical comorbidities and adverse anatomic features¹, CEA need not be contraindicated to warrant consideration of CAS as a reasonable therapeutic alternative. CMS should not require that CAS be superior to CEA to consider it a valid treatment option. The decision to proceed with CAS or CEA is a risk to benefit assessment to be considered by the patient, their family and their treating physician. Without expanded coverage consistent with FDA approved indications, Medicare-covered patients who could benefit from carotid revascularization¹⁹, but who fall into the uncovered “gap” with an symptomatic 50% - 69% stenosis or an asymptomatic $\geq 80\%$ stenosis and are ineligible or unwilling to be enrolled in an FDA sponsored trial and cannot afford to pay for their treatment, will be denied this reasonable and necessary therapeutic option.

In the past, CMS documents have created confusion by mixing outcomes of non-high risk and high risk CEA trials, and also by comparing independently adjudicated CAS outcomes with CEA neurologic outcomes that have not been independently determined. SAPPHERE is the only direct comparison of CAS and CEA in high surgical risk patients and it demonstrated early and late non-inferiority by intention to treat, and superiority by treatment received for CAS compared to CEA.^{2, 3} All of the CAS trials cited and published have benefited from a robust methodology requiring independent assessment and adjudication of neurologic complications. Other than SAPPHERE, there are no reports of CEA in a high surgical risk population that includes an independent neurologic examination. This lack of rigor and independent neurologic evaluation associated with CEA outcome reports may result in under-reporting³⁰, which is why the CEA outcomes in the SAPPHERE randomized data is so very important.

Finally, there has been concern over the risk of CEA and CAS in the very elderly (>80 years). Clearly, as patients age, some but not all, will develop features that increase their procedural risk. Recently published peer-reviewed manuscripts of CAS with emboli protection in the very elderly (>80 years), demonstrate that the recommended CEA benchmark¹⁹ outcomes can be achieved with CAS.²⁷⁻²⁹ However, as is true with any medical treatment option, appropriate recognition of the risks, benefits, and limitations of the operator, the patient, and the technology is a critical component for success. It is acknowledged that experienced operators and careful case selection excluding patients with difficult aortic arch access, and avoiding unfavorable lesion anatomy including excessive vessel tortuosity and/or heavy calcification are required to meet these standards.

CONCLUSION

The crucial question for achieving successful patient outcomes in revascularization is not whether CAS is a superior carotid revascularization technique to CEA, but rather, in which patients is CAS as good and safe as CEA. There is now overwhelming evidence and confidence supporting CAS in selected patients as a valid alternative to CEA in patients with high risk anatomic and comorbid features. The recent peer-reviewed publication of data clearly shows that more than 8,000 high surgical risk patients achieved published carotid revascularization benchmarks¹⁹ for 30-day stroke and death risks, and this evidence makes an irrefutable argument for expansion of CMS' coverage for CAS that is broadly consistent with the FDA labeled indications. Candidates for carotid artery revascularization to prevent stroke, who are identified as high-risk for CEA through anatomic or comorbid characteristics should be allowed to select, in consultation with their physician, the most appropriate treatment option for them, without these current coverage restrictions in the Medicare program.

SCAI, ACC, and SVM are pleased that CMS has responded to publication of the SAPPHIRE data by opening this National Coverage Analysis so promptly. As noted above, our organizations strongly support expansion of Medicare coverage on the basis of these data. The importance of obtaining good outcomes during carotid revascularization (through both CAS and CEA), and the potential implications of severe adverse events (stroke or death), underscore the need for high-level quality improvement programs at all facilities performing these endovascular and surgical procedures. We believe that all facilities and programs should be subjected to review and reaccreditation at regular intervals. Coverage should depend upon fulfillment of the requirements previously delineated by CMS, including proper facilities and equipment, credentialing and recredentialing of physician operators, ongoing measurement of outcomes and implementation of a regular quality improvement initiative.

Furthermore, as part of this accreditation process, institutions should be required to demonstrate acceptable results when compared to national benchmarks. To achieve this necessitates collection of a baseline dataset that may be entered into a "recognized/accredited" robust national registry, such as the NCDR[®] CARE[®] (Carotid Artery Revascularization and Endarterectomy) Registry or the SVS Registry, against which the institutional results can be compared. These registries should include similar elements and definitions, so as to facilitate benchmark comparisons. At the very least, registries should include indications for procedures, patient demographic data, basic procedural data, and outcomes as measured by objective means (e.g., independent neurologic assessment by individuals certified in NIHSS). Analysis of the data collected in this fashion can be utilized to enhance outcomes at individual sites, increase our knowledge and evidence base in carotid revascularization, and drive future appropriateness and coverage decisions in this area.

We believe that robust data collection, such as that available through the CARE Registry, offers excellent opportunities to improve quality of care and gather the data needed to support optimal coverage policies. To

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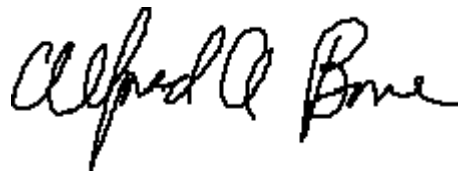
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help CMS answer any outstanding questions, we recommend exploring how we may be able to help develop and implement potential pilots or other programs that utilize registries, such as the CARE Registry, to evaluate and measure specific approaches to achieve quality revascularization outcomes. We look forward to working with CMS to discuss development of these options to help improve Medicare patients' access to appropriate carotid revascularization therapy.

Respectfully submitted,

A handwritten signature in black ink that reads "M. Hijazi". The signature is stylized with a large, sweeping initial "M" and a long horizontal stroke extending to the right.

Ziyad M. Hijazi, M.D., MPH, FSCAI
President
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A handwritten signature in black ink that reads "Alfred A. Bove". The signature is written in a cursive style with a large, prominent initial "A".

Alfred A. Bove, M.D., M.H., Ph.D., F.A.C.C.
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A handwritten signature in black ink that reads "J. Michael Bacharach". The signature is written in a cursive style with a large, prominent initial "J".

J. Michael Bacharach, M.D., M.P.H.
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REFERENCES

1. Bates ER, Babb JD, Casey DE, Jr., et al. ACCF/SCAI/SVMB/SIR/ASITN 2007 clinical expert consensus document on carotid stenting: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents (ACCF/SCAI/SVMB/SIR/ASITN Clinical Expert Consensus Document Committee on Carotid Stenting). *J Am Coll Cardiol* 2007;49:126-70.
2. Yadav JS, Wholey MH, Kuntz RE, et al. Protected carotid-artery stenting versus endarterectomy in high-risk patients. *N Engl J Med* 2004;351:1493-501.
3. Gurm HS, Yadav JS, Fayad P, et al. Long-term results of carotid stenting versus endarterectomy in high-risk patients. *N Engl J Med* 2008;358:1572-9.
4. Gurm HS, Nallamothu BK, Yadav J. Safety of carotid artery stenting for symptomatic carotid artery disease: a meta-analysis. *Eur Heart J* 2008;29:113-9.
5. Gray W. Two-year composite endpoint results for the Archer Trials: Acculink for revascularization of carotids in high risk patients. *Am J Cardiol* 2004;94:62E.
6. Gray WA, Hopkins LN, Yadav S, et al. Protected carotid stenting in high-surgical-risk patients: the ARChER results. *J Vasc Surg* 2006;44:258-68.
7. Hopkins LN, Myla S, Grube E, et al. Carotid artery revascularization in high surgical risk patients with the NexStent and the Filterwire EX/EZ: 1-year results in the CABERNET trial. *Catheter Cardiovasc Interv* 2008;71:950-60.
8. Iyer SS, White CJ, Hopkins LN, et al. Carotid artery revascularization in high-surgical-risk patients using the Carotid WALLSTENT and FilterWire EX/EZ: 1-year outcomes in the BEACH Pivotal Group. *J Am Coll Cardiol* 2008;51:427-34.
9. Security: More good data for protected carotid stenting in high-risk surgical patients. 2003. (Accessed at http://www.medscape.com/viewarticle/461721_print.)
10. United States Food and Drug Administration, Center for Devices and Radiological Health: Abbott Xact® Carotid Stent System, summary of the safety and effectiveness data., 2005. (Accessed at <http://www.fda.gov/cdrh/pdf4/p040038.html>.)
11. White CJ, for the Beach Investigators. BEACH Trial: 30 day outcomes of carotid wallstent and filterwire EX/EZ distal protection system placement for treatment of high surgical risk patients. *J Am Coll Cardiol* 2005;45:28A.
12. Safian RD, Bresnahan JF, Jaff MR, et al. Protected carotid stenting in high-risk patients with severe carotid artery stenosis. *J Am Coll Cardiol* 2006;47:2384-9.
13. Gray WA, Yadav JS, Verta P, et al. The CAPTURE registry: results of carotid stenting with embolic protection in the post approval setting. *Catheter Cardiovasc Interv* 2007;69:341-8.
14. Gray WA, Yadav JS, Verta P, et al. The CAPTURE registry: Predictors of outcomes in carotid artery stenting with embolic protection for high surgical risk patients in the early post-approval setting. *Catheterization and Cardiovascular Interventions* 2007;70:1025-33.
15. Katzen BT, Criado FJ, Ramee SR, et al. Carotid artery stenting with emboli protection surveillance study: thirty-day results of the CASES-PMS study. *Catheter Cardiovasc Interv* 2007;70:316-23.
16. Ramee S, Higashida R. Evaluation of the Medtronic self-expanding carotid stent system with distal protection in the treatment of carotid artery stenosis (Abstract). *Am J Cardiol* 2004;94:61E.
17. Massop D, Dave R, Metzger C, et al. Stenting and Angioplasty with Protection in Patients at High-Risk for Endarterectomy: SAPHIRE Worldwide Registry First 2,001 Patients. *Catheter Cardiovasc Interv* 2008:DOI 10.1002/ccd.21844.
18. Gray W, Chaturvedi S, Verta P. 30-Day Outcomes for Carotid Artery Stenting in 6,320 Patients From Two Prospective, Multicenter, High Surgical Risk Registries. *Circulation Cardiovascular Interventions* 2009.

19. Sacco RL, Adams R, Albers G, et al. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke: co-sponsored by the Council on Cardiovascular Radiology and Intervention: the American Academy of Neurology affirms the value of this guideline. *Stroke* 2006;37:577-617.
20. Creager MA, White CJ, Hiatt WR, et al. Atherosclerotic Peripheral Vascular Disease Symposium II: executive summary. *Circulation* 2008;118:2811-25.
21. White CJ, Beckman JA, Cambria RP, et al. Atherosclerotic Peripheral Vascular Disease Symposium II: controversies in carotid artery revascularization. *Circulation* 2008;118:2852-9.
22. Wennberg D, Lucas F, Birkmeyer J, Bredenberg C, Fisher E. Variation in carotid endarterectomy mortality in the Medicare population. *JAMA* 1998;279:1278-81.
23. Kazmers A, Perkins AJ, Huber TS, Jacobs LA. Carotid surgery in octogenarians in Veterans Affairs medical centers. *J Surg Res* 1999;81:87-90.
24. Miller MT, Comerota AJ, Tzilinis A, Daoud Y, Hammerling J. Carotid endarterectomy in octogenarians: does increased age indicate "high risk?". *J Vasc Surg* 2005;41:231-7.
25. Hobson RW, 2nd, Howard VJ, Roubin GS, et al. Carotid artery stenting is associated with increased complications in octogenarians: 30-day stroke and death rates in the CREST lead-in phase. *J Vasc Surg* 2004;40:1106-11.
26. Roubin GS, Iyer S, Halkin A, Vitek J, Brennan C. Realizing the potential of carotid artery stenting: proposed paradigms for patient selection and procedural technique. *Circulation* 2006;113:2021-30.
27. Chiam P, Roubin G, Iyer S, et al. Carotid artery stenting in elderly patients: Importance of case selection. *Catheterization and Cardiovascular Interventions* 2008;72:318-24.
28. Henry M, Henry I, Polydorou A, Hugel M. Carotid angioplasty and stenting in octogenarians: is it safe? *Catheter Cardiovasc Interv* 2008;72:309-17.
29. Velez CA, White CJ, Reilly JP, et al. Carotid artery stent placement is safe in the very elderly (> or =80 years). *Catheter Cardiovasc Interv* 2008;72:303-8.
30. Rothwell PM, Slattery J, Warlow CP. A systematic review of the risks of stroke and death due to endarterectomy for symptomatic carotid stenosis. *Stroke* 1996;27:260-5.