POEMs

Patient-Oriented Evidence That Matters

Using ACE Inhibitors and ARBs in Advanced Chronic Kidney Disease Does Not Worsen, and May Improve, Renal Outcomes

Clinical Question

In patients with advanced chronic kidney disease (CKD; stages IV or V), does the continued use of renin-angiotensin system inhibitors have a worsening effect on renal function?

Bottom Line

Although some experts have recommended the discontinuation of renin-angiotensin system inhibitors in patients with advanced CKD (glomerular filtration rate [GFR] of less than 30 mL per minute per 1.73 m^2), the study supports their continuation with no evidence of harm and a possible reduction in the need for renal replacement therapy. (Level of Evidence = 1b)

Synopsis

Renin-angiotensin system inhibitors include angiotensin receptor blockers (ARBs) and angiotensin-converting enzyme (ACE) inhibitors. Although their use in mild to moderate CKD (i.e., stages I through III) slows progression of the disease, their use in patients with advanced CKD is not known. The U.K. investigators identified adults with stage IV or V CKD and a decrease in GFR of 2 mL per minute per 1.73 m^2 per year over the past two years who were not on dialysis and used an ACE inhibitor or ARB for at least six months before enrollment. At baseline, the 411 patients had a median serum creatinine level of 3.4 mg per dL (300.6 µmol per L), a median estimated GFR of 18 mL per minute per 1.73 m^2, 45% were 65 years or older, and 36% had type 1 or type 2 diabetes mellitus. The patients were randomized to continue or discontinue their ACE inhibitor or ARB. In both groups, other classes of antihypertensives could be used to control blood pressure at the discretion of the treating physician. Analysis was by intention to treat, and the groups were balanced at baseline. After a median follow-up of three years, the estimated GFR was higher in the group that continued to use renin-angiotensin system inhibitors (13.3 vs. 12.6 mL per minute per 1.73 m^2), but this difference was not statistically significant. Patients in the continuation group had a strong trend toward a lower rate of requiring renal replacement therapy (56% vs. 62%; hazard ratio = 1.28; 95% CI, 0.99 to 1.65). This is an example of a clinically significant difference (number needed to treat = 17) that was not statistically significant, likely because of inadequate sample size and/or duration of follow-up. Hospitalizations, cardiovascular events, and deaths were similar between groups. Adherence to the assigned treatment was very good and there was no difference between groups in serious adverse events.

Study design: Randomized controlled trial (nonblinded)

Funding source: Government

Allocation: Concealed

Setting: Outpatient (any)

Reference: *Bhandari S, Mehta S, Khwaja A, et al.; STOP ACEi Trial Investigators. Renin-angiotensin system inhibition in advanced chronic kidney disease.* N Engl J Med. *2022;387(22):2021-2032.*

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PCI Does Not Improve Outcomes for Patients With Ischemic Heart Disease and LVEF of Less Than 35%

Clinical Question

In patients with severe ischemic heart disease and a left ventricular ejection fraction (LVEF) of less than 35%, does percutaneous coronary intervention (PCI) improve outcomes?

Bottom Line

For patients with extensive ischemic heart disease and an LVEF of less than 35%, PCI provides no clear benefit. (Level of Evidence = 1b)

Synopsis

The investigators identified 700 patients with an LVEF of less than 35%, extensive coronary artery disease, and at least four myocardial segments amenable to revascularization (i.e., proven myocardial viability). Patients were

randomized to receive PCI or optimal medical therapy. At baseline, the mean age was 70 years, 87% were men, and 90% were White. The groups were generally balanced at baseline and analysis was by intention to treat. The study was powered to detect a 30% reduction in a composite of all-cause mortality and hospitalization for heart failure (hazard ratio = 0.70). Among patients assigned to the PCI group, 96.3% underwent PCI and the degree of successful anatomical revascularization was high (71%). After a median follow-up of approximately 3.5 years, there was no significant difference in mortality between groups (31.7% for PCI vs. 32.6% for medical therapy) and no difference in the number of patients with at least one hospitalization for heart failure (14.7% vs. 15.3%). There was no difference in the composite of these outcomes combined. Approximately 10% of patients in the medical therapy group underwent revascularization (largely due to episodes of acute coronary syndrome), and those in the PCI group had higher rates of major bleeding. Although quality-of-life scores favored the PCI group early on, by 24 months there was no longer any difference between groups. There were no differences for any prespecified subgroup analyses.

Study design: Randomized controlled trial (nonblinded)

Funding source: Government

Allocation: Uncertain

Setting: Outpatient (any)

Reference: *Perera D, Clayton T, O'Kane PD, et al.; REVIVED-BCIS2 Investigators. Percutaneous revascularization for ischemic left ventricular dysfunction.* N Engl J Med. *2022;387(15):1351-1360.*

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ADA/EASD Updated Guidelines: Glycemic Control Is Only Part of the Management of Type 2 Diabetes

Clinical Question

What are the current recommendations from the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) for the treatment of type 2 diabetes mellitus?

Bottom Line

The management of type 2 diabetes continues to move away from glycemic goals and toward a more holistic approach to patient care that considers medications, weight management, attention to cardiovascular risk factors, and kidney protection. Metformin is recommended for most patients, although the new classes of medications that affect the heart and kidneys should be considered for many patients. Sulfonylureas, thiazolidinediones, and insulin, all of which have little effect except to lower blood glucose levels, are distinctly de-emphasized. (Level of Evidence = 5)

Synopsis

The guidelines were developed by a working group composed of members from two professional societies and included endocrinologists and researchers (i.e., no patients or primary care clinicians). Most of the working group members had substantial relationships with the pharmaceutical industry. The group systematically reviewed the evidence and assessed its quality. Rather than strict goals, the guidelines continue to move away from an emphasis on markers of glucose control and toward an emphasis on modifiable risk factors to prevent complications and optimize quality of life. However, they recommend an A1C goal of less than 7% in most adults with a life expectancy of 10 years or more. The authors suggest principles of care that are more holistic, including emphasis on social determinants, psychosocial factors, and shared decision-making. The four categories of care include weight management, medications for glycemia management, attention to cardiovascular risk factors, and kidney protection. Metformin remains a mainstay of treatment, although the authors suggest treatment that controls glycemia and offers cardiorenal protection, such as a sodium-glucose cotransporter-2 inhibitor and a glucagon-like peptide-1 receptor agonist, alone or in combination. Insulin should be used when needed to provide further control of blood sugar.

Study design: Practice guideline

Funding source: Foundation

Setting: Various (guideline)

Reference: *Davies MJ, Aroda VR, Collins BS, et al. Management of hyperglycemia in type 2 diabetes, 2022. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD).* Diabetes Care. *2022;45(11):2753-2786.*

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Majority of Grade 2 Cervical Intraepithelial Neoplasia Lesions Regress in Women 25 to 30 Years of Age

Clinical Question

Is watchful waiting a reasonable alternative to invasive treatment for women 25 to 30 years of age with grade 2 cervical intraepithelial neoplasia (CIN2)?

Bottom Line

For women 25 to 30 years of age with CIN2 confirmed with biopsy and a human papillomavirus (HPV) type that is not 16, a majority of lesions regress at least partially within two

years without treatment. Watchful waiting may be appropriate. For women with HPV 16, only 51% had a partial or total regression of CIN2, suggesting that immediate treatment (i.e., loop electrosurgical excision procedure) is warranted. Most progression or regression was evident at 12 months. (Level of Evidence = 1b)

Synopsis

The Swedish multicenter cohort study intended to establish the natural course of CIN2 in patients 25 to 30 years of age at the time of diagnosis. The investigators included 137 patients with a histological diagnosis of CIN2, fully visible squamocolumnar junction, transformation zone type 1 or 2, and available HPV results within three months before biopsy. The authors excluded patients who were immunosuppressed, in cancer treatment, pregnant at the time of diagnosis, or had an HIV infection or previous treatment for CIN. The follow-up evaluation included colposcopy, cytology, HPV testing, and at least two cervical biopsies every six months for up to 24 months. The loop electrosurgical excision procedure was performed in cases with progression to CIN3+ or diagnosis of atypical glandular cells or adenocarcinoma in situ during the study period. Loop electrosurgical excision was also performed at the conclusion of the study for persistent CIN2. In cases of partial regression, patients were followed up until total regression. HPV testing identified HPV 16 and 18, as well as 12 other strains as non-HPV 16/18. Ten patients did not complete the protocol as planned, leaving 127 for the per-protocol analysis. Of these, 21% had been vaccinated for HPV, and one-half were vaccinated before they were sexually active. HPV testing found that 72 patients (56%) had non-HPV 16/18, 45 (35%) had HPV 16, four (3%) had HPV 18, and six (5%) were negative for HPV. In the overall cohort, CIN2 regressed partially or totally in 68 of 82 patients (83%) with HPV status other than HPV 16, but only in 23 of 45 patients (51%) with HPV 16, a statistically significant difference ($P = .0001$). Only one patient (with HPV 16) had progression to stage 1A1 cervical cancer during the study period. Only one patient with HPV 16 had been vaccinated, and the vaccination was administered after they became sexually active.

Study design: Cohort (prospective)

Funding source: Unknown/not stated

Setting: Outpatient (specialty)

Reference: *Kylebäck K, Ekeryd-Andalen A, Greppe C, et al. Active expectancy as alternative to invasive treatment for cervical intraepithelial neoplasia grade 2 in women aged 25 to 30 years: ExCIN2-a prospective clinical multicenter cohort study.* Am J Obstet Gynecol. *2022;227(5):742.e1-742.e11.*

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