V. Assessment for Renovascular Hypertension

DIAGNOSIS AND ASSESSMENT

http://guidelines.hypertension.ca/diagnosis-assessment/renovascular-hypertension/

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Recommendations

1. Patients presenting with ≥ 2 of the following clinical clues, suggesting renovascular hypertension, should be investigated (Grade D):
    i. Sudden onset or worsening of hypertension and age > 55 or < 30 years;
    ii. Presence of an abdominal bruit;
    iii. Hypertension resistant to ≥ 3 drugs;
    iv. Increase in serum creatinine level ≥ 30% associated with use of an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB);
    v. Other atherosclerotic vascular disease, particularly in patients who smoke or have dyslipidemia;
    vi. Recurrent pulmonary edema associated with hypertensive surges.
2. When available, the following tests are recommended to aid in the usual screening for renal vascular disease: captopril-enhanced radioisotope renal scan, Doppler sonography, magnetic resonance angiography, and computed tomography angiography (for those with normal renal function) (Grade B). Captopril-enhanced radioisotope renal scan is not recommended for those with CKD (glomerular filtration rate < 60 mL/min/1.73m2) (Grade D).

Background

1. Patients presenting with ≥ 2 of the following clinical clues, suggesting renovascular hypertension, should be investigated (Grade D):

I. SUDDEN ONSET OR WORSENING OF HYPERTENSION AND AGE > 55 OR < 30 YEARS;

II. PRESENCE OF AN ABDOMINAL BRUIT;

III. HYPERTENSION RESISTANT TO ≥ 3 DRUGS;

IV. INCREASE IN SERUM CREATININE LEVEL ≥ 30% ASSOCIATED WITH USE OF AN ANGIOTENSIN-CONVERTING ENZYME (ACE) INHIBITOR OR ANGIOTENSIN RECEPTOR BLOCKER (ARB);

V. OTHER ATHEROSCLEROTIC VASCULAR DISEASE, PARTICULARLY IN PATIENTS WHO SMOKE OR HAVE DYSLIPIDEMIA;

VI. RECURRENT PULMONARY EDEMA ASSOCIATED WITH HYPERTENSIVE SURGES.

Historical Perspective

Experiments by Goldblatt and colleagues established that narrowing of the renal artery results in significant impairment of renal blood flow, induces renal renin release, increases central sympathetic activity, and leads to arterial hypertension. These experiments were carried out during the first half of the last century. As treatment of severe hypertension at that time was limited to nearly complete dietary salt restriction or dorsal lumbar sympathectomy, surgical treatment (renal autotransplantation and/or bypass of the renal artery) was a reasonable alternative treatment option for renovascular disease. However, early studies showed that revascularization led to cure of hypertension in only in a small number of patients. In the subgroup of patients who did not respond at all to revascularization, it is probable that the renal artery stenosis was not severe enough to cause renovascular hypertension. In those with only a partial response to revascularization, renal artery stenosis likely played only a partial role in the maintenance of hypertension.

With the advent of interventional radiology, surgical revascularization was replaced with renal angioplasty alone and, subsequently, with renal angioplasty and stenting. However, as discussed below, currently there is limited role for angioplasty and stenting in the management of patients with atherosclerotic renovascular disease.

Types of Renovascular Disease

Two major types of renal artery stenosis exist – fibromuscular dysplasia and atherosclerotic renal artery stenosis (the latter is more common). Fibromuscular dysplasia primarily affects younger (<40 year old) females. As the prevalence of hypertension below age 40 is relatively low, the presence of hypertension at this age more likely indicates either secondary form of hypertension and/or use of

drugs/substances causing high blood pressure. In this situation, especially in the absence of an obvious contributor to early onset hypertension (such as obesity), testing for renovascular hypertension appears justified, as fibromuscular dysplasia is treatable by renal angioplasty or surgery. Angioplasty is much less invasive and, therefore, the initial treatment of choice. High cure rates have been reported in early case series of surgery or renal artery angioplasty for fibromuscular dysplasia (4-6). A 2010 meta-analysis of 47 angioplasty (1616 patients) and 23 surgical studies (1014 patients) reported lower (yet still clinically important) cure rates – 36% with angioplasty and 54% with surgery (7).

In contrast, atherosclerotic renal artery stenosis usually occurs after 50 years, when prevalence of hypertension is close to 50%. The presence of renal artery stenosis per se is no longer an automatic indication for revascularization. This is because anatomical renal artery stenosis may not be functionally relevant (i.e., it may not cause sufficient impairment of renal blood flow to precipitate renovascular hypertension) or may already have caused permanent ischemic changes in the affected kidney. In both instances, revascularization would result in no or only a partial response to revascularization.

Recent randomized controlled trials and meta-analyses have shown that neither blood pressure nor cardiovascular events are reduced in patients undergoing renal artery angioplasty compared to optimal medical therapy alone (1-3). Thus, by default, testing for atherosclerotic renal artery stenosis is not routinely warranted; instead cardiovascular risk factors (blood pressure, lipids, smoking, and glycemic control) should be optimized instead. Treatment of renovascular hypertension could be still considered in some instances (for only those patients excluded from trials comparing pharmacotherapy with revascularization), namely those with hypertension resistant to the pharmacotherapy, progressive renal function loss, and those with an episodic acute heart failure secondary to cardiac pressure overload (provided cardiac ischemia has been ruled out).

The criteria cited above that may prompt screening for renovascular hypertension among patients with hypertension have been independently associated with the presence of renal artery stenosis in multivariable analyses. These include age (odds ratio [OR]=l.8/10-year increase), recent onset of hypertension (OR=l.9), the presence of an abdominal bruit (OR=5.4), atherosclerotic vascular disease (OR=1.8) or other vascular risk factors (smoking OR= 1.6, hypercholesterolemia OR=l.7) (8).

While rises in creatinine levels among patients with hypertension may increase suspicion for renovascular cause, this laboratory finding is neither sensitive (less than 10% for bilateral renal artery stenosis (11)) nor specific (particularly for patients on diuretics or low sodium diets (12)). A small rise in creatinine levels of up to 10% with an ACE- inhibitor is a particularly poor indicator of renovascular hypertension. This is because a rise of this magnitude or less occurs with many patients treated with an ACE inhibitor, and likely reflects a drop in intraglomerular pressure. This may be one of the mechanisms whereby ACE inhibitors confer their renal protective effects (13,14). First, a threshold value of 30% or greater for the serum creatinine concentration increase

associated with angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker therapy has been specified to differentiate cases of possible renovascular disease from those of smaller rises in serum creatinine levels that are often normally associated with these agents (15).

2. When available, the following tests are recommended to aid in the usual screening for renal vascular disease: captopril-enhanced radioisotope renal scan, Doppler sonography, magnetic resonance angiography, and computed tomography angiography (for those with normal renal function) (Grade B). Captopril-enhanced radioisotope renal scan is not recommended for those with CKD (glomerular filtration rate < 60 mL/min/1.73m2) (Grade D).

The optimal test for diagnosing renovascular hypertension depends, to a large extent, on local radiological expertise and the underlying clinical situation (e.g., presence of renal failure). Selective renal angiography is the gold standard (16). CT angiography and MR angiography are less invasive and commonly used alternative imaging techniques but they have lower sensitivity and specificity, especially in patients with suspected fibromuscular dysplasia with mid or distal renal artery disease for which these tests could be falsely negative (16) (19). MR angiography is contraindicated in patients with eGFR <30 ml/min/172 m2 because of the risk of gadolinium-induced dermatofibrosis. Duplex ultrasonography is another non-invasive alternative but is technically difficult and operator dependent (17,18).

Based on a 2001 meta-analysis (20), in which angiography was the gold standard and the area under the receiver-operating characteristic curve was used as a measure of the diagnostic performance of the tests, magnetic resonance angiography and computed tomography-angiography had the best performance statistics in detecting radiographic stenoses, followed by Doppler sonography and captopril-enhanced radioisotope renal scan (20).

ACE-inhibited radionucleotide testing (usually the captopril renogram) has historically been a commonly employed screening tool for renovascular hypertension. The test has been estimated to have a sensitivity and specificity of 83% to 91% and 93% to 94%, respectively, when renal angiography is adopted as the reference standard (21-24). Furthermore, Setaro et al (21,22) estimated the sensitivity and specificity to be 83% and 81%, respectively, when using clinical blood pressure response to revascularization as the reference standard. More recently, others have reported lower sensitivity rates (60% to 70%) with radionucleotide testing (25,26), highlighting the importance of clinical judgment and pretest probability. The diagnostic accuracy of captopril-renal scanning is poor in the setting of GFR below 60 mL/min/1.73 m2 (27).

Duplex ultrasound is widely available and can provide both anatomical and functional assessment of renal artery stenosis and is useful in renal failure when other tests are inaccurate or contraindicated. However, the sensitivity and specificity vary considerably among different centres. The technique is time consuming and highly operator dependent (28,29). Galactose-based echocardiography-enhanced duplex ultrasound may produce higher quality images of the renal artery than conventional colour Doppler echocardiography.

The role of gadolinium-enhanced magnetic resonance (MR) angiography as either a screening test or an alternative to conventional angiography remains to be determined. The limiting factors of this technique include inadequate visualization of segmental and accessory renal arteries, a tendency toward overestimation of stenoses, risk of nephrogenic systemic fibrosis if GFR is less than 30 ml/min/1.73 m2, and the high cost and low availability of MR facilities (31-36).

In the setting of a documented anatomical stenosis, evidence that the stenosis is functionally significant can be given by the following: degree of stenosis (>70% of the lumen area), pressure gradient over the stenosis (> 21 mmHg), lateralization of renal vein plasma renin activity, high arterial resistance index on Doppler ultrasound, delayed contrast accumulation and excretion on intravenous pyelogram, and impaired renal blood flow in response to angiotensin converting enzyme inhibitor on captopril renogram (these last two methods are not indicated for patients with eGFR , 30 ml/min/1.72 m2) (38).

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