# IV. Routine and Optional Laboratory Tests for the Investigation of Patients with Hypertension

## DIAGNOSIS AND ASSESSMENT

http://guidelines.hypertension.ca/diagnosis-assessment/lab-tests/

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### Recommendations

1. Routine laboratory tests that should be performed for the investigation of all patients with hypertension include the following:
    i. Urinalysis (Grade D);
    ii. Blood chemistry (potassium, sodium, and creatinine) (Grade D);
    iii. Fasting blood glucose and/or glycated hemoglobin (A1c) (Grade D);
    iv. Serum total cholesterol, LDL, HDL, non-HDL cholesterol, and triglycerides (Grade D); lipids may be drawn fasting or non-fasting (Grade C) (revised recommendation);
    v. Standard 12-lead electrocardiography (Grade C).
2. Assess urinary albumin excretion in patients with diabetes (Grade D).
3. All treated hypertensive patients should be monitored according to the current Canadian Diabetes Association guidelines for the new appearance of diabetes (Grade B).
4. During the maintenance phase of hypertension management, tests (including those for electrolyte, creatinine, and fasting lipids) should be repeated with a frequency reflecting the clinical situation (Grade D).

### Background

**1. Routine laboratory tests that should be performed for the investigation of all patients with hypertension include the following:**

**I. URINALYSIS (GRADE D);**

**II. BLOOD CHEMISTRY (POTASSIUM, SODIUM, AND CREATININE) (GRADE D);**

**III. FASTING BLOOD GLUCOSE AND/OR GLYCATED HEMOGLOBIN (A1C) (GRADE D);**

**IV. SERUM TOTAL CHOLESTEROL, LDL, HDL, NON-HDL CHOLESTEROL, AND TRIGLYCERIDES (GRADE D); LIPIDS MAY BE DRAWN FASTING OR NON-FASTING (GRADE C) (REVISED RECOMMENDATION);**

**V. STANDARD 12-LEAD ELECTROCARDIOGRAPHY (GRADE C).**

There is little direct evidence on which to base recommendations for laboratory testing. Thus, the recommended tests have been based largely on expert opinion. However, the routine laboratory investigations are recommended for the following reasons. First, abnormalities in these tests are common. For example in the Prospective Cardiovascular Muenster (PROCAM) study, 20% of subjects with hypertension had hyperlipidemia and 10% had diabetes mellitus (1). Second, the screening for abnormal serum biochemistry ensures appropriate selection of drug therapy when necessary. For example, caution is warranted if diuretic therapy is considered for patients with hypokalemia or if an angiotensin-converting enzyme (ACE) inhibitor is considered for patients with elevated creatinine levels. Third, these investigations also aid in the determination of the risk of cardiovascular disease for patients with hypertension based on the presence or severity of concomitant vascular risk factors. As such, the results may shorten the diagnostic phase (if target organ damage is present), define a higher risk group or affect the choice of first-line therapy. For example, an EKG may reveal the presence of left ventricular hypertrophy (LVH) or a prior myocardial infarction, both of which portend a higher risk of future cardiovascular events and death (2,3). Finally, both the routine and optional investigations aid in the screening for some of the modifiable causes of hypertension. For example recurrent and/or severe hypokalemia may indicate the presence of primary hyperaldosteronism.

When compared with oral glucose tolerance testing, a systematic review suggests that A1C and fasting glucose levels demonstrate comparable sensitivity and specificity for diabetes detection (4). In a more recent analysis of more than 2000 adults at high risk for diabetes, Hu and colleagues determined the sensitivity and specificity for diabetes of A1C and fasting glucose to be virtually identical (about 80%) at the thresholds evaluated. In addition, when both tests were combined, sensitivity (96.5%) and specificity (96.3%) increased (5). The addition of A1C harmonizes the CHEP recommendations with those of the Canadian Diabetes Association (6).

**2. Assess urinary albumin excretion in patients with diabetes (Grade D).**

Assessment of urinary albumin excretion is no longer used as a basis for targeting lower BP, but is used to guide treatment of hypertension in association with diabetes mellitus. If albuminuria is present, therapy with a renin angiotension system blocker (ACE inhibitor or angiotensin receptor antagonist) is indicated (please see relevant treatment recommendation for further details) (7,8).

In patients without diabetes, urine albumin to creatinine ratio (ACR) is not recommended. Although an independent predictor of future cardiovascular events (9-11), the evidence is not considered strong enough at this time to recommend routine screening of urine albumin levels in people with hypertension who do not have diabetes.

**3. All treated hypertensive patients should be monitored according to the current Canadian Diabetes Association guidelines for the new appearance of diabetes (Grade B).**

The Canadian Diabetes Association guidelines can be found online (www.guidelines.diabetes.ca). In part, hypertensive patients are at higher risk for developing type 2 diabetes because of the tendency of cardiometabolic risk factors to cluster, particularly with central adiposity (12-14). At minimum, new-onset diabetes occurs in 1% to 2% of hypertensive patients per year (15,16) and is independent of the type of antihypertensive therapy (17). Among 18,411 nondiabetic hypertensive patients 55 years of age or older who had follow-up measurements of fasting plasma glucose (43% of the original cohort), the cumulative incidence of diabetes was 8% to 11% at four years (17). Furthermore, the prognosis of patients who develop diabetes is worse than those who do not (15-19). After 14.3 years of follow-up in the placebo arm of the Systolic Hypertension in Elderly Patients (SHEP) trial (18) (age older than 60 years), there was a significant increase in the cardiovascular mortality (hazard ratio [HR] 1.56; 95% CI 1.12 to 2.18) and total mortality (HR 1.35; 95% CI 1.05 to 1.73) among those who developed diabetes.

Although based on weaker evidence, the type of antihypertensive drug treatment also appears to influence future risk of type 2 diabetes (12,13). Studies suggest that both beta-blockers and thiazides are associated with an increased risk of diabetes, and angiotensin-converting enzyme inhibitors, angiotensin receptor blockers and calcium channel blockers are neutral or associated with decreased risk (12). However, in the Diabetes REduction Assessment with ramipril and rosiglitazone Medication (DREAM) trial (20) (three-year randomized controlled trial involving 5269 prediabetic patients), ramipril did not significantly reduce the incidence of type 2 diabetes (HR 0.91, 95% CI 0.81 to 1.03) or mortality. Thus, no specific antihypertensive drugs are currently recommended to prevent the development of diabetes mellitus. It is important to note that there are currently no conclusive data that directly implicate drug-induced type 2 diabetes with increased cardiovascular risk (18). Furthermore, in patients with or without diabetes, thiazide-based treatment regimens reduce cardiovascular and overall mortality to a similar extent as ‘nondiabetogenic’ agents (21). The task force will continue to monitor this area closely and issue updated recommendations as required.

**4. During the maintenance phase of hypertension management, tests (including those for electrolyte, creatinine, and fasting lipids) should be repeated with a frequency reflecting the clinical situation (Grade D).**

Follow-up lab testing may be indicated to monitor for adverse effects of antihypertensive treatment, as surveillance for the development of end-organ damage and/or to re-stratify cardiovascular risk. The need for such testing differs across hypertensive patients and, in the absence of specific studies to define the optimal testing frequency, is left to the judgment of individual clinicians.

## References


1. Assmann G, Schulte H. The Prospective Cardiovascular Muenster (PROCAM) study: prevalence of hyperlipidemia in persons with hypertension and/or diabetes mellitus and the relationship to coronary heart disease. Am Heart J 1988;116: 1713-24.
2. Kahn S, Frishman WH, Weissman S, Ooi WL, Aronson M. Left ventricular hypertrophy on electrocardiogram: prognostic implications from a 10-year cohort study of older subjects: a report from the Bronx Longitudinal Aging Study. J Am Geriatr Soc 1996;44:524-529.
3. Lonn E, Mathew J, Pogue J, et al. Relationship of electrocardiographic left ventricular hypertrophy to mortality and cardiovascular morbidity in high-risk patients. Eur J Cardiovasc Prevent Rehab. 2003;10:420-428.
4. Bennett CM, Guo M, Dharmage SC. HbA1c as a screening tool for detection of Type 2 diabetes: a systematic review. Diabet Med 2007;24: 333-43.
5. Hu Y, Liu W, Chen Y, et al. Combined use of fasting plasma glucose and glycated hemoglobin A1c in the screening of diabetes and impaired glucose tolerance. Acta Diabetol 2010;47:231-6.
6. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2013 clinical practice guidelines for the prevention and management of diabetes in Canada. Can J Diabetes 2013;37(suppl 1):S1-212.
7. Krolewski AS, Warram JH, Freire MB. Epidemiology of late diabetic complications. A basis for the development and evaluation of preventive programs. Endocrinol Metab Clin North Am 1996;25:217-42.
8. Meltzer S, Leiter L, Daneman D, et al. 1998 clinical practice guidelines for the management of diabetes in Canada. Canadian Diabetes Association. CMAJ 1998;159:S1-29.
9. Olsen MH, Wachtell K, Ibsen H, et al; LIFE Study Investigators. Reductions in albuminuria and in electrocardiographic left ventricular hypertrophy independently improve prognosis in hypertension: The LIFE study. J Hypertens 2006;24:775-81.
10. Dyer AR, Greenland P, Elliott P et al; INTERMAP Research Group. Evaluation of measures of urinary albumin excretion in epidemiologic studies. Am J Epidemiol 2004;160:1122-31.
11. Gansevoort RT, Brinkman J, Bakker SJ, De Jong PE, de Zeeuw D. Evaluation of measures of urinary albumin excretion. Am J Epidemiol 2006;164:725-7.
12. Elliott WJ, Meyer PM. Incident diabetes in clinical trials of antihypertensive drugs: A network meta-analysis. Lancet 2007;369:201-7. (Erratum in 2007;369:1518).
13. Padwal R, Laupacis A. Antihypertensive therapy and incidence of type 2 diabetes: A systematic review. Diabetes Care 2004;27:247-55.
14. Gress TW, Nieto FJ, Shahar E, Wofford MR, Brancati FL. Hypertension and antihypertensive therapy as risk factors for type 2 diabetes mellitus. Atherosclerosis Risk in Communities Study. N Engl J Med 2000;342:905-12.
15. Verdecchia P, Reboldi G, Angeli F, et al. Adverse prognostic significance of new diabetes in treated hypertensive subjects. Hypertension 2004;43:963-9.
16. Almgren T, Wilhelmsen L, Samuelsson O, Himmelmann A, Rosengren A, Andersson OK. Diabetes in treated hypertension is common and carries a high cardiovascular risk: Results from a 28-year follow-up. J Hypertens 2007;25:1311 7.

17. Barzilay JI, Davis BR, Cutler JA, et al; ALLHAT Collaborative Research Group. Fasting glucose levels and incident diabetes mellitus in older nondiabetic adults randomized to receive 3 different classes of antihypertensive treatment: A report from the Antihypertensive and Lipid- Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). Arch Intern Med 2006;166:2191- 201.
18. Kostis JB, Wilson AC, Freudenberger RS, Cosgrove NM, Pressel SL, Davis BR; SHEP Collaborative Research Group. Long-term effect of diuretic-based therapy on fatal outcomes in subjects with isolated systolic hypertension with and without diabetes. Am J Cardiol 2005;95:29- 35.
19. Aksnes TA, Kjeldsen SE, Rostrup M, Omvik P, Hua TA, Julius S. Impact of new-onset diabetes mellitus on cardiac outcomes in the Valsartan Antihypertensive Long-term Use Evaluation (VALUE) trial population. Hypertension 2007;50:467-73.
20. The DREAM Trial Investigators. Effect of ramipril on the incidence of diabetes. N Engl J Med 2006;355:1551-62.
21. ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). JAMA 2002;288:2981-2997.