Screening for Adrenal-Endocrine Hypertension: Overview of Accuracy and Cost-effectiveness

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KEYWORDS

• Screening • Secondary hypertension • Adrenal
• Diagnostic accuracy

Hypertension is a highly prevalent disorder afflicting 29% of adults in the United States.[1] It is a major risk factor for cardiovascular disease morbidity and mortality including myocardial infarction, congestive heart failure, stroke, renal disease, and dementia.[2–5] Multiple treatment trials have clearly shown the effectiveness of blood pressure control in preventing cardiovascular disease events.[6,7] Although control rates are improving, approximately 50% of adults with hypertension remain uncontrolled.[1] Most adults with increased blood pressure have primary or essential hypertension for which the cause is unknown. Generally, lifelong treatment is required. The proportion of patients with secondary or identifiable causes of hypertension is uncertain. Older studies suggest that secondary forms account for less than 10% of hypertension.[8] However, with the development of newer screening and diagnostic procedures, the frequency of some secondary forms of hypertension may be higher than previously believed.[9] Detection of secondary hypertension is important because, depending on the cause, it may be possible to cure the hypertension or tailor therapy to achieve control with fewer medications, reducing cost and side effects. In the case of endocrine causes of hypertension, identification is also important because undetected disorders can be fatal and confer adverse effects beyond those caused by increased blood pressure.

This article focuses on issues of accuracy and cost-effectiveness of screening strategies for 2 important endocrine causes of hypertension: primary aldosteronism,

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a common secondary cause of hypertension; and pheochromocytoma, a rare secondary cause of hypertension. Cost-effectiveness of screening involves an understanding of the clinical contexts where the likelihood of these disorders is high enough to justify testing and where the potential adverse clinical consequences of missing the diagnosis justify the expense and risks associated with screening. It also requires an understanding of the diagnostic accuracy of current screening tests and strategies and the effect of positive and negative results on the probability of disease to limit further diagnostic investigations to those most likely to have one of these disorders.

BASICS OF COST-EFFECTIVENESS OF HEALTH INTERVENTIONS

Formal cost-effectiveness analysis is an analytical tool that assesses the costs and effects of an intervention designed to prevent, diagnose, or treat a disease compared with an alternative strategy designed to achieve the same goals.[10,11] A ratio is constructed in which the numerator is the net expenditure of health care resources (a monetary measure) and the denominator is the net improvement in health (a nonmonetary measure). In the context of the present discussion, for each of the endocrine causes of hypertension, the immediate costs are those associated with performing the relevant screening test(s) and any subsequent tests required to confirm the diagnosis and, where necessary, to identify subtypes of disease as well as costs related to any disease-specific interventions. Additional costs considered are those caused by patient time expended (lost wages), caregiving (paid or unpaid), travel expenses, and economic costs to employers. The most common measure of net improvement in health used in the denominator is quality-adjusted life years (QALYs) gained. The final value of the cost-effectiveness ratio represents the marginal effects in both the numerator and the denominator of the intervention compared with the alternative strategy, which, in the context of this discussion, represents the costs related to management of the blood pressure in the setting of an unrecognized endocrine cause and the estimated effect of missing the diagnosis on QALYs. No formal cost-effectiveness analyses have been performed for screening for the endocrine causes of hypertension considered here. The marginal effects on cost and health improvement arising from screening for endocrine causes of hypertension can only be discussed in general terms in this article.

PRINCIPLES UNDERLYING ACCURACY OF DIAGNOSTIC TESTING

Use of a screening test to evaluate for the presence of a disease requires an understanding of the mathematical relationships between test characteristics (ie, sensitivity and specificity) as well as some estimate of the likelihood that the disease is present (pretest probability) in various clinical contexts.[12] The relationship of a screening test result and the presence or absence of a disease is shown in **Fig. 1**. In this scheme, the screening test results are interpreted as either being positive or negative using a defined cut-point value (which is the case for most screening tests for endocrine hypertension). Sensitivity is defined as the proportion of people with the disease who have a positive test result. Specificity is the proportion of people without the disease who have a negative test result. As discussed in more detail later, sensitivity and specificity have not been clearly determined for many of the screening tests used to evaluate for endocrine hypertension. In part, this is because of the lack of an established gold standard used across studies to define the presence of the disease. Different gold standards for diagnosis yield different estimates of sensitivity and specificity. In addition, negative results of screening tests are less well studied than positive results in the medical literature because of a reluctance to perform confirmation