Cardiovascular Revascularization Medicine 20 (2019) 175–176

Contents lists available at ScienceDirect

Cardiovascular Revascularization Medicine

Editorial

The Modern Landscape of Renal Artery Stenosis and Renovascular Hypertension

Benjamin R. Weber *, Robert S. Dieter

In the management of resistant hypertension, a diagnostic evaluation for secondary etiologies is considered to be standard of care, including assessment of the renal arteries [1]. Renovascular hypertension is a prevalent secondary cause of hypertension and is most frequently due to atherosclerotic renal artery stenosis (ARAS). The pathophysiology of ARAS leading to the development of poorly controlled hypertension is well-described, and revascularization of hemodynamically significant renal artery stenosis (RAS) for the treatment of hypertension makes clear mechanistic sense.

In the current issue of *Cardiovascular Revascularization Medicine*, Khan et al. present a single-center, retrospective cohort study of 26 patients with angiographically significant RAS (≥70% unilateral stenosis, or bilateral stenosis) with poorly controlled hypertension (blood pressure 160/90 mmHg) on at least 3 anti-hypertensive medications[2]. The authors described a significant reduction in systolic blood pressure (162 +/- 25 mmHg to 135 +/- 25 mmHg, $p < 0.001$) at 6- to 12-month follow-up, as well as a reduction in the number of anti-hypertensive medications (4.1 +/- 1 to 2.7 +/- 2.1, $p = 0.002$) at 6 months. Both outcomes were sustained at long-term follow-up. This cohort is another example of an observational study lending credence to the possible utility of renal artery stenting in the treatment of hypertension. Yet, in the face of sound mechanistic logic and promising observational data, multiple large, randomized controlled clinical trials have failed to demonstrate a clinically significant benefit of endovascular revascularization save for a slight reduction in antihypertensive medications [3–6].

Admittedly, many of the randomized controlled trials to date have been widely criticized for their loose inclusion criteria as well as significant crossover. These flaws have left space for lingering doubt and the suggestion of a more highly selected subgroup of patients with ARAS and hypertension who might still derive benefit from renal artery stenting. The CORAL trial is thought to have corrected for several of the flaws of its predecessors, including more stringent criteria of lesion severity (at least 80% diameter stenosis or at least 60% stenosis with a pressure gradient of at least 20 mm Hg) [7]. That being said, the limitations of angiographic severity of coronary lesions are well-described. Modern adjunctive technologies known to derive added benefit to angiography alone in the selection of lesions for coronary revascularization (intravascular imaging and fractional flow reserve) have yet to be fully evaluated in the treatment of RAS in a large randomized controlled setting.

Revascularization of ARAS currently receives a class IIa recommendation by the American College of Cardiology Foundation/American Heart Association (ACCF/AHA) guidelines for patients with hemodynamically significant RAS and accelerated hypertension, resistant hypertension, malignant hypertension, hypertension with an unexplained unilateral small kidney, and hypertension with intolerance to medication [1]. Of note, these guidelines are from 2013 and predate the CORAL trial and subsequent updated meta-analyses [8]. The more recent European Society of Cardiology (ESC) guidelines (2017) have relegated routine revascularization of ARAS to a class III indication [3]. Both guidelines give similarly weak recommendations for revascularization for the preservation of renal function. It should be noted that the one clinical scenario in which renal artery stenting is clearly indicated by ACCF/AHA is recurrent congestive heart failure or sudden unexplained pulmonary edema with hemodynamically significant RAS (class I).

The current iterations of the ACCF/AHA (2013) and ESC (2017) guidelines prefer medical therapy over revascularization as the first-line treatment of atherosclerotic RAS [1,3]. Angiotensin-converting enzyme inhibitors (ACEis), angiotensin receptor blockers (ARBs), calcium channel blockers, beta-blockers, and diuretics all receive class I indications for unilateral RAS. ARBs/ACEis can even be considered in the bilateral severe RAS or a solitary functioning kidney if closely monitored after initiation (class IIb). The ESC guidelines additionally recommend statins and antiplatelet therapy. Interestingly, one criticism of the CORAL study was that both study arms benefited from a similar degree of blood pressure reduction (~15mmHg). This finding suggests that medical therapy was not fully optimized prior to the trial and that enrollment in the trial alone resulted in improved blood pressure control. A potential explanation for this phenomenon includes more frequent contact with the medical system, more extensive counseling and education, improved medication titration and adherence and, thus, improved blood pressure outcomes equivalent to an invasive procedure. It stands to reason, then, that in many patients, in routine practice with "resistant hypertension" with known RAS, there is likely room for improvement in medical therapy before subjecting patents to a, to-date, unproven invasive therapy with known risks.

References

[1] Anderson JL, Halperin JL, Albert NM, Bozkurt B, Brindis RG, Curtis LH, et al. Management of patients with peripheral artery disease (compilation of 2005 and 2011 ACCF/AHA guideline recommendations): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation 2013;127(13):1425–43.

* Corresponding author.

https://doi.org/10.1016/j.carrev.2019.01.021

[2] Khan Z, Tolia S, Sanam K, Gholkar G, Zughaib M, Naik S, et al. Is There still a Role for Renal Artery Stenting in the Management of Renovascular Hypertension - A Single-Center Experience and Where Do We Stand? Cardiovasc Revasc Med 2019;20:202–6.
[3] Aboyans V, et al, ESC Scientific Document Group. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries Endorsed by: the European Stroke Organization (ESO)The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). Eur Heart J 2017;32(22):2851–906.
[4] van Jaarsveld BC, Krijnen P, Pieterman H, et al. The effect of balloon angioplasty on hypertension in atherosclerotic renal-artery stenosis. Dutch Renal Artery Stenosis Intervention Cooperative Study Group. N Engl J Med 2000;342(14):1007–14.
[5] Bax L, Woittiez AJ, Kouwenberg HJ, et al. Stent placement in patients with atherosclerotic renal artery stenosis and impaired renal function: a randomized trial. Ann Intern Med 2009;150(12):840–1 [W150].
[6] Wheatley K, Ives N, Gray R, et al, ASTRAL Investigators. Revascularization versus medical therapy for renal-artery stenosis. N Engl J Med 2009;361(20):1953–62.
[7] Cooper CJ, Murphy TP, Cutlip DE, et al, CORAL Investigators. Stenting and medical therapy for atherosclerotic renal-artery stenosis. N Engl J Med 2014;370(1):13–22.
[8] Jenks S, et al. Balloon angioplasty, with and without stenting, versus medical therapy for hypertensive patients with renal artery stenosis. Cochrane Database Syst Rev 2014 (12):CD002944.