adverse events included death, ESRD, and renal artery stenosis. The two groups had similar baseline characteristics; just over half of patients were taking three classes of antihypertensive medications. Mean 24-hour ambulatory BP was 152.1/97.2 mm Hg in the renal denervation group and 151.3/97.9 mm Hg in the sham control group.

At 6 months, the renal denervation group had significant reductions in BP measurements. Mean baseline-adjusted treatment differences in 24-hour BP were −7.0 mm Hg systolic and −4.3 mm Hg diastolic. For office BP, the differences were −6.6 and −4.2 mm Hg, respectively. Compared to the sham group, the difference in the renal denervation group was −7.4/−4.1 mm Hg for 24-hour BP and −6.8/−3.5 mm Hg for office BP.

Analysis of hourly data showed significant reductions in BP throughout the 24-hour monitoring period in patients assigned to renal denervation. The between-group differences in BP were not significant at 3 months’ follow-up. Laboratory tests showed medication adherence of about 60%, with significant variation for individual patients throughout the study. No patient in either group experienced major adverse events.

Previous studies of renal denervation for treatment of hypertension have yielded conflicting results. The recent SPYRAL HTN-OFF MED trial showed “significant and meaningful” reductions in BP in the absence of antihypertensive medications. The SPYRAL HTN-ON MED study evaluated the outcomes of renal denervation in a clinically representative situation in which this procedural approach might be integrated with continued antihypertensive drug treatment.

The results show greater reductions in BP with renal denervation compared to a sham procedure in patients with uncontrolled hypertension who continue taking antihypertensive drugs. The authors note that about half of patients did not follow their prescribed antihypertensive regimen during follow-up, even though they were aware that adherence would be monitored as part of the study [Kandzari DE, et al. Effect of renal denervation on blood pressure in the presence of antihypertensive drugs. 6-month efficacy and safety results from the SPYRAL HTN-ON MED proof-of-concept randomised trial. Lancet 2018; https://doi.org/10.1016/S0140-6736(18)30951-6].

Metformin Appears Safe for Most Diabetics with CKD


The community-based cohort study included 75,413 patients with type 2 diabetes in a large regional healthcare system who had serum creatinine measurements between 2004 and 2017. Metformin use and dose were analyzed for association with hospital admission for acidosis, accounting for time-related changes in eGFR. The study included replication in a sample of 67,578 new metformin users and 14,439 new sulfonylurea users, drawn from an individual-level inpatient and outpatient claims database.

The healthcare system cohort was 51% female, with a mean age of 60.4 years. At a median 5.7 years’ follow-up, there were 2355 hospitalizations with acidosis. Of these, only 20 had acidosis as the primary diagnostic code.

Overall, there was no significant association between time-dependent metformin use and incident acidosis, compared to alternative diabetes treatment. The risk of acidosis increased along with eGFR. However, the association became significant only at an eGFR of less than 30 mL/min/1.73 m²: adjusted hazard ratio 2.07. The association remained significant after adjustment for time-dependent use of a wide range of other medications. Lower eGFR was associated with a higher incidence of acidosis, whether or not the patients were using metformin.

The results were similar on analysis of new metformin versus sulfonylurea users, in a propensity-matched cohort, and on analysis excluding patients using insulin at baseline. In the replication analysis, there was no significant difference in acidosis risk for metformin versus sulfonylurea users, even at eGFR values less than 30 mL/min/1.73 m².

About 20% of patients with type 2 diabetes have an eGFR of less than 60 mL/min/1.73 m². Metformin is the first-line treatment for type 2 diabetes. However, it may be avoided in diabetic patients with CKD due to concerns about drug accumulation and lactic acidosis.

The new study, based on extensive data from two real-world settings, finds no association between metformin and incident acidosis in patients with type 2 diabetes and eGFR of 30 to 60 mL/min/1.73 m². Metformin appears to increase acidosis risk only for diabetic patients with eGFR of less than 30 mL/min/1.73 m². The researchers write, “From a public health perspective, the potential benefits of using metformin for patients with [diabetes] and CKD are vast, given the increasing number of people affected with both diseases worldwide” [Lazarus BN, et al. Association of metformin use with risk of lactic acidosis across the range of kidney function: a community-based cohort study. JAMA Intern Med 2018; DOI:10.1001/jamainternmed.2018.0292].