

The future of renal artery stenting

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The future of renal artery stenting for atherosclerotic renal artery stenosis

Recently, the CORAL trial was published [1]. The overall finding of the CORAL trial was that stenting of atherosclerotic renal artery stenoses did not reduce the composite end point of cardiovascular or renal death, myocardial infarction, stroke, congestive heart failure hospitalization, progressive renal insufficiency, or the need for renal replacement therapy. This study is the most recent of several randomized trials to look at renal artery revascularization [2–6], all of which have been negative. Many of the prior trials faced criticism due to perceived limitations in trial size, design or conduct. The earliest of these studies (EMMA, the Scottish and New Castle trial and DRASTIC) [2–4] were limited by small size and a predominant use of angioplasty without stenting. The more recent of these trials, STAR and ASTRAL [5,6], may have been limited by other methodologic issues such as inclusion criteria and the lack of core lab analyses. These limitations have been pointed out in many prior publications, perhaps most famously in an editorial by Christopher White [7]. However, with the consistently negative outcomes of all the randomized studies of renal artery revascularization, there should be little debate that renal artery revascularization has a very limited, if any, role in the management of atherosclerotic renal artery stenosis.

Why was revascularization of renal artery stenosis an important public health issue?

When considering renal artery revascularization, it is essential to understand why a bene-

fit has been thought to exist. The physiologic mechanisms supporting the concept of renal artery stenosis as a potential health hazard relate to a number of adverse effects of renal artery stenosis (RAS). The negative effects of RAS include drug-resistant hypertension, activation of the renin–angiotensin–aldosterone axis, activation of the sympathetic nervous system, and development of ischemic nephropathy. These are relevant since these adverse pathophysiologic consequences may result in serious health consequences including stroke, myocardial infarction, congestive heart failure and kidney failure. Furthermore, several studies have documented the high risk of death and adverse cardiovascular and renal outcomes in patients with atherosclerotic renal artery stenosis [8–10]. While stenting for RAS may reduce these negative neuro-humoral effects, some may also be managed with medications such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers and β -blockers, amongst others. We now know from the randomized trials that medical therapy directed at these maladaptive mechanisms is as beneficial as renal artery revascularization for the prevention of clinical events in the majority of people with atherosclerotic renal artery stenosis.

Should anyone with atherosclerotic renal artery stenosis be considered for renal stenting?

If stenting is not needed to prevent the negative effects of neuroendocrine activation, and especially the adverse events that occur as a consequence, is there any potential role? The answer to this question may be a limited yes.



William R Colyer

Author for correspondence:
Division of Cardiology,
Department of Medicine,
University of Toledo Medical
Center, 3000 Arlington
Avenue, Mail Stop 1118,
Toledo, OH 43614, USA
Tel.: +1 419 383 3697
william.colyer@utoledo.edu



Christopher J Cooper

Division of Cardiology,
Department of Medicine,
University of Toledo Medical
Center, 3000 Arlington
Avenue, Mail Stop 1118,
Toledo, OH 43614, USA

Specifically, renal artery revascularization with stenting may be useful in patients with advanced kidney disease, and very severe stenoses, in whom the need for dialysis is imminent and in whom medical therapy has failed. Biologically it is clear that the kidney requires blood flow to function and that at some point RAS must become detrimental; however, this point is not well defined. The CORAL trial found no subgroup that benefited from renal artery stenting, including global renal ischemia, or in those with a stenosis over 80% [1]. Unfortunately, unlike other vascular territories, there are no reliable tests to identify renal ischemia *per se*, nor are there symptoms which suggest renal ischemia. This is also relevant since much of the benefit for revascularization in other vascular beds is derived from treating acute ischemia (acute coronary syndrome, threatened limb loss) or eliminating symptoms (angina, claudication). Without these types of treatment targets, patients who may benefit from renal artery stenting are difficult to identify and the benefit is difficult to demonstrate.

“...in individuals with severe renal dysfunction the role for renal artery stenting is uncertain and future trials would be helpful to address this uncertainty...”

This leads back to the concept of stenting to preserve the kidney itself. One of the limitations of all trials of renal artery revascularization is the relatively small number of enrolled subjects with advanced renal dysfunction in the presence of severe renal stenosis. Kalra *et al.* has previously published data that suggest the benefit of renal stenting may be among the patients with the worst renal function, specifically those with stage 4 or 5 chronic kidney disease [11]. Similarly, data from the RESIST trial suggested that the likelihood of an improvement in kidney function after renal artery revascularization is proportional to the severity of renal dysfunction [12]. However, it should be noted that in CORAL, neither patients with glomerular filtration rate below 45 ml/min nor those with serum creatinines over 1.6 mg/dl were any more likely to have a favorable result with stenting [1]. Thus, in individuals with severe renal dysfunction the role for renal artery stenting is uncertain and future trials would be helpful to address this uncertainty, although enrollment in such trials may be challenging.

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A cautionary note though, is that some may be tempted to extend the results of these studies in what may be inappropriate directions. First, angioplasty without stenting appears to be a reasonably effective strategy for management of the young patient with fibromuscular dysplasia with an intent to improve blood pressure control. This point was well made in a recent meta-regression analysis suggesting that patients who were younger were more likely to have a favorable response [13].

Second, there should be great caution in moving from percutaneous to surgical revascularization of atherosclerotic renal artery stenoses. Recent observational studies in Medicare beneficiaries suggest a very high in-hospital mortality for patients that undergo surgical revascularization of atherosclerotic renal artery stenosis [14–15]. This is on a background where others have observed similar clinical outcomes with surgery and balloon angioplasty when these were contrasted directly in a randomized trial [16]. Thus, when atherosclerotic renal artery stenosis is encountered, the best available evidence is that treatment of choice for the vast majority of patients is medical therapy alone.

Conclusion

The future of renal artery stenting appears to be quite limited, although it may exist for a small minority of patients with atherosclerotic renal artery stenosis. Currently, renal stenting might be considered in patients with progressive renal failure who are approaching dialysis and who are failing aggressive medical therapies to preserve renal function. This is a cohort of patients who ideally should be studied in a randomized trial to see if there is a measurable benefit to renal stenting in this setting. Although such a trial may face challenges, it would be valuable to patients, physicians and payers who are uncertain about the future of this therapy.

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