

# Aliskiren Renography Detects Renal Artery Stenosis

*Aliskiren renography can be used to categorize high-risk hypertensive patients for optimal therapy.*

BY MIRIAM E. TUCKER  
Senior Writer

LAKE BUENA VISTA, FLA. — Aliskiren used with a nuclear camera to measure split glomerular filtration rate in a same-day basal and stimulated study shows promise as a diagnostic screening test for functional renal artery stenosis in high-risk hypertensive patients.

Aliskiren (Tekturna) renography can be used to categorize high-risk hypertensive patients—such as those with heart failure, peripheral vascular disease, or resistant hypertension, and those with paradoxical blood pressure response to medications—for optimal hypertension therapy. Moreover, the agent itself—the first widely available direct renin inhibitor—also has renoprotective potential because of its preservation of glomerular function, Dr. Harold T. Pretorius and his associates said in a poster presentation at the annual meeting of the American Association of Clinical Endocrinologists.

“This may prove to be an improvement on the captopril renogram test, which has sort of fallen out of favor for a few reasons. Some patients had severe reactions to captopril, and the accuracy and sensitivity were not what we’d like. So instead of an angiotensin-converting enzyme inhibitor, we use a direct renin inhibitor and we’ve had much better results, especially in assessing renin-dependent hypertension,” Dr. Pretorius, an endocrinologist who practices in Cincinnati, said in an interview held at the meeting.

The method involves an initial basal scan of both kidneys, using an intravenous tracer such as 10-25 mCi Tc-99m diethyl-

enetriamine penta-acetic acid (DTPA). Almost any other renal nuclear tracer would work—all are nontoxic to the kidneys—but DTPA has the advantage of low cost, noted Dr. Pretorius, who is also a nuclear medicine specialist.

Details of the procedure contributing to accurate and reproducible results include proper bolus injection, calibrated gamma camera-based renal depth measurements, and attention to proper background corrections for same-day studies in a physiological state as similar as practicable.

Split glomerular filtration rate was measured using a modification of a nonlinear formula and normalized to a standard body surface area of 1.73 m<sup>2</sup> (Nucl. Med. Commun. 2007;28:407-13). After a 10-minute basal renal scan, the patient is given a 150- to 300-mg (depending on size and basal blood pressure) oral dose of aliskiren, and the renal scan is repeated an hour later.

In a series of 61 high-risk patients, 43 (70%) had bilateral increases in glomerular filtration rate (GFR), suggesting that no functional renal artery stenosis (RAS) was present and that those patients would respond positively to renin-angiotensin-aldosterone system (RAAS) inhibition with agents such as angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs).

In 16 of the 61 patients (26%), the response to aliskiren was abnormal, meaning that they either had no response or had a drop in GFR—suggesting bilateral RAS or a very low renin state such as hyperaldosteronism—or they had an asymmetrical split GFR, suggesting unilateral functional RAS. In these scenarios, inhibition

of RAAS with ACE inhibitors or ARBs is generally contraindicated because it could exacerbate the renal insufficiency and the hypertension.

These findings are consistent with the literature, which suggests that approximately 20%-30% of resistant hypertension is attributable to RAS, Dr. Pretorius commented.

Of the 16 patients with abnormal aliskiren renography, there were 6 with diabetes in whom ACE inhibitors or ARBs would otherwise have been indicated.

“Instead of giving the drugs and waiting 3 months to find out that the patient might be doing worse, you can do this test in 1 day and know who is going to do well with ACE inhibitor or ARB treatment,” Dr. Pretorius said.

And, he added, the test can also distinguish the patients who simply aren’t taking their prescribed antihypertensive medications from those who truly have resistant hypertension because of RAS or another form of secondary hypertension, such as hyperaldosteronism.

“Often the patients are compliant. They’re taking their pills, but they’re just not working.” Such patients could then be referred for renal angiography and, when suitable, for renal angioplasty, he said.

Aliskiren renography was inconclusive in only 2 of 61 patients (3.3%), in contrast to the 20%-30% typically seen with captopril renography.

And with captopril, the equivocal results often occurred in the patients with mild renal insufficiency.

The aliskiren test works better in such patients, in whom the agent improves renal blood flow and thereby provides an opportunity to treat for a longer period of time, he noted.

Concurrent antihypertensives including ACE inhibitors or ARBs, calcium channel blockers, diuretics, or  $\alpha$ -blockers do not generally interfere with aliskiren renography.

However, aspirin, other nonsteroidal anti-inflammatory drugs, irbesartan (Avapro), or prior aliskiren therapy may reduce the response. “Remarkably, cigarette smoking has little acute effect,” Dr. Pretorius and his associates commented in the poster.

And one more advantage: “The beauty of this test is that all the nuclear lab has to figure out is whether the GFR goes up or down for either kidney. The old captopril test had to be performed quite accurately. If you didn’t have a real expert, it was often not done right. With the aliskiren, even a novice nuclear technologist almost always gets the right answer.”

Dr. Pretorius is now pursuing further studies with a protocol he has submitted to an institutional review board for human studies. He has also filed a provisional use patent on the method, which he hopes will attract a commercial sponsor to help fund further research. He has been a speaker about hypertension for Novartis, the maker of Tekturna, but the company did not fund this research. Funding to file the provisional patent came from a patient who was happy with his test result and subsequent treatment. ■

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## Diabetes Not a Risk Factor for Adverse CABG Outcomes

BY MARK S. LESNEY  
Senior Editor

Diabetes is not an independent risk factor for adverse early outcomes after coronary artery bypass grafting surgery, according to a large, retrospective study of patients who underwent the procedure over a 10-year period at a single institution.

This result may be due to improvements in management of glucose levels, according to a report by Dr. Pedro E. Antunes and his colleagues.

Up to one-quarter of the patients who undergo coronary artery bypass grafting (CABG) surgery have diabetes.

Previous reports have been conflicting regarding the negative impact of diabetes on short-term mortality and morbidity in patients undergoing CABG, with older studies finding a clearer relationship between diabetes and worse outcomes, the authors wrote.

In this study, 4,567 patients underwent isolated CABG over a 10-year period at the Hospitais da Universidade, Coimbra, Portugal.

Overall, the rate of diabetes mellitus was 22% in

these patients, ranging from 19% at the beginning of the study in 1992 to 27% at the end of the study in 2001—a significant decade-long trend (Eur. J. Cardiothorac. Surg. 2008;34:370-5).

The study did not distinguish type 2 from type 1 diabetes, the authors noted.

The diabetic patients showed a significantly worse case mix, compared with the nondiabetic patients, according to the researchers.

**‘Better blood glucose management in the perioperative period improves early outcomes in diabetic patients subjected to CABG.’**

Diabetic patients had a higher mean age, a higher mean body mass index, and a higher proportion of patients with dyslipidemia, anemia, cardiomegaly, renal failure, peripheral vascular disease, and cerebrovascular and other comorbidities.

Perioperative glucose control in diabetic patients was aimed at achieving levels between 120 and 160 mg/dL. They received a standard sliding scale

of subcutaneous insulin injection pre- and postoperatively; in the operating room and the ICU they received continuous intravenous insulin infusions.

The overall in-hospital mortality was 0.96% (44 patients). There was no significant difference in mortality rate for the diabetic and nondiabetic groups: The mortality rates for the two groups were 0.9% and 1.0%, respectively,

Dr. Pedro E. Antunes and his colleagues reported.

Multivariate analysis showed that the presence of diabetes was not an independent predictor of in-hospital mortality.

However, increasing age, reoperation, peripheral vascular disease, left ventricular dysfunction with an ejection fraction less than 40%, and nonelective surgery were all independent predictors of in-hospital death.

As for in-hospital morbidity events, univariate analysis showed that diabetes was significantly associated only with cerebrovascular accident and prolonged length of stay.

However, these associations disappeared in multivariate analysis, and only the development of mediastinitis in the diabetic patients showed significance.

“Better blood glucose management in the perioperative period improves early outcomes in diabetic patients subjected to CABG,” the authors reported.

The researchers concluded that “despite the worsening case mix, in our experience diabetic patients could be surgically revascularized with low mortality and morbidity rates, comparable to those of nondiabetic patients.”

Limitations of the study reported by the authors include that it is observational and retrospective, although they commented that it was based on prospectively collected data and had a large cohort size, which adds strength to the power of the analysis. ■