the results of previous renal-denervation studies. [Bhatt DL, et al: A controlled trial of renal denervation for resistant hypertension. *N Engl J Med.* 2014; 370: 1393–1401].

HbA_{1c} Doesn't Aid Risk Prediction in Nondiabetic Patients

Glycated hemoglobin (HbA1c) does not provide additional information on cardiovascular risk in patients without diabetes or cardiovascular disease (CVD), suggests a meta-analysis in the *Journal of the American Medical Association*.

The meta-analysis included individual-level data on 294,998 participants, all initially without known diabetes or CVD, from 73 prospective cohort studies. Glycated hemoglobin level was evaluated as a predictor of initial cardiovascular events in patients in different 10-year cardiovascular risk categories: low, less than 5 percent; intermediate, 5 percent to less than 7.5 percent; or high, 7.5 percent or greater. The analysis included measures of risk discrimination and reclassification.

The data included 20,840 fatal and nonfatal CVD events—13,237 coronary heart disease and 7603 stroke outcomes—at a median follow-up time of 9.9 years. After adjustment for some conventional cardiovascular risk factors, the slope of the association between HbA1c and CVD risk was approximately J-shaped. There was little effect of further adjustment for total cholesterol and triglyceride levels or estimated GFR. The association was attenuated by adjustment for high-density lipoprotein cholesterol and C-reactive protein.

Risk discrimination was little improved by the addition of HbA1c data to a model incorporating conventional cardiovascular risk factors, and net reclassification improvement was not improved at all. The results were similar in all 10-year CVD risk categories. The additional risk information from HbA1c was similar to or greater than that provided by fasting, random, or postload plasma glucose levels.

Higher levels of glycemia have been linked to increased CVD risk, suggesting a role of HbA1c for cardiovascular risk assessment in asymptomatic, nondiabetic adults. However, the new analysis showed limited value of adding HbA1c to conventional models for predicting initial CVD events. The authors call for further studies to evaluate the significance of the "consistent J-shaped associations between various glycemia measures and CVD incidence" [The Emerging Risk Factors Collaboration. Glycated hemoglobin measurement and prediction of cardiovascular disease. *JAMA* 2014; 311:1225–1233].

ACEIs, but Not ARBs, Reduce Mortality in Patients with Diabetes

Two classes of renin-angiotensin system blockers have differing effects on mortality in diabetic patients, concludes a meta-analysis in *JAMA Internal Medicine*.

A systematic review identified 35 randomized trials evaluating the effects of renin-angiotensin system blockers on all-cause and cardiovascular mortality and major cardiovascular events in patients with diabetes. There were 23 trials comparing angiotensin-converting enzyme inhibitors (ACEIs) with placebo or active drugs, including 32,287 patients, and 13 trials comparing angiotensin II receptor blockers (ARBs) with no treatment, including 23,867 patients. The outcomes with ACEIs and ARBs were separately evaluated in random-effects meta-analyses.

With ACEIs, there were significant reductions in all-cause mortality, odds ratio (OR) 0.87; cardiovascular death, OR 0.83; and major cardiovascular events, OR 0.86. The reduction in cardiovascular events was significant for both

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myocardial infarction, relative risk (RR) 0.79; and heart failure, RR 0.81.

Neither mortality outcome was significantly reduced by treatment with ARBs. Overall cardiovascular events were unaffected as well, although there was a significant reduction in heart failure risk: RR 0.70. Neither class of drug reduced stroke risk. Metaregression analysis suggested that ACEIs reduced mortality independently of baseline blood pressure or proteinuria, patient age, type of ACEI, or presence of diabetes.

Treatment with ACEIs or ARBs is recommended for diabetic patients with high blood pressure. However, these two drug classes have differing mechanisms and may differ in their clinical effects.

The new meta-analysis found significant reductions in overall and cardiovascular mortality in diabetic patients receiving ACEIs but not ARBs. The ACEIs were also associated with a reduced risk of cardiovascular events, whereas ARBs reduced only heart failure risk. The results support ACEIs as "first-line therapy to limit the excess mortality and morbidity" in hypertensive patients with diabetes [Cheng J, et al. Effect of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers on all-cause mortality, cardiovascular deaths, and cardiovascular events in patients with diabetes mellitus: a meta-analysis. *JAMA Intern Med* March 31, 2014. doi:10.1001/jamainternmed.2014.348].

STONE Score Helps in Assessing Ureteral Stones

A five-item clinical prediction rule performs well in identifying patients with uncomplicated ureteral stones, according to a report in the *British Medical Journal*.

The score was developed in a retrospective cohort of 1040 adults undergoing noncontrast computed tomography (CT) for suspected uncomplicated kidney stones under a "flank pain protocol." The factors associated with CT findings of symptomatic ureteral stones were incorporated into a scoring system identifying groups at low, moderate, and high probability of stones. The resulting 13-point STONE score was tested in a prospective validation cohort of 491 patients.

The five strongest predictors of ureteral stones were male sex, short duration of pain, nonblack race, nausea and vomiting, and microscopic hematuria. In the derivation cohort, the rates of ureteral stones were 8.3 percent in patients with a low-probability STONE score (0 to 5 points), 51.6 percent in those with a moderate probability score (6 to 9 points), and 89.6 percent in those with a high-probability score (10 to 13 points).

In the validation cohort, the rates were 9.2 percent, 51.3 percent, and 88.6 percent, respectively. Among patients with high-probability STONE scores, there was a 0.3 percent rate of acutely important alternative findings in the derivation cohort and 1.6 percent in the validation cohort.

Computed tomography is an accurate test for kidney stones, but it may not affect important clinical outcomes. The STONE score provides an easily calculated, objective clinical prediction rule for the assessment of renal colic patients.

The results suggest that the STONE score accurately predicts the likelihood of ureteral stones, which is inversely associated with the likelihood of acutely important alternative findings. With further validation, this score could help to select patients who could be treated without CT or with reduced-dose CT [More CL, et al. Derivation and validation of a clinical prediction rule for uncomplicated ureteral stone—the STONE score: retrospective and prospective observational cohort studies. *BMJ* 2014; g2191].