March 28, 2007

Centers for Medicare & Medicaid Services  
Department of Health & Human Services  
7500 Security Boulevard  
Baltimore, MD 21244

Re: CAG-00085R4

Dear Sir/Madam:

On behalf of the American Heart Association (AHA), including the American Stroke Association (ASA) and over 22.5 million AHA and ASA volunteers and supporters, we appreciate the opportunity to submit our comments in response to the Centers for Medicare and Medicaid Services (CMS) national coverage analysis for percutaneous transluminal angioplasty (PTA) and stenting of the renal arteries.

Since 1924, the American Heart Association has dedicated itself to reducing disability and death from cardiovascular disease and stroke – the #1 and #3 leading causes of death in the United States – through research, education, community based programs and advocacy. AHA’s efforts include the development of evidence-based clinical practice guidelines and scientific statements designed to raise awareness and advise physicians and other providers on the prevention, treatment, and management of cardiovascular disease and stroke. These are developed jointly with the American College of Cardiology (ACC) using rigorous methodology and an intensive review process. The subject of atherosclerotic renal artery stenosis (ARAS) is covered in the ACC/AHA 2005 Practice Guidelines for the Management of Patients with Peripheral Arterial Disease (Lower Extremity, Renal, Mesenteric, and Abdominal Aortic).1 These guidelines were developed in collaboration with and endorsed by the American Association for Vascular Surgery/Society for Vascular Surgery, the Society for Cardiovascular Angiography and Interventions, the Society for Vascular Medicine and Biology, and the Society of Interventional Radiology. Our comments are based on those guidelines.

1 See http://circ.ahajournals.org/cgi/reprint/113/11/e463.
At the end of February, CMS announced its intention to examine the best treatment options for patients with ARAS and develop a national coverage determination for PTA and stenting of the renal arteries. As part of this analysis, CMS will examine what patient population and under what circumstances Medicare coverage of renal artery stenting is reasonable and necessary. AHA supports the Agency’s efforts to evaluate this procedure and identify the appropriate patient population. PTA and stenting is an effective treatment option for appropriately selected patients; the procedure has become one of the most frequently used revascularization techniques, despite a limited evidence base. Without additional trials examining PTA and stenting and comparing the procedure to surgical revascularization and medical management, it will be difficult to correctly identify the appropriate patient population for this treatment option.

**Current Evidence**

Current Medicare policy provides coverage for PTA of the renal arteries for patients in whom there is an inadequate response to a thorough medical management for symptoms and for whom surgery is the likely alternative. AHA agrees that physicians should compare both medical treatment and revascularization techniques for patients with ARAS, and consider revascularization when it has a likely or definite advantage to medical therapy. Medical therapy should follow the recommendations detailed in the ACC/AHA guidelines.

There is some evidence, although limited in nature, that revascularization may benefit selected patients with significant renal artery stenosis (RAS). Based on the evidence currently available, the ACC/AHA guidelines offer the following Class I (there is evidence for and/or general agreement that a given procedure or treatment is beneficial, useful, and effective) or Class IIa (there is conflicting evidence or a divergence of opinion about the usefulness/efficacy of a procedure or treatment; the weight of evidence/opinion is in favor of usefulness/efficacy) recommendations for revascularization:

### Congestive Heart Failure & Unstable Angina

**Class I Recommendation**

1. Percutaneous revascularization is indicated for patients with hemodynamically significant RAS and recurrent, unexplained congestive heart failure or sudden, unexplained pulmonary edema (*Level of Evidence: B*).

2. Percutaneous revascularization is reasonable for patients with hemodynamically significant RAS and unstable angina (*Level of Evidence: B*)

### Hypertension

**Class IIa Recommendation**

1. Percutaneous revascularization is reasonable for patients with hemodynamically significant RAS and accelerated, resistant, or malignant hypertension; hypertension with an unexplained unilateral small kidney; or hypertension with intolerance to medication (*Level of Evidence: B*)

---

2 See [http://circ.ahajournals.org/cgi/reprint/106/12/1572](http://circ.ahajournals.org/cgi/reprint/106/12/1572), Pg. 1573.
3 See [http://circ.ahajournals.org/cgi/reprint/106/12/1572](http://circ.ahajournals.org/cgi/reprint/106/12/1572), Pgs. 1573-1574.
Preservation of Renal Function  
Class IIa Recommendation  
1. Percutaneous revascularization is reasonable for patients with RAS and progressive chronic kidney disease with bilateral RAS or a RAS to a solitary functioning kidney (Level of Evidence: B)

We would suggest that these specific patient groups are currently appropriate for coverage.

There are additional patient groups that have Class IIb (there is conflicting evidence or a divergence of opinion about the usefulness/efficacy of a procedure or treatment; the usefulness/efficacy is less well established by evidence/opinion) recommendations:

Preservation of Renal Function  
Class IIb Recommendation  
2. Percutaneous revascularization may be considered for patients with RAS and chronic renal insufficiency with unilateral RAS (Level of Evidence: C)

Asymptomatic Stenosis  
Class IIb Recommendation  
1. Percutaneous revascularization may be considered for the treatment of an asymptomatic bilateral or solitary viable kidney with a hemodynamically significant RAS (Level of Evidence: C)  

2. The usefulness of percutaneous revascularization of an asymptomatic unilateral hemodynamically significant RAS in a viable kidney is not well established and is presently clinically unproven (Level of Evidence: C)  

The current justification for coverage in these patients is weaker.

It is important to emphasize that the recommendations are based on the current evidence base. The Class I and IIa recommendations are Level of Evidence B, i.e., data derived from a single randomized trial or nonrandomized studies. The prospective clinical trials that have been published generally have significant methodological problems. While revascularization with stent-assisted angioplasty has gained increasing acceptance and has undergone tremendous procedural growth,\(^4\) replacing much of what had been done with traditional surgery, “many questions remain, partly because of the continuing evolution of tools and techniques and partly because of the paucity of large prospective randomized trials.”\(^5\) For example, the Class IIb recommendations for patients with asymptomatic stenosis are largely based on expert opinion (Level of Evidence C) instead of evidence that this treatment improves any renal or systemic outcome. (See Attachment A for additional information on the classification of recommendations and levels of evidence).

The relative paucity of clinical trial evidence has created controversy around the role of revascularization in patients with ARAS. Questions remain over the clinical clues that should be

---

\(^4\) See http://circ.ahajournals.org/cgi/reprint/106/12/1572, Pg. 1572.  
\(^5\) See http://circ.ahajournals.org/cgi/reprint/109/21/2643, Pg. 2463.
considered when selecting medical versus revascularization therapy, the degree of renal arterial narrowing that justifies an attempt at revascularization, and the relative effect of the different treatment options on patient outcomes. As acknowledged in AHRQ’s report on renal artery stenosis, “there remains considerable uncertainty on which intervention provides the best clinical outcome… Overall, the evidence does not currently support one treatment approach over the other for the general population of people with ARAS.” Simply put, “It is still unknown if percutaneous renal artery angioplasty or stent placement is superior to medical therapy or surgical revascularization in reducing cardiovascular mortality, providing prolonged improvements in blood pressure control, or preserving renal size and function.”

The need to resolve this controversy and identify the appropriate patient population for PTA and stenting of the renal arteries appears to be at least partially responsible for the Agency’s decision to develop a national coverage determination for this procedure under Medicare. According to the CMS tracking sheet, the Agency initiated this coverage analysis because of a “recent increase in concern regarding renal artery PTA and stenting and external questions regarding Medicare’s impact on current research and utilization of these procedures.” We support CMS’ efforts to examine this revascularization technique and attempt to identify the patients who are likely to benefit from it.

Additional Evidence is Needed

PTA with stent placement across the stenosis may ultimately prove to be the treatment standard for patients with ARAS; however, we do not yet have enough clinical evidence to adequately compare the treatment options and accurately identify the appropriate patient population. “Despite extensive clinical experience over the past 10 years and the publication of multiple articles describing renal revascularization with renal artery stents, renal angioplasty, and surgical renal revascularization, few prospective randomized controlled trials have been reported.”

The need for additional studies is supported by AHRQ’s review of the existing scientific evidence related to revascularization. As AHRQ found, there is no published evidence comparing aggressive medical therapy with PTA and stenting; and of the limited studies that have been completed to date, almost two-thirds were of poor methodological quality and more than half were of limited applicability to the population of interest.

Data from research studies currently in-progress such as the National Institutes of Health-sponsored Cardiovascular Outcomes in Renal Atherosclerotic Lesions (CORAL) trial and other broad-based studies will play a significant role in helping the medical community determine the appropriate role for stent-assisted angioplasty in patients with ARAS. Without this additional evidence from well-designed, controlled randomized trials, it will be difficult to identify the patient population and circumstances under which Medicare coverage of PTA and stenting of renal arteries is reasonable and necessary.

---

6 See http://circ.ahajournals.org/cgi/reprint/106/12/1572, Pg. 1573.
8 See http://circ.ahajournals.org/cgi/reprint/106/12/1572, Pg. 1573.
10 See http://circ.ahajournals.org/cgi/reprint/106/12/1572, Pg. 1572.
11 See http://effectivehealthcare.ahrq.gov/repFiles/RAS_Executive_Summary.pdf, Pg. 3.
Conclusion
In closing, we reiterate our support for CMS’ decision to examine the best treatment for patients with ARAS. The patient population that could potentially benefit from some form of revascularization therapy is substantial; approximately 30% of patients with coronary artery disease and approximately 50% of the elderly and those with diffuse atherosclerotic vascular diseases are afflicted with ARAS.\textsuperscript{12} A growing number of these patients are being treated with PTA and stenting, and the procedure has become the standard for revascularization in many patients with ARAS.

The number of PTA and stenting procedures has grown rapidly despite a lack of strong supporting clinical evidence. While there is some evidence that revascularization will benefit the specific patient groups described above, the overall evidence base is generally far less than desirable. This reinforces the need for additional data from well conducted clinical trials (such as CORAL) to strengthen the evidence in support of this procedure. Data from such clinical trials is crucial to the advancement of this treatment option for patients with ARAS. Without these data, physicians will be forced to continue to make treatment decisions, and CMS will be forced to make coverage decisions, based on a limited and incomplete database of evidence. Given the magnitude of the patient population that could benefit from selection of the appropriate treatment, this is not an acceptable option.

We strongly support efforts by CMS to encourage enrollment in the ongoing CORAL trial and other studies of treatment options for ARAS. To encourage enrollment, we suggest that the Agency consider aligning reimbursement for this procedure with participation in clinical trials. If providers continue to offer PTA and stenting outside of a clinical trial, patients have little incentive to enroll in a clinical trial and it will be difficult, if not impossible, to obtain strong, scientific data that compares the benefits and risks of this procedure.

If you have any questions or need any additional information, please do not hesitate to contact Susan Bishop, MA, Regulatory Relations Manager, at 202-785-7908 or via email at susan.k.bishop@heart.org.

Sincerely,

Raymond Gibbons, MD, FAHA
President, AHA

\textsuperscript{12} See http://effectivehealthcare.ahrq.gov/repFiles/RAS_Executive_Summary.pdf, Pg. 1.
Classification of Recommendations

Class I: Conditions for which there is evidence for and/or general agreement that a given procedure or treatment is beneficial, useful, and effective.

Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.

   Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.

   Class IIb: Usefulness/efficacy is less well established by evidence/opinion.

Class III: Conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful.

Level of Evidence

Level of Evidence A: Data derived from multiple randomized clinical trials or meta-analysis.

Level of Evidence B: Data derived from a single randomized trial or nonrandomized studies.

Level of Evidence C: Only consensus opinion of experts, case studies, or standard of care.