Cost Efficacy of the Diagnosis and Therapy of Renovascular Hypertension

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Numerous competing diagnostic modalities and the lack of data about therapeutic benefit result in controversy concerning the identification and treatment of renovascular hypertension. **Methods:** Meta-analyses were used to examine the cost efficacy of renovascular hypertension diagnosis and treatment. Sensitivity, specificity and predictive value were calculated for captopril renography, Doppler, the captopril test and arteriography. Sensitivities and specificities were used to project cost per patient cured or improved for each modality. This was compared with the lifetime cost of medical therapy. Cost efficacy was calculated using a hypothetical population (1000 patients, a prevalency rate of 30% for renal artery stenosis, expected cure or improvement rate of 0.77 after angioplasty). **Results:** The sensitivity, specificity and positive predictive values were similar for all modalities except the captopril test, which had a significantly lower sensitivity. The specificity was similar for all procedures; Doppler was highest but was mitigated by a 17% technical failure rate. The cost per patient cured or improved is greatest for arteriography and lowest for the captopril test. The relationship between cost per patient cured and the number of patients diagnosed in the population was calculated (relative value = (1/cost) × number patients detected). The relative value of captopril renography and arteriography is similar. Doppler and the captopril test have the lowest relative value. If angioplasty reduces medication by three drugs, the savings is $5807 to $8046 per patient. Surgical therapy is not cost-effective. **Conclusion:** Screening for renovascular hypertension is not cost-effective at a prevalence less than 30%, but captopril renography is equally cost-effective as arteriography and obviates the need for an arteriogram in many patients.

Key Words: renovascular hypertension; captopril renography; arteriography; cost efficacy

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In 1934, Goldblatt (*1*) dramatically proved that hypertension could be induced by narrowing a dog's renal artery. His finding has served as a stimulus for extensive investigation. Proof of this phenomenon in humans was provided 4 yr later in the case report of a patient with renal artery stenosis cured by surgical repair (*2*). Sixty years later, there is still considerable controversy over the role of renovascular disease in the diagnosis and treatment of hypertension.

Estimates of the prevalence of renovascular hypertension range from less than 1% in the general population (*3*) to as much as 30% or 40% in highly selected populations (*4*). Numerous screening procedures have been introduced, but their roles in the diagnostic process have not been clearly defined. Reports on the relative costs of the various screening procedures are remarkably few in view of the extensive literature devoted to the subject (*5,6*). Perhaps even more important is the lack of any recent data on the long-term benefit to the patient of anatomic correction of renovascular hypertension.

During the past decade, medical therapy of hypertension has changed dramatically (*7*) and pharmacologic agents have been introduced that are usually successful even for the most severe forms of hypertension. The availability of these agents has raised serious questions about the relative merit of pharmacologic therapy of renovascular hypertension versus anatomic correction of renal artery stenosis. The most recent report devoted to this subject fails to demonstrate a significant prolongation in life expectancy from correction of renal artery stenosis compared with pharmacologic therapy in patients with renovascular hypertension (*8*).

In view of these findings, it is appropriate to review the costs of the differential diagnosis of renovascular hypertension and its remediation versus the cost of medical therapy without any associated diagnostic tests.

This study was designed to evaluate the costs, sensitivities and specificities of the most commonly used tests in the detection of renovascular hypertension. The cost benefit of correction of renal artery stenosis in patients with renovascular hypertension compared to accepted forms of medical therapy also was examined.

METHODS

Literature Search

A MEDLINE literature search for articles directed at screening procedures for renovascular hypertension and renal artery stenosis was performed. The search was limited to English language articles published during 1983–1993. Additional articles were identified from the references of these reports.

Criteria for inclusion in the final analysis were:

1. Data were reported during the last five years (1988–1993).
2. Studies had angiographic corroboration of results.
3. Patients included in more than one report were analyzed only once.
4. No multicenter studies were found with uniform protocols; therefore, none were included.
5. No renal transplant studies were included.
6. To represent a clinically screened general population, no studies with patients selected solely for fibromuscular disease or atherosclerotic disease were included.
7. True-positive, true-negative, false-positive and false-negative rates must have been calculable from the data presented.

No true-negative or false-negative rates could be identified for angiography since angiographically negative studies do not proceed to angioplasty or surgical repair. Therefore, this requirement was omitted for this category. Since angiography is the gold standard for renal artery stenosis, there are, by definition, no false-positives.

Forty-seven articles fulfilled these criteria. Five categories were

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TABLE 1
Cost of Medical Therapy for Renovascular Hypertension

Average age at angioplasty	55 yr
Average life expectancy	20 yr
Average diastolic blood pressure	108 mmHg
Average cost of medications, assuming at least two drugs for control (beta blocker, diuretic, potassium supplement in 50% of patients)	$680/yr
Lifetime cost (two drugs)	$13,600
Add calcium channel blocker or ACE inhibitor (three drugs)	$1,080/yr
Lifetime cost (three drugs)	$21,600

included as screening methods for renovascular disease. Captopril renography was analyzed as a screening test for renovascular hypertension if post-therapy blood pressure data were reported (*9–13*) and it was analyzed as a screening test for renal artery stenosis only if correlation with angiography was reported (*14–22*). Doppler ultrasonography (*23–29*) and the captopril test (plasma renin response to captopril) (*30–22*) were analyzed as screening tests for renal artery stenosis if angiographic correlation was reported. Insufficient data were available to evaluate the Doppler and captopril tests with respect to blood pressure response. Angiography was analyzed for renovascular hypertension if post-therapy blood pressure data were reported (*9,12,13,22,34–44*).

Race, sex, age and minor technical variations were disregarded. Captopril renography was treated as two separate studies if two separate agents were used so that separate true-positive, true-negative, false-positive and false-negative rates could be calculated. Angioplasty and surgical repair data were treated as separate datasets even if they were combined in a single report.

Meta-Analyses

Data were analyzed using meta-analyses with an adjustment for sample size (*46,47*). No significant qualitative difference among studies was identified. The 5-yr time frame eliminated the need for any chronologic adjustments. By utilizing the equations in Appendix A, we used meta-analysis to calculate a study-adjusted sensitivity, specificity, positive predictive values and their associated confidence intervals. Angiography data for the detection of renovascular hypertension allow calculation only of the positive predictive value since only true-positives and false-positives (for renovascular hypertension) are available.

Fees for the various diagnostic and therapeutic procedures (angioplasty and surgical repair) were obtained from the Charge Master of the Montefiore Medical Center for 1993 (*48*). Complication rates, as well as time in the hospital, were factored into the analysis. The costs of medical therapy were based on an average age at angioplasty of 55 yr and an average diastolic blood pressure of 108 mmHg (see angiography references). An average life expectancy of 20 yr in a treated patient was anticipated based on this age and blood pressure (*49*). Costs of two- and three-drug medical regimens were determined using data from the 1993 Red Book (*50*) and adding a 10% retail markup plus a $2.00 pharmacy fee per 100 units of medication. It was assumed that patients would receive a minimum of two medications, which were likely to be a low-cost diuretic and beta-blocker or equivalent. Fifty percent of the patients receiving a diuretic were projected to receive potassium supplementation as well. Another algorithm was used based on a three-drug treatment program. This program added a converting enzyme inhibitor or a calcium channel blocker or equivalent (Table 1).

Costs from the complications of hypertension, medication and laboratory tests were not factored into the analysis and were assumed to be similar for the two groups. There are no current data to support a change in life expectancy or hypertensive complications from interventional relief of renal artery stenosis versus medical therapy. Physician visits are not added in the final analysis. Life expectancy was assumed to be similar for patients treated by angioplasty as for medical therapy (*7*).

Analytic schemes were designed based on a population of 1000 patients with a 30% prevalence of renal artery stenosis (Fig. 1). The 30% prevalence was chosen as one which could reasonably be achieved with careful screening based on clinical criteria (see Ref. 61). A cure or improvement rate of 0.77 was used for patients treated with angioplasty (see angiography references). Sensitivity, specificity, positive predictive values and the costs for the five screening procedures were used to determine the number of patients partially cured or cured and the cost for detecting disease by each modality. Diagnostic, therapeutic and complication costs were summed for each screening procedure and divided by the number of patients improved or cured to obtain a cost per patient improved or cured for each modality. This cost could then be compared to medical therapy based on the two or three drug lifetime regimens. Accordingly, the total cost or savings for each screening test could be determined. An additional cost would be incurred in patients requiring a second procedure. This number would vary greatly from institution to institution and was not factored into the analysis.

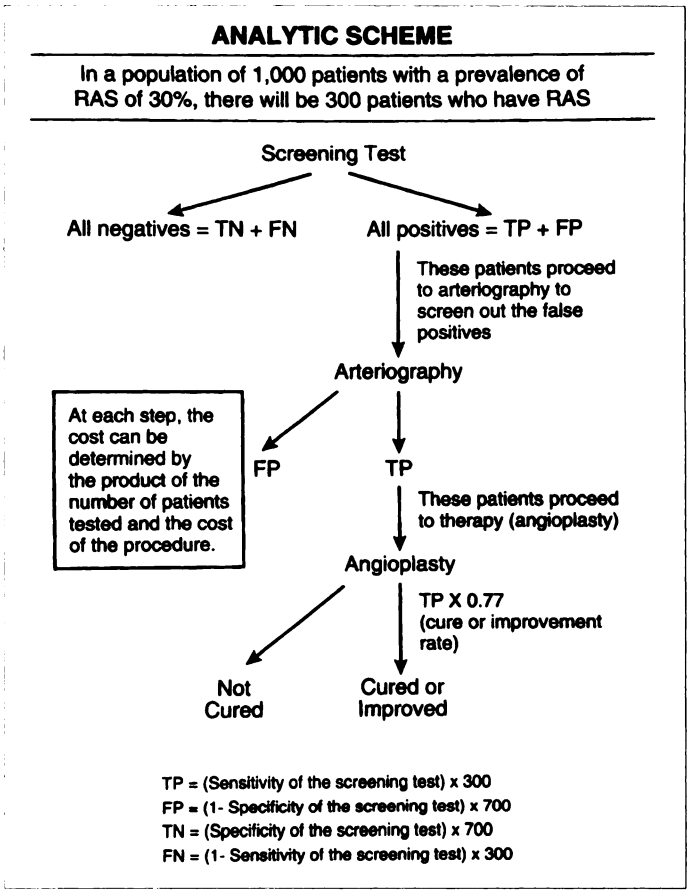

FIGURE 1. Schematic illustrates the basic approach to calculating the relative cost of diagnostic and therapeutic procedures available for renovascular hypertension. "Successfully treated patients" include those whose blood pressure reverts to normal and those who show a reduction in medication requirements. The absolute cost efficacy of the procedure depends on the total reduction in medication requirements which is achieved by the therapy.

TABLE 2
Meta-Analysis Values

Test	Sensitivity	Specificity	(30% RAS) PPV	(RVH) PPV
Captopril renogram (RAS)	89 (86,92)	92 (89,95)	83 (78,88)‡	64 (60,68)
Captopril renogram (RVH)	90 (88,92)	86 (79,93)	NC	66 (56,76)
Captopril test	61 (54,68)	86 (83,89)	65 (60,70)	50 (46,54)
Doppler*	90 (86,94)	98 (97,99)	95 (88,100)	73 (68,78)
Arteriography (RVH)†	NC	NC	100	77 (74,80)

*Only 83% success rate.
†Based on angioplasty data.
‡Numbers in parentheses are 95% confidence intervals.
PPV = positive predictive value; RAS = renal artery stenosis; RVH = renovascular hypertension; NC = not calculable.

RESULTS

Five studies (256 patients) included in the meta-analysis for captopril renography in the evaluation for renovascular hypertension provided data on the blood pressure response to angioplasty or surgical repair. The calculated study-adjusted sensitivity, specificity, positive predictive values and the corresponding 95% confidence intervals (numbers in parentheses) were 90%(88,92), 86%(79,93), and 93%(89,97), respectively. Ten studies (712 patients) were included in the meta-analysis for captopril renography for renal artery stenosis (blood pressure response was not reported). The study-adjusted sensitivity, specificity and positive predictive value were 89% (86,92), 92%(89,95) and 91%(88,94). The meta-analysis for the captopril test (peripheral plasma renin activity) comprised six studies with 656 patients. The study-adjusted sensitivity, specificity and positive predictive value were 61%(54,68), 86%(83,89) and 61%(55,67). Seven studies were included in the meta-analysis for Doppler sonography in the evaluation of renal artery stenosis with 479 patients and a calculated study-adjusted sensitivity, specificity and positive predictive values of 90%(86,94), 98%(97,99), and 96%(93,99). The average technical success rate for the Doppler studies was 83%, with 17% representing technical failures. The technical failure rate for the other diagnostic procedures was negligible.

Nineteen studies (875 patients) reported the blood pressure response to intervention after renal artery stenosis was depicted by angiography. The study-adjusted positive predictive value for improvement in blood pressure based on a renal artery stenosis of >50% was 77%(74,80). These results are summarized in Table 2, with a positive predictive value calculated for a 30% prevalence of renal artery stenosis. The probability of renal artery stenosis or renovascular hypertension given a positive (i.e., positive predictive value) or negative test result (1-negative predictive value) (Fig. 2) and the accuracy curves (Fig. 3) graphically depict the prevalences of renal artery stenosis or renovascular hypertension as ranging from 0% to 100%.

Diagnostic study charges were $799 for captopril renography (baseline renogram followed by captopril renogram), $745 for renal ultrasound with Doppler, $300 for the captopril (Renin) test and $1727 for renal angiography (*48*). Therapeutic procedure charges were $3354 for renal angioplasty. Angioplasty requires an average 2-night hospital stay (@$1305), resulting in a total cost of $5964. These charges would be modified in centers in which diagnostic angiography and therapeutic angioplasty are performed at one sitting. The cost for surgical repair of renal artery stenosis is $18,107, including the cost of hospitalization (*48*).

No costs for complications of angiography were factored into the analysis since inadequate data were available and the effect on cost would be minimal. The major complications of angioplasty occur in approximately 8.6% of patients (Trost D, *personal communication*) and were calculated to average $440 per patient having angioplasty based on a minimum stay of 1 day in the ICU and 2 regular days in the hospital. Minor complications occur in approximately 3.4% of patients, but the costs are minimal and were not factored into the analysis.

Analytic schemes for the various screening tests were constructed as described to determine the cure or improvement rate utilizing the costs for the diagnostic studies, therapeutic procedures and the calculated study-adjusted sensitivity, specificity and positive predictive values. A prevalence of 30% for renal artery stenosis (chosen on the basis of strict clinical screening criteria) and 21% for renovascular hypertension (30% × 0.77) was used in the analytic schemes. Approximately 77% of all patients with renal artery stenosis show an improvement or cure of hypertension after angioplasty. About 29% of those patients with a response to angioplasty were cured of their hypertension and 71% showed improvement during a follow-up of 3 mo to 6 yr (average 22 mo) (*12,34,36,37,38,40–43,45*). For analytic

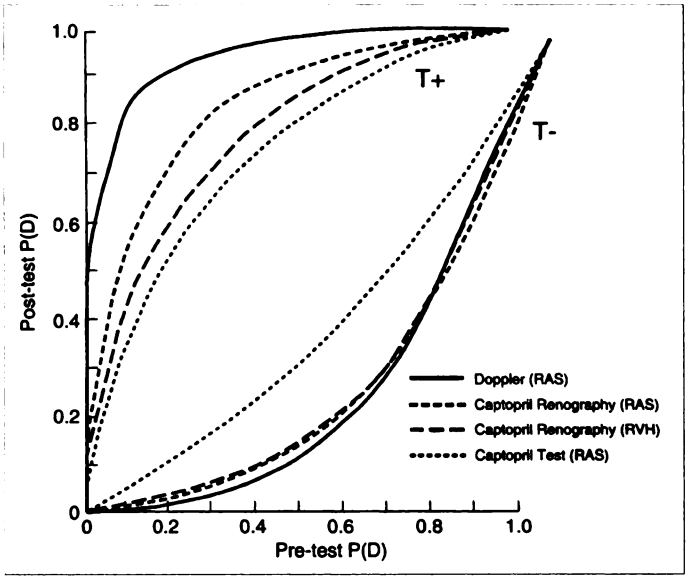

FIGURE 2. The positive predictive value (T+) and negative predictive value (T−) are plotted against prevalences of renal artery stenosis (Pre-test P(D)) from 0 to 100% for the three diagnostic procedures. For the captopril renogram renovascular hypertension, it is plotted against the prevalence of renovascular hypertension. Arteriography is not shown in this figure since it is used as the standard. There is no correction for the reported 17% failure rate for Doppler, which would significantly alter the curve.

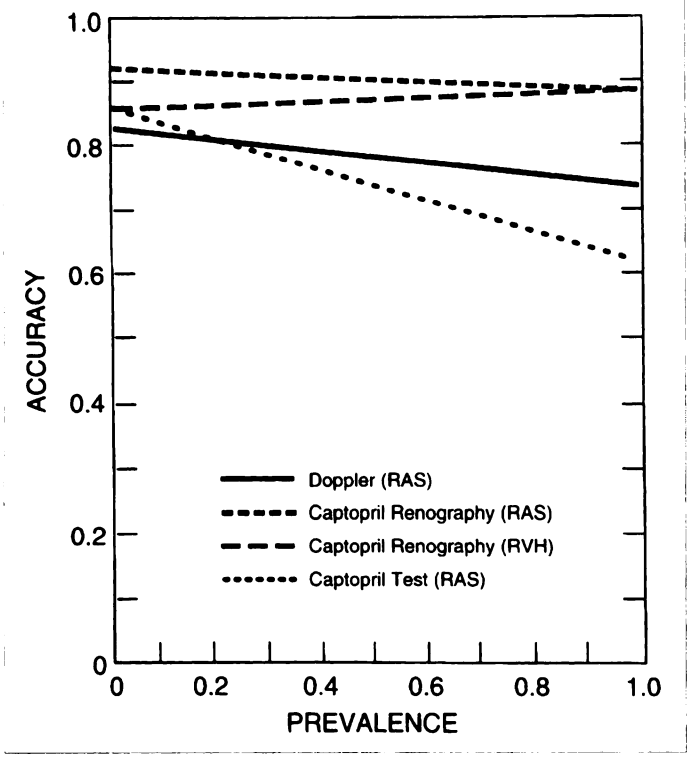

FIGURE 3. Diagnostic accuracy (Acc = P(Se) + (1 − P)Sp), in which the first term represents TP and the second TN. Thus, when P = 0, Acc = Sp and p = 1, Acc = Se and Acc is a straight line joining the two endpoints as in Figure 4. Each of the diagnostic procedures is plotted against the prevalence. The captopril test which performs comparably to the other tests at lower prevalences becomes increasingly inaccurate as the prevalence increases. The remaining three tests do relatively well across a wide range of prevalences. The accuracy for Doppler does not exceed 83% because of the 17% failure rate which leaves 17% of patients with an unknown diagnosis.

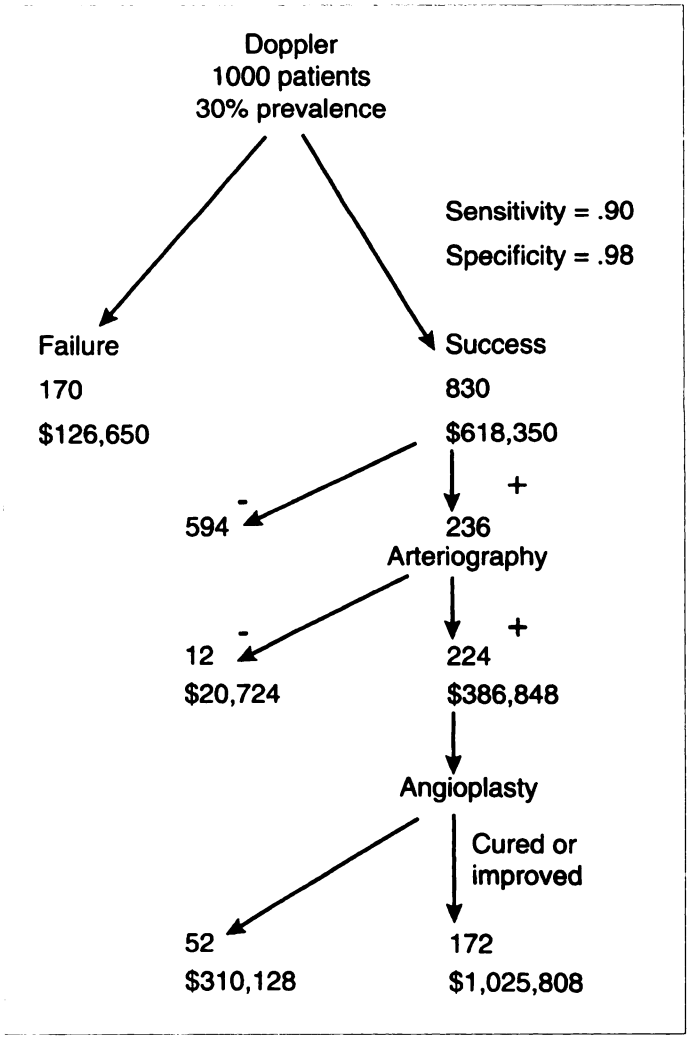

FIGURE 4. Captopril renography, the captopril test and Doppler precedes arteriography if there is a preselected population for arteriography as shown in the sample flow scheme. Because of the 17% failure rate due to Doppler, a significant number of patients do not proceed beyond the initial diagnostic attempt. Eighty-three percent (830 patients) of patients have a successful Doppler. The number with a positive test is based on the (sensitivity × prevalence) and [1 − specificity × (1 − prevalence)]. The cured or improved rate for angioplasty uses the study-adjusted value of 0.77. The costs per patient are calculated using the same factors shown in Figures 1 and 5. All diagnostic, therapeutic and complication costs in the entire population are added and divided by the number improved or cured.

purposes, the benefit is based on reduced medication requirements. These figures can be factored easily when making a decision about the appropriateness of the work-up and treatment of renovascular hypertension for an individual patient. Correction for a technical failure rate of 17% was incorporated into the Doppler flow scheme (Fig. 4).

In this hypothetical population, the number of patients with diagnosed renovascular hypertension and the number of patients missed were determined. The number of patients diagnosed with renovascular hypertension was highest for arteriography and lowest for the captopril test. The diagnostic and therapeutic cost per 1000 patients screened was then determined for each screening test. Based on a 77% cure or improvement rate by angioplasty, the cost per patient improved or cured for each test was determined to be $15,793 using angiography as the initial screening test, $14,041 for Doppler ultrasonography, $14,875 for captopril renography (renal artery stenosis), $13,554 for captopril renography (renovascular hypertension) and $13,881 for the captopril test. These figures represent the sum of all of the diagnostic and therapeutic procedures as well as complication costs in the hypothetical population for each of the diagnostic tests used divided by the number of patients cured or improved (Fig. 4). Savings by omitting baseline captopril renography are small and were calculated to be only $373 per patient. Relative quality values were calculated for each screening test and are summarized in Table 3.

An average cost of medications for pharmacologic treatment of renovascular hypertension with two drugs (plus potassium supplements) was calculated to be $680 per year, and the lifetime cost was calculated at $13,600 based on an average of 20 yr of treatment. If a third drug was added to the medical regimen, then the lifetime cost was calculated to be $21,600 (*50*). Complication costs from pharmacologic therapy could not be determined accurately and were not factored into the analysis.

A comparison was made of the cost of surgical or angioplasty therapy with two or three drug regimens. The most cost-effective screening test proved to be captopril renography in detecting renovascular hypertension, with a savings of $46 or $8046 for two and three drug regimens, respectively. The least cost-effective test was arteriography, which showed a loss of $2193 compared with a two-drug regimen and a savings of $5807 compared with three-drug regimen. The cost savings or losses are summarized in Table 4.

The cost of continued medical follow-up at more frequent intervals for patients on continued pharmacologic therapy versus those who have been cured of their hypertension is not included in the final data. On average, it would be expected that

TABLE 3
Relative Quality Values

Value directly related to a number of patients cured or improved.
Value inversely related to cost per patient cured or improved.

	[(1/Cost) × Patients × 1000]		
Captopril renography (RVH)	1/13,554 × 208	=	15.35
Captopril renography (RAS)	1/14,875 × 206	=	13.85
Arteriography*	1/15,793 × 231	=	14.63
Doppler	1/15,041 × 172	=	11.44
Captopril test	1/13,881 × 141	=	10.16

*Arteriography will result in 5% complications which are not factored into the quality score.
RVH = renovascular hypertension; RAS = renal artery stenosis.

a patient who has been treated successfully would require about one medical visit with a complete work-up annually. Only 29% of 77% or 22% of all patients treated would, however, actually fall into this category. Patients whose blood pressure was improved but not cured would require the same amount of medical follow-up as those on continuing therapy. Since only 29% of all patients showing improvement are cured, the difference in follow-up costs from the medically treated group would be relatively small. Surgical therapy was not cost-effective for any of the procedures tested.

DISCUSSION

Effect of Prevalence

Although there are too few data on the long-term follow-up of patients with renovascular hypertension, this study provides many insights into their work-up and treatment. Most striking is the clear lack of cost benefit of any of the diagnostic modalities in low prevalence populations. For prevalence rates below 30% (cured or improved), the cost of detecting and treating renovascular hypertension is far greater than pharmacologic therapy. This conclusion is based on the observation that significant savings are not observed at a 30% prevalence unless the drug requirement is reduced by at least three medications. For example, the diagnostic and therapeutic costs for arteriography is $15,793 per patient cured or improved at a 30% prevalence. For a 20% prevalence, this cost rises to $19,546. The influence of prevalence rates on cost is depicted in Figure 5 for captopril renography (renal artery stenosis). The cost, however, levels off at about 30% prevalence. This relationship is similar for all of the modalities tested. Even at a prevalence of 30%, there is doubtful cost benefit to a patient unless the pharmacologic regimen can be reduced by at least two drugs, and real savings do not occur unless the treatment program is reduced by three drugs. Patients whose blood pressure responds to therapy with low-cost generic medications will have a far less cost benefit than individuals with refractory blood pressure elevations requiring more expensive therapy.

TABLE 4
Savings (− Loss) per Patient Cured or Improved

	Two drugs	Three drugs
Captopril test	−281	7,719
Captopril renogram (RVH)	46	8,046
Captopril renogram (RAS)	−1,275	6,725
Doppler	−1,441	6,559
Arteriogram	−2,193	5,807

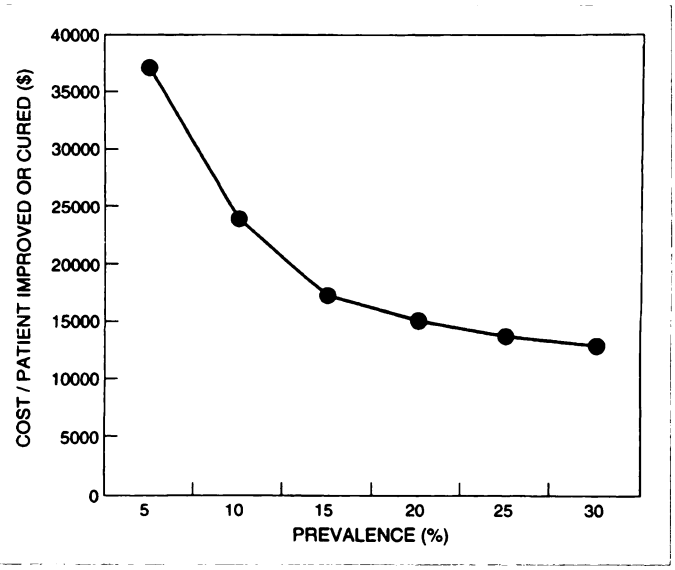

FIGURE 5. The relationship between cost of diagnosis and therapy and prevalence of disease is shown for captopril renography renal artery stenosis. There is a significant effect on cost when the prevalence is <30%.

Relative Test Performance

The most effective initial screening test was arteriography which will miss few patients with significant renal artery stenosis. The tradeoff for a nearly 100% detection rate is that this procedure is the most invasive and expensive test available. This study did not factor the cost of complications after arteriography due to lack of adequate data. It is, however, certain that arteriography results in far greater patient discomfort and undoubtedly there will be some expenses associated with side effects and patient reaction to the procedure.

Captopril renography as an alternative to arteriography is almost as effective as arteriography but greatly reduces the number of individuals who will have unnecessary arteriograms. Published studies also suggest that the likelihood of a patient with a positive captopril renogram and proven renal artery stenosis of responding to angioplasty may be greater than that of a patient with a lesion detected by anatomic methods alone with no confirming physiologic test. The downside of a less invasive approach is that a few patients with potentially curable lesions will not be screened.

Published reports on the efficacy of Doppler studies for renal artery stenosis are highly enthusiastic. These reports, however, almost universally fail to factor the high technical failure rate of this test. Even in centers with highly trained and accomplished specialists, the failure rate of Doppler averages about 17%. Therefore, Doppler as a screening test will miss at least twice as many patients with renal artery stenosis and potentially curable renovascular hypertension as captopril renography. In centers with less experienced staff, the technical failure rate is probably higher.

Surprisingly, the captopril test, based on sampling of plasma renin activity after captopril administration, does not do well at all in this analysis. The captopril test did not screen almost twice as many patients as Doppler and four times as many as captopril renography.

Cure Rate

A disappointing finding is that among the few studies with significant long-term follow-up, the cure rate for renovascular hypertension is low in the general population. Only 29% of the 77% of patients who show a response are actually cured of

hypertension during an observation period from 3 mo to 6 yr (average follow-up 22 mo). The remaining patients showed improvement. Since drug therapy of renovascular hypertension can be difficult, even a reduction in the therapeutic requirement may be beneficial in some patients, especially those who can reduce their medication requirement by two or more expensive drugs.

Other Considerations

Several other considerations also merit discussion. Are there tangible benefits to angioplasty other than reduction in blood pressure? Current data suggest that drug therapy of hypertension can reduce risks (e.g., mortality, stroke) considerably (*51,52*). This may not be true for renovascular hypertension, which is more severe and difficult to treat. Hollenberg (*53*) observed the occurrence of azotemia in patients with bilateral renal artery stenosis or stenosis in a single kidney. Devoy et al. also reported on irreversible azotemia associated with captopril therapy and renal artery stenosis (*54*).

McNeil (*55*) reported that the perioperative mortality in repair of atherosclerotic renal artery stenosis largely negated the benefits of surgical therapy. MacNeil's study was made in 1975, however, and there has been considerable improvement in interventions and refinements in angioplasty. Patients with fibromuscular disease have a much greater cure rate than patients with atherosclerotic disease (*56*). Response to treatment of atherosclerotic renal artery stenosis also varies with the location and extent of the lesion. If angioplasty is withheld in patients with a low probability of cure at the time of angiography, there might be a positive effect on the cost efficacy. This is a worthwhile approach which requires the development of specific criteria in determining the therapeutic regimen.

Regardless of whether the high risk of surgery is still comparable to that reported by McNeil (*55*), the present study clearly shows no cost benefit from surgical therapy. Because the cost of surgery is excessive, unless a significant change in life expectancy or in the associated complications of hypertension can be demonstrated, there is no possible cost benefit of surgical treatment of renal artery stenosis.

Isles et al. (*8*) have the most recent follow-up data comparing survival in medically versus surgically treated patients with renovascular disease. Their study included 121 patients diagnosed between 1975 and 1982 to allow for 10-yr survival calculations. These data are notable, although there have been many changes both in medical and surgical in therapy since then. Ten-year survival in the group who had surgery was 71% compared to 62% in the medical group (p = ns). Both groups had a lower survival rate than hypertensive controls and all values were lower than those for the general population.

Another concern for renovascular disease is the progressive loss of renal function and the possible progression of the stenosis. Some data support the view that renal artery stenosis is a cause of progressive renal failure and should be corrected for this reason regardless of the blood pressure effect (*57,58*). Patients who progress to end-stage renal disease would incur an additional enormous cost for treatment. If remediation of renal function is the justification for treatment of renal artery stenosis, then serum creatinine becomes part of the decision process. In azotemic patients, however, diagnostic tests are less accurate and the patient's life expectancy is shorter. The present analysis cannot be generalized to the subgroup of patients with bilaterally reduced renal function, except as they occur in a general screened population.

Evaluation of a patient for a differential diagnosis of renovascular hypertension should include the presence or absence of renal function changes, the severity of the hypertension, the drug requirement and the occurrence of hypertension-related episodes of acute illness. In the patient who is easily treated for hypertension and whose medication requirement is two or fewer drugs, there can be no expectation of a cost benefit. Patients in whom three or more drugs are required or whose hypertension cannot be readily controlled are most likely to benefit if renovascular hypertension is the underlying cause of their illness.

CONCLUSION

In deciding which screening test to use, several considerations emerge. If the patient is azotemic, most of the screening tests are less effective. If the physician is also concerned about restoring renal function, arteriography, although the most expensive approach, is also probably the most effective. Patients with relatively well preserved renal function may be effectively screened with any of the available tests, although captopril renography appears to be the most cost-effective. Renography also offers the benefit of providing lateralizing information and is a useful noninvasive test for patient follow-up if an intervention is performed (*59*). The test is also preferable in diabetic patients and patients with known contrast media sensitivity who may be at some risk even with the administration of nonionic contrast (*60*).

The search for a renovascular cause of hypertension has been the focus of great attention since Goldblatt proved the existence of the entity. It is, however, a relatively uncommon cause of hypertension which makes the screening process difficult. These data provide some guidelines for selecting a screening test and deciding which patients benefit the most from that particular test. Although angioplasty is potentially a highly cost-effective treatment, surgical therapy appears prohibitive except in highly selected patients.

APPENDIX

A meta-analysis was performed using the following equations (*1*):

$$P_{av} = \frac{\sum_{i=1}^{n} w_i p_i}{\sum_{i=1}^{n} w_i}, \qquad \text{Eq. A1}$$

in which, for each screening test, n_i is the number of patients in the ith study and p_i is the probability (sensitivity or specificity) for the ith study. Using a weighting factor for sample size (w_i), which is indirectly related to the variance of p_i, the average probability (P_{av}) was calculated for each of the screening tests:

$$\text{Where: Variance } (p_i) = p_i(1 - p_i)/n_i$$

$$W_i = 1/\text{variance (pi)}. \qquad \text{Eq. A2}$$

To calculate each of the 95% confidence intervals, the variance of P_{av} was calculated.

$$\text{Variance } P_{av} = \frac{1}{\sum_{i=1}^{n} W_i}. \qquad \text{Eq. A3}$$

The 95% confidence interval for P_{av} then is:

$$\pm 1.96 \times \sqrt{\frac{1}{\sum_{i=1}^{n} W_i}}. \qquad \text{Eq. A4}$$

The positive predictive value (PPV) at a prevalence of 30% for renal artery stenosis and 23% for renovascular hypertension was calculated for the screening tests:

$$PPV = \frac{Se \cdot C}{(Se \cdot C) + (1 - Sp)(1 - C)}, \qquad \text{Eq. A5}$$

in which C = prevalence, Se = sensitivity and Sp = specificity.

By the delta method (142), the variance (V) for the PPV at prevalence = C is:

$$V(PPV) = \frac{[(1 - Sp) \cdot C \cdot (1 - C)]^2}{[(Se \cdot C) + (1 - Sp)(1 - C)]^4} \cdot V(Se) + \frac{[Se \cdot C \cdot (1 - C)]^2}{[(Se \cdot C) + (1 - Sp)(1 - C)]^4} \cdot V(Sp). \qquad \text{Eq. A6}$$

The 95% confidence interval for PPV then is:

$$\pm 1.96 \cdot \sqrt{V(PPV)}.$$

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