demics, may play a valuable role. The effectiveness of screening is unproven, however. The quality of auscultation depends on the examiner, and this study suggests that it will be difficult to prove a benefit of screening in asymptomatic patients. It is likely that patients will be better served by focusing time and resources on reducing known and modifiable risk factors for stroke such as hypertension and cigarette smoking.

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Calcium Channel Blockers and Cardiovascular Complications in Hypertensive Diabetics

Estacio RO, et al. The effect of nisoldipine as compared with enalapril on cardiovascular outcomes in patients with non-insulin-dependent diabetes and hypertension. New Eng J Med 1998; 338:645-52.

Clinical question **What is the risk of cardiovascular complications in hypertensive patients with type 2 diabetes mellitus who take a long-acting calcium channel blocker (CCB)?**

Background Case-control studies have described an association between CCBs and an increased risk of cardiovascular events and mortality. There is also evidence that angiotensin-converting enzyme (ACE) inhibitors increase the survival rate after an acute myocardial infarction (MI), and may delay the progression of renal disease in diabetics. This study, a subanalysis of the Appropriate Blood Pressure Control in Diabetes (ABCD) Trial, compared the incidence of cardiovascular complications in hypertensive patients with type 2 diabetes treated with either a CCB or an ACE inhibitor.

Population studied Subjects were patients aged 40 to 74 years who had type 2 diabetes, a diastolic blood pressure >80 mm Hg, and were taking no antihypertensive agents. Exclusion criteria included allergy to study medications, an absolute indication for use of one of the study drugs, recent MI, stroke, unstable angina, coronary artery bypass surgery, and renal insufficiency or dialysis.

Study design and validity This was a double-blind, randomized, controlled trial. Four hundred seventy patients were randomly assigned to: (1) intensive vs moderate blood pressure goals (diastolic blood pressure <75 mm Hg or diastolic blood pressure 80 to 89 mm Hg, respectively), and (2) nisoldipine or enalapril. If the target blood pressure was not attained by the study medication, either metoprolol or hydrochlorothiazide was added. Patient baseline characteristics were similar except for a higher incidence of angina, a higher incidence of abnormal ankle-brachial index, and a lower HDL in the enalapril group. Follow-up was complete, and analysis followed the intention-to-treat principle. Within the hypertensive arm of the ABCD trial, a significant increase in cardiovascular events was noted in one group during study follow-up. The safety committee unblinded the study, analyzed the results, and recommended discontinuation of nisoldipine. This study reports only these results; evaluation in the normotensive group continues as part of the larger trial.

Outcomes measured The primary outcomes of this report were the incidence of cardiovascular events (sudden death, progressive heart failure, MI, fatal arrhythmias, stroke, ruptured aortic aneurysm, and pulmonary infarct) and mortality; both were secondary outcomes of the ABCD trial. The mean duration of follow-up was 5 years.

Results No significant difference was found in blood pressure control between the two groups. However, significantly more patients in the ACE inhibitor group compared with the CCB group required the addition of a second antihypertensive medication to reach the target blood pressure (42.1% vs 37.9% metoprolol, 50.6% vs 39.6% hydrochlorothiazide). No differences were noted between groups regarding glycosylated hemoglobin or lipid levels. Rates of medication discontinuation were similar in both groups.

Patients assigned to an ACE inhibitor suffered significantly fewer deaths because of cardiovascular disease (5 vs 10), fewer nonfatal MIs (5 vs 22), and fewer combined fatal and nonfatal MIs (5 vs 25) than those assigned to the CCB. This association was maintained whether moderate or intense blood pressure control was sought. Adjusting for potential confounders, including baseline differences, the CCB group was 7.0 times more likely to have a fatal or nonfatal MI (95% CI, 2.3 - 21.4). No difference was found between groups for stroke, progressive heart failure, or cardiovascular or all-cause mortality.

Recommendations for clinical practice **This study clearly shows an increased risk of MIs for diabetic hypertensives receiving a long-acting CCB compared with those receiving an ACE inhibitor. The interpretation of these results, however, is less clear. These findings may result from a harmful effect of CCBs, a protective effect of ACE inhibitors, or a combination of the two. Another consideration is that more patients in the ACE inhibitor group required the addition of hydrochlorothiazide or a beta-blocker, both of**

which have proven cardiovascular and mortality benefits for patients with hypertension. While the mounting evidence about the potential harm of CCBs has frequently been attributed only to short-acting drugs, this study also raises concern about the long-acting variety. We therefore recommend that antihypertensive treatment focus on effective and inexpensive medications (such as diuretics and beta-blockers), or medications such as ACE inhibitors with potential benefit for patients with diabetes, and avoid medications such as CCBs that are both costly and potentially harmful.

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FINASTERIDE FOR BPH

McConnell JD, Bruskewitz R, Walsh P, et al. The effect of finasteride on the risk of acute urinary retention and the need for surgical treatment among men with benign prostatic hyperplasia. N Engl J Med 1998; 338:557-63.

Clinical question **Does finasteride reduce symptoms, the incidence of acute urinary retention, and the need for surgery in men with benign prostatic hyperplasia (BPH)?**

Background Fifty percent of 50-year-old men have BPH, and the incidence increases by approximately 10% every decade. Finasteride, a selective 5α-reductase inhibitor, has previously been shown to modestly improve urinary symptoms and reduce the gland volume in men with enlarged prostates because of BPH. However, the long-term effectiveness of any medical therapy for BPH has not been previously studied.

Population studied Predominately white men with moderate to severe BPH symptoms (scores of 8 to 34 on a "quasi-American Urologic Association [AUA] Symptom Score"), maximum flow rates <15 mL per second, and an enlarged prostate on digital rectal examination (DRE) were studied. Men taking alpha-blockers or antiandrogens and those with a history of chronic prostatitis, recurrent urinary tract infections, prostate cancer, bladder cancer, or a prostate-specific antigen (PSA) of 10 ng/mL or more were excluded.

Study design and validity This was a 4-year, randomized, double-blind, placebo-controlled trial. Patients were randomized to receive either finasteride 5 mg or placebo daily. Symptoms, side effects, and urinary flow rates were assessed every 4 months. After the initiation of the study, the AUA symptom score was adopted as the standard symptom assessment tool. Answers to the original questionnaire were adjusted to approximate the AUA symptom score. Serum PSA levels were measured every 4 months for 1 year and every 8 months thereafter. Patients with baseline PSA levels of 4 ng/mL or higher required a negative prostate biopsy to be admitted into the study. Biopsies were repeated at the study's end. Physical examinations, including DRE and routine blood work, were performed yearly. The intervention and control groups were similar at baseline and subjects were analyzed in the groups to which they were assigned (intention-to-treat analysis). Follow-up was available for 92% of subjects. Shortcomings of this study include that the duration of complaints and previous treatments were not documented, patient satisfaction was not evaluated, there was no description of how the decision for surgery was made, and there was no comparison to alpha-blockers (another common treatment for BPH).

Outcomes measured The primary outcome was the self-administered "quasi-AUA Symptom Score." The secondary endpoints were the need for prostate surgery and the occurrence of acute urinary retention.

Results Of the 3040 men who were randomized, 524 (34%) of the finasteride group and 633 (42%) of the placebo group discontinued treatment, most commonly because of adverse drug effects or treatment failures. The mean decrease in symptom score was 2.6 in the finasteride group and 1.0 in the placebo group. Acute urinary retention developed in 99 men in the placebo group and 42 men in the treatment group (7% vs 3%). The most clinically relevant estimate of effect is the number needed to treat (NNT). In this case, 25 patients would have to be treated for 4 years to prevent one episode of urinary retention (NNT = 25). Surgery was performed on 152 patients in the placebo group and 69 in the finasteride group (10% vs 5%, NNT = 20). Potential harm can be expressed in a similar manner with the number needed to harm (NNH). There was a clinically significant increase in the incidence of impotence (NNH=33) and decreased libido (NNH=23) during the first year of use. These adverse effects were not seen in the second and fourth years of the study.

Recommendations for clinical practice **In this Merck-sponsored study (the makers of finasteride), the finasteride group had a 1.6 point absolute improvement in their symptom score over placebo. While statistically significant, this is not clinically significant: Patients usually report symptomatic improvement only when this score improves by 3 or more. While there was a clinically significant decrease in acute urinary retention and the need for surgery, this is balanced by an equally significant increase in impotence and**