Secondary Hypertension: Diagnosis and Management of an Adrenal Adenoma

Case Study and Commentary, Miho Tagawa, MD, and Debbie L. Cohen, MD

Abstract

- **Objective:** To review the assessment of secondary hypertension and the management of an adrenal adenoma.

- **Methods:** Literature review focusing on recent guidelines on hypertension (especially resistant hypertension and secondary hypertension), primary aldosteronism, and adrenal adenoma. Original articles were reviewed when indicated.

- **Results:** Secondary hypertension should be suspected in selected patients. Primary aldosteronism is more prevalent than previously thought. If suspected, patients should be screened for primary aldosteronism using a plasma aldosterone-to-renin ratio. Adrenal venous sampling plays an important role in deciding whether surgery is an option in the management of adrenal adenoma. The management of atherosclerotic renal artery stenosis should be individualized and percutaneous revascularization should be considered cautiously.

- **Conclusion:** It is important to identify patients with secondary hypertension as they often require different management strategies and may have a potentially curable form of hypertension.

Hypertension remains a major public health issue. Approximately 65 million adults in the United States have hypertension [1,2]. Although rates of hypertension control have increased from 27% to 35%, the prevalence of hypertension has also continued to increase [1,2]. Hypertension is associated with an increased risk of cardiovascular morbidity and mortality [3]. Treatment of hypertension is worthwhile: clinical trials have shown that by lowering blood pressure with the use of antihypertensive medications there is a decreased risk of stroke, myocardial infarction, end-stage renal disease, and heart failure [4].

However, compliance with medications remains problematic as many of the antihypertensive medications are associated with side effects. It has also been noted that some forms of secondary hypertension, such as renal artery stenosis and primary aldosteronism, may be associated with a higher risk of cardiovascular morbidity compared with essential hypertension even with the same level of hypertension [5,6]. Given these costs and risks, it is imperative to diagnose and manage potentially curable forms of secondary hypertension in appropriately selected patients.

**CASE STUDY**

**Initial Presentation**

A 65-year-old white woman was referred to the hypertension clinic for refractory hypertension.

**History**

The patient had been diagnosed 6 months ago with hypertension by her primary care physician. She had been strictly adhering to lifestyle modifications, including dietary sodium restriction and increased aerobic exercise regimen, and had required the addition of 3 antihypertensive medications (valsartan 320 mg daily, hydrochlorothiazide 25 mg daily, and amlodipine 10 mg daily). Despite being compliant with both lifestyle modification and medications, her blood pressure remained in the range of 160–170/90–100 mm Hg. The patient had regular annual physical examinations and blood pressure had been normal at prior office visits.

The patient reported no symptoms. She denied taking any over-the-counter medications or herbal or vitamin supplements. She was currently taking potassium supplements with her antihypertensive regimen. She had a negative family history of hypertension, renal disease, and endocrine disease.

**Physical Examination**

On physical examination height was 5’7” and weight was 170 lb, with a body mass index of 26.6. Blood pressure was 174/96 mm Hg and when repeated after 5 minutes was 168/84 mm Hg. Pulse rate was 86 bpm and regular. Funduscopic examination showed arteriolar narrowing. Heart and lung examinations were normal. The abdomen was benign.
and there was no epigastric bruit present. Examination of the extremities showed good peripheral pulses and no pedal edema.

**Testing**

A 12-lead electrocardiogram was normal. Serum creatinine, electrolytes (on potassium supplement), fasting glucose, and lipid profile were normal. Urinalysis was normal.

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**What is essential in the clinical evaluation of the hypertensive patient?**

The first step of evaluation of hypertensive patients is a thorough medical history. It should include the onset of hypertension, review of systems to assess associated symptoms, all the medications including over-the-counter medication, supplements (eg, herbal, vitamins), the use of illicit drugs, habitual history (alcohol and smoking), family history of hypertension, renal, or endocrine diseases. Anxiety, the presence of panic attacks, depression, and quantitative and qualitative nature of sleep should also be assessed.

The physical examination should include body weight to calculate the body mass index, appropriate blood pressure measurements in all 4 extremities (to exclude coarctation of the aorta), an examination of the fundi to assess for changes seen with hypertensive retinopathy, auscultation for carotid, abdominal and femoral bruits, palpitation of the thyroid gland, thorough examination of the heart and lungs, examination of the abdomen for enlarged kidneys, masses or bladder distention, and abnormal aortic pulsation, palpation of the lower extremities for edema and pulses and neurological examinations.

Laboratory tests should include urinalysis, a chemistry panel including measurement of serum creatinine, potassium, and fasting glucose, and a lipid panel. Urinalysis and serum creatinine are for the evaluation of renal parenchymal diseases and fasting serum glucose for the screening for diabetes. Low serum potassium may indicate primary aldosteronism. Hyperlipidemia should be treated according to the National Cholesterol Education Program guidelines [9]. Twelve-lead electrocardiography should be performed to assess for left ventricular hypertrophy. Optional tests include urinary albumin/creatinine ratio and echocardiogram (echocardiogram has higher sensitivity for left ventricular hypertrophy than electrocardiogram [10]).

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**What is the etiology of hypertension?**

About 90% of patients have primary, or essential, hypertension; the remaining 10% have hypertension attributed to secondary causes [7]. With the advance of screening tests and increasing awareness that secondary causes of hypertension are more prevalent than previously thought, the reported rate of secondary causes of hypertension is increasing (Table 1). Common and uncommon forms of secondary hypertension are shown in Table 2 [8]. There are 2 common types of secondary hypertension: renal and adrenal. These 2 causes account for more than 90% of all cases of secondary hypertension. Other causes of secondary hypertension include medications (nonsteroidal anti-inflammatory drugs, nasal decongestants,

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**Table 1. Incidence of Essential and Secondary Hypertension Among Hypertensive Patients in Comparison with Previous Reports**

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Number of patients examined</td>
<td>1020</td>
<td>4429</td>
<td>3783</td>
<td>1000</td>
<td>665</td>
</tr>
<tr>
<td>Essential hypertension (%)</td>
<td>90.9</td>
<td>89.5</td>
<td>92.1</td>
<td>95.3</td>
<td>94.0</td>
</tr>
<tr>
<td>Renal hypertension (%)</td>
<td>0*</td>
<td>1.8</td>
<td>5.6</td>
<td>2.4</td>
<td>5.0</td>
</tr>
<tr>
<td>Primary aldosteronism (%)</td>
<td>6.0</td>
<td>1.5</td>
<td>0.3</td>
<td>0.1</td>
<td>ND</td>
</tr>
<tr>
<td>Renovascular hypertension (%)</td>
<td>0.5</td>
<td>3.3</td>
<td>0.7</td>
<td>1.0</td>
<td>0.2</td>
</tr>
<tr>
<td>Cushing's syndrome (%)</td>
<td>1.0</td>
<td>0.6</td>
<td>0.1</td>
<td>0.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Preclinical Cushing's syndrome (%)</td>
<td>1.0</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Pheochromocytoma (%)</td>
<td>0.6</td>
<td>0.3</td>
<td>0.1</td>
<td>0.2</td>
<td>ND</td>
</tr>
<tr>
<td>Others (%)</td>
<td>0</td>
<td>0</td>
<td>1.0</td>
<td>0.8</td>
<td>0.4</td>
</tr>
</tbody>
</table>

ND = not determined. (Reprinted with permission from reference 7.)

*Patients with renal failure were excluded from this investigation.
When should secondary hypertension be suspected?

As discussed above, more than 90% of patients with hypertension have essential hypertension. Thus, performing screening tests for secondary causes of hypertension for all patients with hypertension is neither necessary nor cost-effective. Screening for secondary causes should be performed in selected cases where there is an increased suspicion of secondary hypertension (Table 3). Epigastric bruit, recurrent flash pulmonary edema, and worsening of renal function with the initiation of angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers are suggestive of renal artery stenosis. Unprovoked hypokalemia or severe diuretic-induced hypokalemia is suggestive of primary aldosteronism, although normal serum potassium does not preclude the possibility. Triad of headache, palpitations, and sweating is suggestive of pheochromocytoma. Differential blood pressure measurements in the arms and legs or radiofemoral pulse delay are suggestive of coarctation of the aorta. Drug-resistant hypertension or refractory hypertension is defined as blood pressure that remains above goal in spite of the concurrent use of 3 antihypertensive agents of different classes. Ideally, 1 of the 3 agents should be a diuretic and all agents should be prescribed at optimal dose amounts [8]. One should note that common causes of resistant hypertension are noncompliance to lifestyle modification or pharmacological treatment, inadequate or inappropriate treatment or exogenous substances such as cocaine, or over-the-counter medication including nonsteroidal anti-inflammatory drugs, and sympathomimetics, rather than secondary causes.

Is there reason to be concerned about a secondary cause or component to the patient’s elevated blood pressure?

The patient developed hypertension at age 65. She has refractory hypertension despite taking appropriate doses of 3 antihypertensive medications and unprovoked hypokalemia. Consideration of primary aldosteronism in this patient is appropriate.

Further History

The patient had an episode of abdominal pain 2 months ago and visited an emergency room, where a computed tomography (CT) scan of the abdomen and pelvis was performed. She was diagnosed with acute gastroenteritis, and abdominal pain resolved with symptomatic treatment. The CT scan incidentally revealed a 1.5 cm right adrenal mass.

What is the workup of an adrenal mass?

Adrenal masses are not uncommon findings in the general population. In a review of 25 studies, the overall frequency of adrenal adenomas in 87,065 autopsies was 6% [11,12]. The incidence of adrenal incidentaloma by abdominal CT taken for various reasons was reported to be 4% in a recent study [13]. The prevalence of adrenal adenoma increases with increasing age [11,12]; the probability of finding an unsuspected adrenal adenoma on abdominal CT in a patient

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**Table 2. Secondary Causes of Hypertension**

<table>
<thead>
<tr>
<th>Common</th>
<th>Uncommon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obstructive sleep apnea</td>
<td>Pheochromocytoma</td>
</tr>
<tr>
<td>Renal parenchymal disease</td>
<td>Cushing’s disease</td>
</tr>
<tr>
<td>Primary aldosteronism</td>
<td>Hyperparathyroidism</td>
</tr>
<tr>
<td>Renal artery stenosis</td>
<td>Aortic coarctation</td>
</tr>
<tr>
<td>Uncompromised</td>
<td>Intracranial tumor</td>
</tr>
</tbody>
</table>

Adapted with permission from reference 8.

**Table 3. Findings That Should Increase Suspicion for Secondary Hypertension**

- New-onset hypertension in patients < 30 years or > 50 years
- Drug-resistant hypertension
- Hypertension that has been easy to control but is now resistant
- Accelerated hypertension
- Negative family history for hypertension
- Abnormal renal function or urinalysis
- Unprovoked hypokalemia
- Epigastric bruit, especially if a diastolic component is present
- Recurrent flash pulmonary edema
- Worsening of renal function with the initiation of angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers
- Differential blood pressure measurements in the arms and legs or radiofemoral pulse delay
- Triad of symptoms: headache, sweating, and palpitations

Adapted with permission from reference 8.
between 20 and 29 years of age would be approximately 0.2%, as compared with approximately 7% in a patient over 70 years of age. The majority of adrenal masses are nonfunctional and benign adenomas [14].

Although the optimal diagnostic approach to a patient who has an adrenal incidentaloma has not been established, one reasonable algorithm suggested is shown in Figure [15].

The screening for primary aldosteronism is the measurement of aldosterone-to-renin ratio (ARR). One should note that there are different assays and units for renin (plasma renin activity [ng/mL/hr] and direct renin concentration [mU/L]) or aldosterone (1 ng/dL converts to 277 pmol/L). The cut-off values for ARR for the screening of primary aldosteronism have been debated. In 1 study, the sensitivity and specificity of different cut-off values were examined using a receiver-operating characteristics curve. In that particular study, upright ARR of 40 gave 100% sensitivity and 84.4% specificity, whereas ARR of 25 gave 100% sensitivity and 73% specificity [16]. A commonly used cut-off value for a positive screening for primary aldosteronism is an ARR of 30 (plasma aldosterone concentration in ng/dL divided by plasma renin activity in ng/mL/hr) [17]. Most investigators also require a plasma aldosterone concentration greater than 15 ng/dL for a positive screening test [18,19], although it is controversial and 1 study found a smaller concentration in 36% of patients with confirmed primary hyperaldosteronism [20]. It should be noted that hypokalemia suppresses plasma aldosterone concentration and optimally should be corrected when ARR is
measured. Mineralocorticoid antagonists must be stopped at least for 4 weeks before the measurement of ARR. Preferably, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, β blockers and diuretics should be replaced by α1 blocker, doxazosin, or long-acting calcium channel blockers [19]; however, it is not mandatory [21] and is rarely done as it is not practical.

More than 50% of patients with pheochromocytoma present with hypertension, though some may be asymptomatic [22,23], and 25% of patients with pheochromocytoma will have chronic hypertension. The best screening test for pheochromocytoma is the measurement of plasma free metanephrines and normetanephrine. It offers 97% sensitivity and 96% specificity for the diagnosis of pheochromocytoma [24].

For the screening for Cushing’s or subclinical Cushing’s syndrome, an overnight dexamethasone (1 mg) suppression test is recommended. Though the optimal cut-off value is debated, cortisol level greater than 1.8 μg/dL is often used as suggested by Endocrine Society guidelines [25].

### Additional Testing in This Patient

After valsartan and hydrochlorothiazide were replaced with doxazosin, the plasma renin activity was 0.1 ng/mL/hr and plasma aldosterone concentration was 55 ng/dL. Plasma metanephrine and normetanephrine were normal. Overnight dexamethasone suppression test revealed a cortisol level of 1.5 μg/dL.

- **Can we make a diagnosis of primary aldosteronism?**

It is recognized that the prevalence of primary aldosteronism is higher than previously thought. A large prospective study showed that the prevalence of primary aldosteronism was 11% in newly diagnosed hypertensives referred to a hypertension clinic [26]. Clinical manifestations of primary aldosteronism include hypertension (often resistant hyper tension), hypokalemia, and metabolic alkalosis. However, only 9% to 37% of patients with primary aldosteronism have hypokalemia [27]; the absence of hypokalemia does not preclude the diagnosis of primary aldosteronism.

As mentioned above, the most commonly used cut-off value for a positive screen for primary aldosteronism is ARR of 30 (plasma aldosterone concentration in ng/dL divided by plasma renin activity in ng/mL/hr) [17]. This patient had ARR of 550. The most recent guidelines from the Endocrine Society recommend performing 1 confirmatory test for primary aldosteronism (Table 4) [17].

### Diagnosis

A diagnosis of primary aldosteronism was made after saline infusion test and spironolactone 50 mg daily was started, which was titrated up to 100 mg twice daily over a 3-month period. Most recent blood pressure was 126/74 mm Hg on spironolactone 100 mg twice daily and amlodipine 10 mg daily. The valsartan and hydrochlorothiazide have been discontinued.

- **Does this patient have an aldosterone-producing adenoma on the right adrenal gland?**

There are 3 major subtypes of primary aldosteronism: aldosterone-producing adenoma, bilateral adrenal hyperplasia, and unilateral adrenal hyperplasia. Although high-resolution CT or magnetic resonance imaging of the abdomen and pelvis is recommended for the workup for patients with primary aldosteronism, the presence of adrenal mass does not automatically lead to the diagnosis of aldosterone-producing adenoma because nonfunctioning adrenal adenomas are common in the general population and may occur incidentally in patients with unilateral or bilateral adrenal hyperplasia. The gold standard for differentiating between

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**Table 4. Confirmatory Tests for Primary Aldosteronism**

<table>
<thead>
<tr>
<th>Test</th>
<th>Procedure</th>
<th>Positive result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral salt loading test</td>
<td>Oral sodium intake &gt; 6 g/day for 3 days then measure 24-hr urine aldosterone</td>
<td>24-hr urinary aldosterone &gt; 12 μg</td>
</tr>
<tr>
<td>Saline infusion test</td>
<td>Measurement of PAC before and after the infusion of 2 L of normal saline at recumbent position</td>
<td>PAC &gt; 10 ng/dL after the infusion</td>
</tr>
<tr>
<td>Fludrocortisone suppression test</td>
<td>0.1 mg oral fludrocortisone every 6 hr for 4 days and then measure PRA and PAC at 10 AM</td>
<td>Upright PAC &gt; 6 ng/dL at 10 AM</td>
</tr>
<tr>
<td>Captopril challenge test</td>
<td>25–50 mg captopril and measure PRA and PAC at time 0, 1, and 2 hr after challenge</td>
<td>No suppression of PAC</td>
</tr>
</tbody>
</table>

PAC = plasma aldosterone concentration; PRA = plasma renin activity. (Adapted with permission from reference 17.)
unilateral (aldosterone-producing adenoma or unilateral adrenal hyperplasia) and bilateral (bilateral adrenal hyperplasia) causes of primary aldosteronism is adrenal venous sampling. In adrenal venous sampling, adrenocorticotropic hormone is infused during the procedure and blood samples for the measurement of aldosterone and cortisol are taken separately from the right and left adrenal veins and inferior vena cava to localize the source of autonomous secretion of aldosterone [28]. Adrenal venous sampling is technically challenging and its success rate ranges from 44% to 95% [29–31]. We generally use lateralization index (ipsilateral plasma aldosterone to cortisol ratio/contralateral plasma aldosterone to cortisol ratio) greater than 4 as a criteria for a lateralization, though there is considerable debate over the criteria [29,32–38].

When CT shows unilateral adrenal abnormality, adrenal venous sampling shows bilateral aldosterone oversecretion or lateralization to the contralateral adrenal gland in 40% to 59% [30,31,39]. On the other hand, when CT shows no abnormality or bilateral adrenal abnormalities, adrenal venous sampling shows lateralization to an adrenal gland in 45% to 67% [30,31,39]. The most recent guideline from the Endocrine Society recommends that adrenal venous sampling should be performed by an experienced radiologist to distinguish between unilateral and bilateral adrenal disease when surgical treatment is considered for primary aldosteronism [17]. Although some groups suggest that adrenal venous sampling is not necessary for patients younger than age 40 with adrenal adenoma on imaging, we agree with the recommendation by Endocrine Society, and all our patients undergo adrenal venous sampling before proceeding with surgery.

Adrenal Venous Sampling

The patient underwent adrenal venous sampling while spironolactone was held for 6 weeks to avoid interference of spironolactone on plasma aldosterone concentration. The results were as follows:

<table>
<thead>
<tr>
<th></th>
<th>Aldosterone (ng/dL)</th>
<th>Cortisol (mg/dL)</th>
<th>A/C</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVC</td>
<td>116</td>
<td>29.5</td>
<td>3.93</td>
</tr>
<tr>
<td>Right adrenal vein</td>
<td>1254</td>
<td>1061</td>
<td>1.18</td>
</tr>
<tr>
<td>Left adrenal vein</td>
<td>7732</td>
<td>753</td>
<td>10.3</td>
</tr>
</tbody>
</table>

Lateralization index is 8.67

A/C= aldosterone to cortisol ratio; IVC = inferior vena cava.

The results of adrenal vein sampling showed lateralization to the left side, which was opposite to the side of the mass on the imaging study.

- Should adrenalectomy be performed and if so, on which side?

There are 2 treatment options when unilateral oversecretion of aldosterone is causing primary aldosteronism: medical treatment with mineralocorticoid antagonists or unilateral adrenalectomy. Although there is no firm evidence that one is superior over another, 1 study showed that medical treatment may be as effective as unilateral adrenalectomy in blood pressure control and prevention of left ventricular hypertrophy [40]. On the other hand, hypertension may be improved or cured by adrenalectomy and antihypertensive medications may be decreased or stopped, cost for medical care could be decreased, and side effects from long-term antihypertensive medications could be avoided. One study estimated that adrenalectomy saves CAD $31,132 per patient compared with medical therapy alone for primary aldosteronism [41].

Not all patients with unilateral disease of primary aldosteronism are cured of hypertension after unilateral adrenalectomy, probably due to the presence of preexisting essential hypertension with changes in the renovascular system due to persistent hypertension. The factors associated with residual hypertension after adrenalectomy are age, longer duration of hypertension, higher plasma aldosterone concentration, family history of hypertension in a first-degree relative, the number of antihypertensive medications before adrenalectomy and serum creatinine [38–45]. We recently reported that patients with primary aldosteronism may still benefit from adrenalectomy even with these factors as long as adrenal venous sampling clearly shows lateralization [31]. The patient had a short duration of hypertension, no family history of hypertension, and normal serum creatinine, which all favor a good response to adrenalectomy.

This patient had an adrenal mass on the right side and adrenal venous sampling showed lateralization to the left adrenal gland. As described above, it is not uncommon to see discordance between the results of imaging and adrenal venous sampling. She should undergo left adrenalectomy if she is going to consider surgical treatment.

Adrenalectomy and Follow-up

After the discussion of benefit and risk of adrenalectomy, the patient decided to undergo laparoscopic adrenalectomy. She underwent left adrenalectomy uneventfully. Pathology showed a 3-mm adenoma in the excised left adrenal gland. Postoperatively, her blood pressure normalized. Her blood pressure is now 125/74 mm Hg without any antihypertensive medications.

- What is medical therapy for primary aldosteronism?

Patients with bilateral adrenal hyperplasia and those with aldosterone-producing adenomas or unilateral hyperplasia
who are not candidates for or who decline surgery should receive a mineralocorticoid receptor antagonist. Excessive aldosterone not only causes hypertension through extracellular volume expansion, but it also induces perivascular fibrosis and cardiac remodeling [46,47]. Mineralocorticoid receptor antagonists that are currently available are spironolactone and eplerenone. Spironolactone has affinity for both androgen and progesterone receptors. This affinity can induce adverse effects such as gynecomastia and sexual dysfunction in men, and menstrual irregularities in women. Gynecomastia was reported in 6.9% of men who received 50 mg of spironolactone daily and in 52% of those who received 150 mg daily. Thus, men do not tolerate the higher doses of spironolactone [48] that are usually necessary to treat hyperaldosteronism appropriately. Substitution of the 17α-thioacetyl group of spironolactone with a carbomethoxy group generates eplerenone. The affinity of eplerenone for progesterin and androgen receptors is as much as 500-fold lower than that of spironolactone, and thus eplerenone does not cause gynecomastia. Eplerenone has no active metabolites and a shorter half-life than spironolactone and appears to have a reduced risk of hyperkalemia, although the mechanism of this is unclear. Eplerenone has less potency on a per mg basis compared with spironolactone. From a health economics perspective, however, spironolactone is recommended as a first-line drug; the average wholesale price for a year of eplerenone therapy (50 mg twice daily) is US $1453 in 2010 (as eplerenone is now generic) while generic spironolactone is available for $10 per month from discount pharmacies. Amiloride is effective in lowering blood pressure and normalizing serum potassium. However, it does not block the effect of aldosterone on perivascular fibrosis or cardiac remodeling and should be reserved for male patients who do not tolerate mineralocorticoid receptor antagonists.

- **What is the approach to patients with other causes of secondary hypertension?**

The approach for patients with primary aldosteronism has been discussed in detail above. When there is a high suspicion for renal artery stenosis, either CT angiography or magnetic resonance angiography (MRA) can be used. Fibromuscular dysplasia (FMD) is present in the distal renal arteries and branches and may not be seen on MRA, so if one has a high suspicion for FMD, CT angiography is a better imaging modality. Renal artery angiography, however, remains the gold standard [49]. Percutaneous revascularization is the best treatment option for renal artery stenosis due to FMD. There is substantial debate over the optimal management of patients with atherosclerotic renal artery stenosis, especially unilateral renal artery stenosis. There are multiple reports of benefit from percutaneous revascularization [50–52]. On the other hand, all the randomized controlled trials performed to date failed to demonstrate the benefit of percutaneous revascularization (either balloon angioplasty or stent placement) over medical treatment [53–55], although there are many critiques about these studies (eg, definition of renal artery stenosis [50%–75% by imaging study vs. pressure gradient during angiography], cross-over between intervention and control group). The decision to refer a patient with atherosclerotic renal artery stenosis for percutaneous revascularization should be made on an individual basis bearing in mind that revascularization has not been shown to be superior to medical therapy thus far, although trials are ongoing.

- **How should hypertensive patients be monitored?**

In general, we recommend follow-up visits every 6 to 12 months for monitoring of stable patients depending on other existing comorbidities. We typically do annual routine blood testing (measurement of potassium, creatinine, glucose, lipids), unless medication adjustments are made or renal function is declining. When medications are adjusted, especially when angiotensin-converting enzyme inhibitors or angiotensin II receptor blocker are added, creatinine and potassium should be measured 1 to 2 weeks after the initiation of these agents. Hypertension is one of the major causes of chronic kidney diseases. When serum creatinine is checked, estimated glomerular filtration rate (GFR) should be calculated [56]. Frequently, the primary care provider will make the diagnosis of chronic kidney disease. In general, patients with estimated GFR of less than 30 mL/min/1.73 m² should be referred to a nephrologist [57]. When there is a faster decline in GFR than expected or significant proteinuria, patients should be referred to a nephrologist sooner. Late referral to a nephrologist (defined as 3 months before the first dialysis session) greatly compromises the nephrologist-patient relationship, and in diabetic patients leads to greater mortality in the first year on dialysis [58].

**SUMMARY**

- Secondary hypertension should be suspected in selected patients with history, physical examination and laboratory study suggestive of secondary causes of hypertension.
- Primary aldosteronism accounts for 5% to 10% of hypertension and is more common than previously thought.
- The best screening test for primary aldosteronism is aldosterone-to-renin ratio. Adrenal venous sampling is recommended in all patients before proceeding with
unilateral adrenalectomy.

- The management of atherosclerotic renal artery stenosis is controversial and should be decided on a case-by-case basis tending to conservative medical therapy.
- It is important to identify patients with secondary hypertension because they may require different management from patients with essential hypertension and they may have a potentially curable form of hypertension.

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References