Pretreatment Imaging Workup for Patients with Intermittent Claudication: A Cost-Effectiveness Analysis

Karen Visser, PhD, Karen M. Kuntz, ScD, Magruder C. Donaldson, MD, G. Scott Gazelle, MD, PhD, and M.G. Myriam Hunink, MD, PhD

PURPOSE: To determine the optimal imaging strategy in pretreatment workup of patients with intermittent claudication with use of noninvasive imaging modalities and intraarterial digital subtraction angiography (DSA).

MATERIALS AND METHODS: A decision-analytic model that considered test characteristics such as sensitivity, complications induced by the test, implications of missing lesions, and the consequences of overtreating patients, was developed to evaluate the societal cost-effectiveness (CE) of magnetic resonance (MR) angiography, duplex ultrasonography (US), and DSA. Our main outcome measures were quality-adjusted life years (QALYs), lifetime costs (in dollars), and incremental CE ratios. The base-case analysis considered a cohort of 60-year old male patients without a history of coronary artery disease who presented with severe claudication to undergo pretreatment imaging workup.

RESULTS: The range in effectiveness and lifetime costs among different diagnostic workup strategies was small (largest difference in effectiveness: 0.025 QALYs; largest difference in lifetime costs: $1,800). If treatment was limited to angioplasty in patients with suitable lesions, MR angiography had an incremental CE ratio of $35,000 per QALY compared with no diagnostic workup, and DSA had an incremental CE ratio of $471,000 per QALY compared with MR angiography. If treatment options included both angioplasty and bypass surgery, DSA had an incremental CE ratio of $179,000 per QALY compared with no diagnostic workup, and MR angiography and duplex US were less effective and more costly.

CONCLUSIONS: The differences in costs and effectiveness among diagnostic imaging strategies for patients with intermittent claudication are slight and MR angiography or duplex US can replace DSA without substantial loss in effectiveness and with a slight cost reduction.

Index terms: Cost-effectiveness • Extremities, blood supply • Peripheral vascular disease

J Vasc Interv Radiol 2003; 14:53–62

Abbreviations: CAD = coronary artery disease, CE = cost-effectiveness, DSA = digital subtraction angiography, PAD = peripheral arterial disease, QALY = quality-adjusted life year

THE pretreatment workup for patients with intermittent claudication involves selecting the most appropriate intervention for each patient and varies by institution. Some centers advocate the use of duplex ultrasonography (US) as the initial modality, followed in many cases by intraarterial digital subtraction angiography (DSA), whereas others advocate the use of magnetic resonance (MR) angiography as the only imaging modality. So far, most studies on the pretreatment imaging workup of peripheral arterial disease (PAD) have focused on the diagnostic accuracy of these tests. For the detection of significant stenoses, duplex US has reasonable accuracy compared with DSA, whereas MR angiography is nearly as accurate as DSA (1). Currently, in some clinics, angioplasty procedures, and sometimes even bypass surgery,

From the Program for the Assessment of Radiological Technology (ART) Program, Department of Epidemiology and Biostatistics (K.V., M.G.M.H.), and Department of Radiology (K.V., M.G.M.H.), Erasmus MC University Medical Center Rotterdam, The Netherlands; Department of Health Policy and Management (K.M.K., G.S.G., M.G.M.H.), Harvard School of Public Health; Division of Vascular Surgery (M.C.D.), Brigham and Women's Hospital; and Decision Analysis and Technology Assessment Group (G.S.G.), Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts. Received June 10, 2002; revision requested July 18; revision received August 6; accepted August 8. **Address correspondence to** K.V., Assessment of Radiological Technology (ART) Program, Department of Epidemiology and Biostatistics and Department of Radiology, Erasmus MC, Room EE21-18; Dr. Molewaterplein 50, 3015 GE Rotterdam, The Netherlands; E-mail: k.visser@epib.fgg.eur.nl

None of the authors has identified a potential conflict of interest.

© SIR, 2003

DOI: 10.1097/01.RVI.0000052291.26939.82

are planned on the basis of the findings of duplex US (2–4). Likewise, the results of MR angiography for planning invasive treatment are also promising (5,6). Intraarterial DSA, conversely, is considered to be the reference ("gold") standard and is still often used despite its slight risk of morbidity and mortality (7,8) and its expense. The question arises as to which imaging workup strategy is preferred.

To determine which test(s) are preferred in clinical practice, we need to take into account not only the diagnostic accuracy of each test, but also the related effects of diagnostic imaging tests on the treatment plan, long-term prognosis, quality of life, and costs. Although, ideally, one would like to perform a clinical study to address all these issues, such a study would be complicated and time-consuming. Alternatively, a cost-effectiveness (CE) analysis with use of a decision-analytic approach can shed light on the trade-offs involved. A model integrates all relevant effects and costs and has the ability to compare numerous diagnostic strategies. The purpose of this study was to assess the CE of MR angiography, duplex US, and intraarterial DSA for the pretreatment imaging workup of patients with lifestyle-limiting intermittent claudication with use of a decision-analytic approach.

MATERIALS AND METHODS

Decision Model

A previously developed decision-analytic model (9) that evaluated treatment and follow-up in patients with intermittent claudication was extended with an additional model of imaging workup to assess which workup is most appropriate for the patient. Three different workup strategies were considered: (i) MR angiography in all patients, (ii) duplex US in all patients, and (iii) intraarterial DSA in all patients. A reference strategy consisting of exercise therapy without imaging workup was also considered.

The information obtained from the imaging workup was used to make treatment decisions. The **Figure** represents a simplified outline of the model. The test results indicated whether the lesion was located in a suprainguinal or infrainguinal location and which treatment (angioplasty with selective stent placement, bypass surgery, or supervised exercise) was preferable. Intraarterial DSA was considered to be the reference standard and yields all information necessary to make the correct treatment decision. A treatment decision cannot always be made based on the MR angiography or duplex US results. Therefore, we assumed that additional workup with DSA was performed if the test yielded technically inadequate results (eg, bowel gas for duplex US), no treatment plan could be determined on the basis of the test result, no lesion was localized, or the test could not be performed (eg, if there were contraindications to MR angiography such as claustrophobia or having a pacemaker).

False test outcomes.—MR angiography and duplex US could induce false test results, which could lead to treatment of an incorrect location and/or inappropriate treatment. For example, a patient with a suprainguinal lesion suitable for angioplasty could be diagnosed with MR angiography as having a lesion not suitable for angioplasty. Because of the limited data reported in the literature, the following assumptions were made for the implications of false test results.

For angioplasty, we assumed that the preceding diagnostic DSA as part of an angioplasty procedure would detect incorrectly located lesions and/or lesions incorrectly referred for angioplasty. For depicting incorrectly located lesions, we assumed that, in 10% of the cases, another angioplasty session would be necessary on another day (eg, because of contrast material overload or incorrect puncture for the angioplasty procedure). The costs of a planned angioplasty procedure that had to be stopped after DSA were assumed to be equal to a DSA procedure plus an additional amount of money for inefficient use of personnel, equipment, and room time (**Table 1**).

When bypass surgery was performed on nonsuitable lesions, it was assumed that postoperative success rates would be lower. For patients in whom bypass surgery was performed at the wrong location because of a false test result, we assumed that repeat DSA would be performed for persistent symptoms, followed by repeat surgery.

Treatment.—The treatment options for lifestyle-limiting intermittent claudication included percutaneous transluminal angioplasty with stent placement if necessary, bypass surgery, and supervised exercise. There seems to be disagreement on whether the presence of claudication justifies the use of bypass surgery and, therefore, we modeled two different treatment scenarios. In the first scenario, treatment was limited to angioplasty only and patients with lesions not suitable for angioplasty entered a supervised exercise program (minimally invasive treatment scenario). In the second scenario, angioplasty was performed if feasible and bypass surgery was performed otherwise (more-invasive treatment scenario). The results available from the previously developed decision-analytic model on treatment and follow-up for intermittent claudication showed that the more-invasive treatment scenario was more effective than the minimally invasive treatment scenario, but against a very high cost (9). For the strategy with no diagnostic workup, all patients entered a supervised exercise program and invasive treatment was performed only if patients developed critical limb ischemia.

Patients with recurrent lifestyle-limiting claudication (defined as maximum walking distance less than 250 meters), graft failure, or development of symptoms in the contralateral limb underwent further treatment (9). Critical limb ischemia (defined as rest pain, ulcer, or gangrene) was always treated invasively and, if necessary, an amputation was performed.

Data Sources

Test characteristics.—**Table 2** presents the data on gadolinium-enhanced MR angiography and color-guided duplex US that were incorporated in the model (1,4–6,10,11). To our knowledge, no major side effects caused by MR angiography or duplex US have been reported. DSA, conversely, has a slight risk of morbidity and mortality. The probability of systemic complications caused by DSA was 0.029 (range, 0.017–0.052)

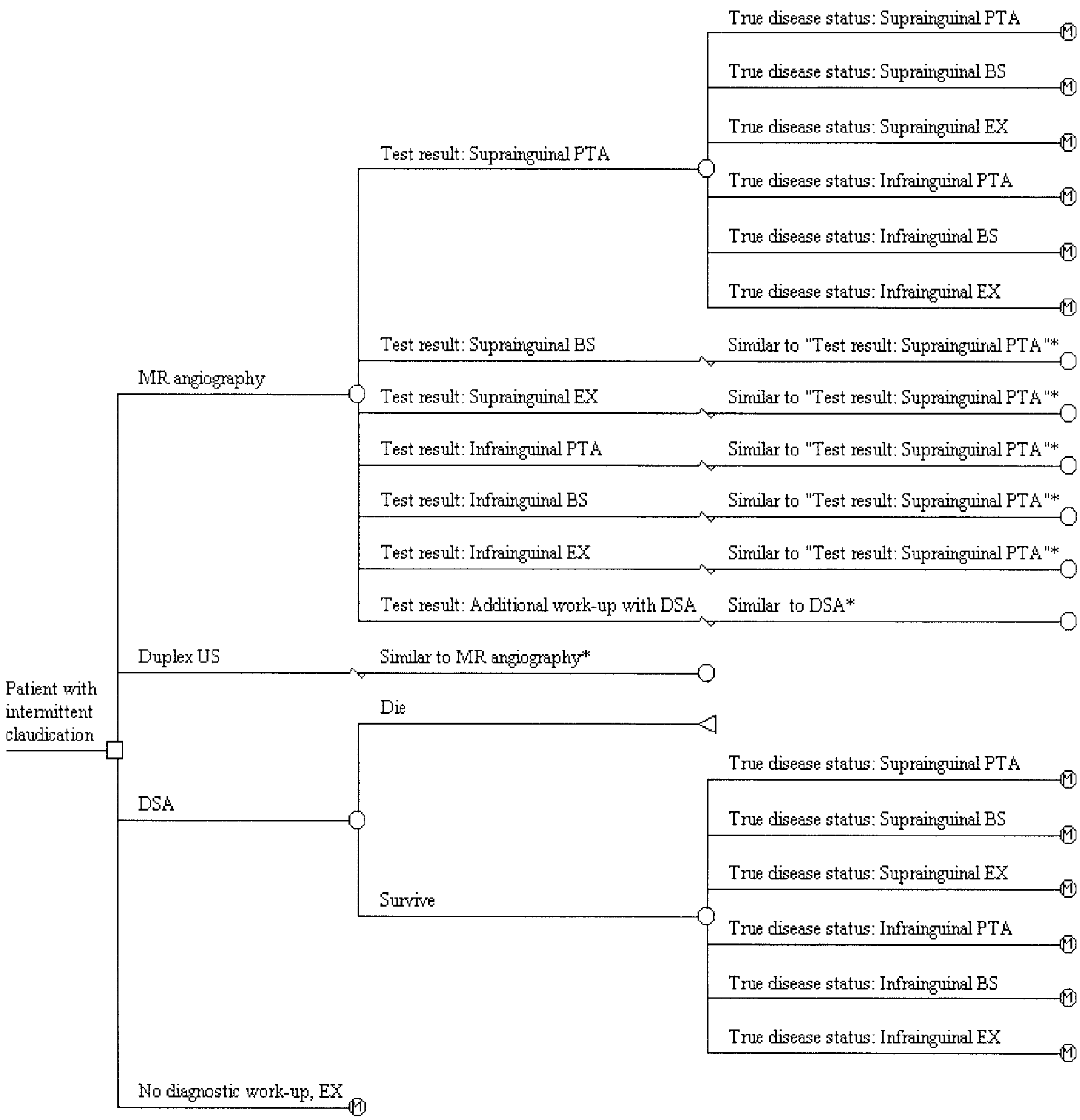

Figure. Schematic representation of the structure of the decision model. Patients who undergo diagnostic workup will be treated according to the diagnostic test result. In the Markov model, treatment of patients and lifetime follow-up is modeled. Test results are considered true if the test result and true disease status are the same, whereas test results are considered false if the test result and true disease status are discrepant. Patients who do not undergo diagnostic workup enter a supervised exercise program. PTA = percutaneous transluminal angioplasty with selective stent placement; BS = bypass surgery; EX = supervised exercise program; (M) = Markov model. *The structure of the subsequent subtree is similar to a structure used elsewhere in the tree.

(8) and the mortality risk was 3.3×10^{-4} (range, $2.9–16.2 \times 10^{-4}$) (7,12).

For the baseline analysis, we assumed that the DSA strategy consisted of a complete DSA (ie, from abdominal aorta to ankles) for the diagnostic workup of PAD and that the information obtained from the DSA would first be discussed by the vascular surgeon and radiologist before proceeding with treatment. If the patient had a lesion that would be suitable for angioplasty, an angioplasty procedure preceded by selective DSA was scheduled. In a sensitivity analysis, we explored the effect of combining DSA and angioplasty during one procedure. It should be noted that the definitive choice of treatment before DSA is unknown.

Table 1
Health-related Quality of Life and Costs

Variable	Base-case Value	Range*	Source (Ref. No.)
Health values			
Severe intermittent claudication†	0.71	0.67–0.75	(19)
Mild intermittent claudication†	0.79	0.75–0.83	(19)
Critical limb ischemia‡	0.35	0.15–0.55	(20)
History of angina pectoris§	0.90	0.60–1.00	(21)
Systemic long-term complications after interventions§	0.72	0.60–0.90	(22)
Costs			
MR angiography	574	287–861‖	Medicare
Duplex US	243	121–365‖	Medicare
DSA	1,183	1,822¶	Medicare
Mortality from vascular interventions	12,758	3,950–21,960	(24)
Complications of DSA	7,393	4,100–10,690	(24)
Extra costs for planned but not performed angioplasty#	316	158–474	(23)
Aortic bifurcation bypass surgery	25,790	23,300–28,300	(24)
Suprainguinal angioplasty with selective stent placement	8,290	5,600–11,000	(24, 25)
Infrainguinal bypass surgery	18,110	15,800–20,400	(24)
Infrainguinal angioplasty	4,480	1,600–7,500	(24)
One year supervised exercise**	4,150	880–9,500	(9)

Note.—Total Costs = US $1998.
* Range or alternative numbers were used for sensitivity analysis.
† Health values were EuroQol responses from participants in an exercise program transformed to time trade-off values.
‡ Values were based on time trade-off.
§ These health values were incorporated by assuming a simple multiplicative relation.
‖ Ranges in costs represent 50% and 150% of baseline estimate.
¶ Inclusive costs of overnight stay in the hospital.
# Extra costs for one hour of inefficient use of personnel, equipment, and room time were counted if an angioplasty was planned but not performed. The costs of the planned-but-not-performed angioplasty equaled the costs of an angiography plus the extra costs for inefficient use.
** Main source of costs was patient time spent on walking.

Treatment and follow-up.—Probabilities for location of disease and suitability for treatment were available from a vascular registry (9). There were more suprainguinal lesions than infrainguinal lesions and a higher proportion of suprainguinal lesions than infrainguinal lesions was suitable for angioplasty (**Table 3**) (9,13). Of all patients undergoing diagnostic workup for PAD, we assumed that 95% would be eligible for invasive treatment after workup. Patency rates were available from published meta-analyses (14–16). Probabilities and rates are presented in **Table 3** (9,14–18).

Health-related quality of life.—Quality-adjusted life years (QALYs) were calculated as the sum of health values for each health state multiplied by the amount of time spent in those states. Health-related quality of life was expressed as health values ranging from 0 (dead) to 1 (full health). The health values used are presented in **Table 1** (19–22).

Costs.—Costs were divided into medical costs, including costs of diagnostic tests, treatment, and follow-up, and nonmedical costs, including transportation costs and patient time spent on diagnostic testing, interventions, and follow-up visits. All costs were converted to 1998 United States dollars with use of the Consumer Price Index (United States Bureau of Labor Statistics Data). We used Medicare reimbursement rates, which include technical and professional fees, for the costs of MR angiography, duplex US, and DSA (**Table 1**). Extra costs for inefficient use of personnel, equipment, and housing in the case of an incorrectly scheduled angioplasty procedure were available from a CE analysis (23). The costs for invasive treatment were available from a cost-identification analysis in patients with PAD (24), except for the costs of angioplasty with selective stent placement for suprainguinal disease (25).

Cost-effectiveness Analyses

The principal outcomes in the model were QALYs and lifetime costs and both were discounted at an annual rate of 3% (26). QALYs and lifetime costs for downstream treatment and follow-up of all possible diagnostic outcomes were calculated in the Markov model with first-order Monte Carlo simulations of 100,000 patients and combined with the costs and effectiveness of the pretreatment workup. The time period between pretreatment workup and subsequent treatment was assumed to be negligible in comparison to the patients' life expectancy.

To determine the CE of alternative diagnostic strategies we used incremental CE ratios. The strategies were ordered according to increasing effectiveness, and (extended) dominated strategies were eliminated. A strategy was considered to be dominated by another strategy if the latter yielded

Table 2
Test Characteristics of MR Angiography and Duplex US

Variable	MR Angiography Base-case value	MR Angiography Range*	MR Angiography Source (Ref. No.)	Duplex US Base-case value	Duplex US Range*	Duplex US Source (Ref. No.)
Sensitivity >50% stenosis†	0.96	0.91–0.97	(1)	0.90	0.89–0.90	(1)
Specificity >50% stenosis	0.96	0.94–0.98	(1)	0.95	0.93–0.96	(1)
Probability of:						
Uninterpretable test result‡	0.07	0.05–0.10	§	0.11	0.0–0.23	(10)
Indeterminate test result‖	0	–	(5#, 6**)	0.089	0.036–0.14	(4)
Test result suggests angioplasty given that lesion is suitable for angioplasty¶	0.79	0.87	(5, 6)	0.60	0.93	(4‡‡, 11††)
Test result suggests angioplasty given that lesion is suitable for bypass surgery¶	0.03	0.065	(5, 6)	0.08	0.10	(4, 11)
Test result suggests angioplasty given that lesion is not suitable for invasive treatment¶	0	0.065	(5, 6)	0.09	0.24	(4, 11)
Test result suggests bypass surgery given that lesion is suitable for bypass surgery¶	0.97	0.87	(5, 6)	0.87	0.90	(4, 11)
Test result suggests bypass surgery given that lesion is suitable for angioplasty¶	0.14	0.065	(5, 6)	0.36	0.07	(4, 11)
Test result suggests bypass surgery given that lesion is not suitable for invasive treatment¶	0	0.065	(5, 6)	0.09	0.29	(4, 11)

* Range or alternative numbers were used for sensitivity analysis.
† Sensitivity was calculated based on specificity with use of summary receiver operating characteristics regression equation available from a meta-analysis (1).
‡ An uninterpretable test result was defined as a technical inadequate test result (eg, bowel gas for duplex US) or the test could not be performed (eg, claustrophobia for MR angiography).
§ Including 5% of patients who had a contraindication for MR angiography (personal communication, Ky H., MD, PhD, 2000).
‖ An indeterminate test result was defined as a technically adequate test result on which no treatment plan could be determined.
¶ We assumed for MR angiography and duplex US that the probabilities for assessing the treatment option were independent of location.
# Probabilities were estimated from a cross-tabulation of treatment plans based on MR angiography and DSA. Because only the margin totals of the cross-tabulation were known, it was assumed that the highest proportion of possible agreement between MR angiography and DSA was achieved based on these totals. Criteria for suitability of lesions for angioplasty were iliac artery stenoses and occlusions less than 20 mm in length.
** Treatment plans based on DSA were compared with treatment plans based on DSA with additional MR angiography. We assumed that the proportion of discrepant treatment plans was equally divided over the other two categories. No criteria for suitability of lesions for angioplasty were reported.
†† Study was performed with grayscale duplex US and included the complete spectrum of patients with PAD. In all patients, treatment plans based on duplex US and DSA were compared. No criteria for suitability of lesions for angioplasty were reported.
‡‡ In only 64 of 112 patients, treatment plans of duplex US and DSA were compared. No criteria for suitability of lesions for angioplasty were reported.

more QALYs at lower costs. A strategy was considered to be extended dominated if another strategy yielded more QALYs and had a lower incremental CE ratio. Incremental CE ratios were then calculated as the difference in average lifetime costs divided by the difference in average QALYs for one particular strategy compared to the next-best strategy (27). The model was programmed in the DATA computer program (Decision Analysis by TreeAge, version 3.5.6; Treeage Software, Williamstown, MA).

Base-case analysis.—The base-case analysis evaluated a cohort of 60-year-old men with a 1-year history of severe unilateral claudication, an initial ankle-brachial index (systolic ankle blood pressure divided by systolic brachial blood pressure) of 0.70, and no history of coronary artery disease (CAD). The analysis was done separately for the scenario in which angioplasty was the only treatment option (minimally invasive treatment scenario) and that in which angioplasty and bypass surgery were available (more-invasive treatment scenario).

In an additional analysis, two other patient cohorts were considered: 40-year old men (all other characteristics similar to the base case) and 70-year old men with a history of CAD (all other characteristics similar to the base case). For patients with a history of CAD, we assumed that the more-invasive treatment scenario was not possible because these patients have high complication rates after bypass surgery.

Sensitivity analysis.—In one-way sensitivity analyses, we used parameters that varied in a range of plausible values (**Table 2**). Extensive sensitivity analyses for the treatment and follow-up model were previously performed (9); therefore, our sensitivity analysis focused on diagnostic parameters. We evaluated some of our base-case assumptions and varied the threshold walking distance from 250 meters to 175 meters (probabilities and

Table 3
True Disease Status and Patency Rates for Patients with Intermittent Claudication

Variable	Base-case value	Range*	Source (Ref. No.)
True disease status			
Probability of suprainguinal disease	0.56	0.12–0.85	(9)
Probability that a suprainguinal lesion is suitable for angioplasty†	0.51	0.43–0.59, 0.74	(9, 13)
Probability that an infrainguinal lesions is suitable for angioplasty†	0.18	0.11–0.25, 0.50	(9, 13)
Probability that lesions are suitable for invasive treatment	0.95	0.85	(6, 9)
Annual rate of progression of invasively untreated disease§	0.20	–	(17)
Annual rate of changing diseased location‖	0.15	–	(18)
Two-year patency			
Aortic bifurcation bypass surgery	0.95	–	(15)
Angioplasty of suprainguinal lesions			
Stenosis	0.84	–	(16)
Occlusion	0.67	–	(16)
Infrainguinal bypass surgery			
Autologous vein	0.89	–	(14)
PTFE, above-knee anastomosis	0.86	–	(14)
PTFE, below-knee anastomosis	0.80	–	(14)
Angioplasty of infrainguinal lesions			
Stenosis	0.75	–	(14)
Occlusion	0.46	–	(14)

Note.—PTFE = polytetrafluoroethylene.
* Range or alternative numbers were used for sensitivity analysis.
† A lesion was considered suitable for angioplasty if there was one focal stenosis 50%–99% above the knee joint.
‡ In the Markov model, analyzing treatment and follow-up, it was assumed that 5% of the lesions were not suitable for invasive treatment.
§ For patients with lesions suitable for angioplasty who incorrectly participated in the supervised exercise program, it was assumed that the proportion of lesions suitable for angioplasty decreased over time, and, consequently, the proportion of lesions suitable for bypass surgery increased, which equaled the rate of progression of disease.
‖ For patients who entered the supervised exercise program, it was assumed that the predominant disease location could change over time as long as the patient was not treated invasively, and it was assumed that the rate of changing diseased location equaled the rate of developing symptoms in the contralateral limb.

health values were adjusted accordingly). Only the most influential and clinically relevant sensitivity analyses were reported in detail.

We also explored the CE of two additional diagnostic strategies for the more-invasive treatment scenario. The first strategy was MR angiography in all patients followed by DSA to plan bypass surgery in those who required it. The second strategy was duplex US with DSA for planning bypass surgery.

RESULTS

Base-case Analysis

Considering the minimally invasive treatment scenario (**Table 4**) for the base-case analysis (60-year old men with no history of CAD), no diagnostic workup yielded the lowest effectiveness and costs. The incremental CE ratio for MR angiography yielded $35,000 per QALY compared with no diagnostic workup. DSA was the most effective strategy and the incremental CE ratio was $471,000 per QALY compared with MR angiography. Duplex US was less effective and more costly than MR angiography; however, the differences in QALYs and costs were slight. Under the more-invasive treatment scenario (**Table 5**), DSA was the most effective strategy, with an incremental CE ratio of $179,000 per QALY compared with no diagnostic workup. MR angiography and duplex US were both dominated by DSA.

For 40-year-old men, the results were quite similar, even though the incremental CE ratios decreased (minimally invasive treatment scenario, $18,000 per QALY for MR angiography; more-invasive treatment scenario, $119,000 per QALY for DSA). For 70-year-old men with a history of CAD, only the minimally invasive treatment scenario was considered and MR angiography had an incremental CE ratio of $95,000 per QALY.

Sensitivity Analysis

The results were not sensitive to changes in the diagnostic test characteristics, except that use of the alternative values for the treatment recommendations by duplex US (4) (**Table 2**) changed the results in favor of duplex US under the minimally invasive treatment scenario. Duplex US then became the optimal strategy (6.1503 QALYs and $21,928) and had an incremental CE ratio of $34,000 per QALY.

In a sensitivity analysis, we assumed that angioplasty could immediately follow DSA and found that, for DSA, the QALYs increased by 0.0007

Table 4
QALYs, Costs, and Incremental CE Ratios for the Base-case Analysis, Minimally Invasive Treatment Scenario

Diagnostic Strategy*	QALY	Cost ($)	Incremental CE Ratios
No diagnostic workup	6.0606	18,912	–
Duplex US	6.1465	22,042	D
MR angiography	6.1487	21,959	35,000
DSA	6.1498	22,497	471,000

Note.—D = dominated. Numbers of incremental CE ratios could be slightly different from calculating based on the numbers in the table because of rounding. Incremental CE ratios were calculated compared to the next best strategy after excluding dominated strategies.
* Strategies were ordered on increasing effectiveness (QALYs).

Table 5
QALYs, Costs, and Incremental CE Ratios for the Base-Case Analysis, more Invasive Treatment Scenario

Diagnostic Strategy*	QALY	Cost ($)	Incremental CE Ratios
No diagnostic workup	6.0606	18,912	–
Duplex US	6.2002	50,178	D
MR angiography	6.2136	48,980	D
DSA	6.2254	48,411	179,000

Note.—D = dominated. Numbers of incremental CE ratios could be slightly different from calculating based on the numbers in the table because of rounding. Incremental CE ratios were calculated compared to the next best strategy after excluding dominated strategies.
* Strategies were ordered on increasing effectiveness (QALYs).

and the costs decreased by $217, but only the incremental CE ratio for DSA under the minimally invasive treatment scenario changed to $195,000 per QALY. Also, when we broadened the criteria of suitability for angioplasty for patients with intermittent claudication (0.74 for suprainguinal lesions and 0.50 for infrainguinal lesions; **Table 3**), the results changed in favor of DSA. Effectiveness and costs for DSA were 6.2449 QALYs and $24,640 for the minimally invasive treatment scenario, and the incremental ratio for DSA relative to MR angiography decreased to $91,000 per QALY. Effectiveness and costs were 6.3024 QALYs and $40,714 for the more-invasive treatment scenario, and the incremental ratio for DSA relative to the no-diagnostic-workup strategy decreased to $90,000 per QALY.

By defining severe intermittent claudication by a walking distance shorter than 175 meters (base-case analysis, 250 meters), the effectiveness increased and the costs decreased. For both the minimally invasive treatment scenario and the more-invasive treatment scenario, the incremental CE ratio of DSA increased ($968,000 per QALY and $233,000 per QALY, respectively).

Finally, we explored the CE of MR angiography (6.2253 QALYs and $48,587) and duplex US (6.2257 QALYs and $48,374) in combination with DSA for planning bypass surgery for the more-invasive treatment scenario, and these strategies were similar to DSA. The strategy of duplex US with DSA for planning bypass surgery was the optimal strategy, with an incremental CE ratio of $179,000 per QALY compared with the no-diagnostic-workup strategy.

DISCUSSION

We found that differences in costs and effectiveness between the various diagnostic imaging strategies for patients with intermittent claudication were slight. Differences between the strategies arise from differences in costs of the tests, risks of the tests, and the proportion and consequences of false test results, all of which seem important at the time of testing. However, what may seem to be a large difference at the time of testing becomes relatively small when considering long-term overall outcomes such as lifetime costs and quality-adjusted life expectancy. In addition, the results were dependent to some extent on the treatment options considered. When treatment was limited to angioplasty, MR angiography, duplex US, and DSA yielded similar costs and effectiveness, whereas if both angioplasty and bypass surgery were considered as treatment options, DSA yielded slightly lower costs and higher effectiveness compared to the other strategies. The reason that the optimal diagnostic strategy depended on the available treatment options can be explained by considering that the consequences of a false diagnostic test result were more influential if the treatment scenario included bypass surgery than if only angioplasty was considered. For example, if bypass is performed in an incorrect arterial segment, a second bypass procedure is necessary, which yields high costs and has a risk of complications; DSA preceding the angioplasty procedure would prevent treatment of an incorrect arterial segment. Also, bypass surgery was more expensive than angioplasty, resulting in higher incremental CE ratios for the more-invasive treatment scenario.

We found two other studies (28,29) that analyzed the CE of the pretreatment workup for PAD. In one study (29), duplex US and DSA were compared and it was concluded that duplex US was not a cost-effective alternative because of its low sensitivity. The other study (28) reported that MR angiography alone or in combination with selective use of DSA might be a cost-effective alternative compared with DSA. The inflow and outflow assessments were evaluated in that analysis, which was comparable to our analysis, in which we evaluated whether the lesion was located in a suprainguinal or infrainguinal location and which treatment was preferable. Three key differences between their analysis and ours were that they considered patients with limb-threatening PAD instead of intermittent claudication, they did not consider angioplasty as a possible treatment option, and they performed MR angiography without gadolinium enhancement.

Rather than performing a clinical trial, we developed a decision model and retrieved data from various literature sources. The use of such secondary data has limitations in that data are not always fully applicable to the question under study. For instance, much of the radiologic literature on the diagnostic workup of PAD has focused on the diagnostic performance of the imaging modalities for arterial segments, whereas, in our analysis, we estimated the lifetime costs and quality-adjusted life expectancy for patients. With use of various modeling strategies, we were able to integrate the per-segment diagnostic performance data to a more meaningful patient level. Also, many studies have been published on treatment recommendations according to MR angiography and duplex US, but most do not give sufficient detail for use in a decision model. The data for duplex US on treatment recommendations were available from an older study (11) in which no color guidance was used, implying that the diagnostic performance of duplex US is probably better than our baseline estimate. When we used data from a more recent study (4) in the sensitivity analysis, the results of strategies including duplex US improved. Besides, criteria for the suitability of lesions for angioplasty were reported in only one (5) of the quoted studies (4–6,11) and, therefore, we were unable to compare the criteria.

Another limitation of decision analysis is that assumptions have to be made to keep the model tractable. We had to make assumptions about outcomes after false test results because not all the consequences are known. In our model, all false test results entailed a decrease in quality-adjusted life expectancy and/or an increase in costs. Another assumption that may be questionable is the assumption of DSA to be the reference standard. Earlier studies (30,31) reported that MR angiography detected more patent runoff vessels than DSA, which may be important for assessing the feasibility of bypass surgery and the optimal distal anastomosis. Also, the definition of severe intermittent claudication (walking distance less than 250 meters) may be arbitrary. We found that the use of a more stringent cutoff value (175 meters) did not change the conclusions. Finally, we did not model the option of workup for CAD before proceeding with imaging workup and treatment for PAD because this is a different question than we set out to address and is beyond the scope of our paper. However, we did consider the presence of CAD in patients with intermittent claudication. In our analyses, we assumed that patients with a history of CAD would not undergo bypass surgery for symptoms of intermittent claudication because the results of an earlier CE analysis (9) showed that bypass surgery for these patients was less effective and more costly than supervised exercise or angioplasty.

In our base-case analysis, we assumed that DSA for the pretreatment workup of PAD and a subsequent angioplasty procedure would be scheduled in separate sessions. However, in clinical practice, diagnostic DSA and angioplasty may be planned as one procedure, even though the definite choice of treatment is unknown before the procedure. If the lesion is not suitable for angioplasty, the procedure will be terminated after the diagnostic DSA procedure and, depending on the flexibility of the work process, the angiography room may remain unused. This implies inefficient use of personnel, equipment, and room time, which increases costs. The advantages of combining DSA and angioplasty into one procedure are that the patient is exposed only once to the risks of a percutaneous procedure and that it is cost-saving as a result of more efficient use of room time, personnel, and other resources. In a sensitivity analysis, we assumed that 10% of patients needed a second session for angioplasty. The cost savings of performing the procedures in one session outweighed the cost increase of inefficient use of personnel, equipment, and room time, and there was a slight increase in effectiveness, which suggests that planning diagnostic DSA and angioplasty as one procedure is preferred to performing initial noninvasive imaging.

The incremental CE ratios in our baseline analysis ranged from $35,000 to $471,000 per QALY. Society's willingness to pay for health care interventions is unknown and depends on many aspects such as the health care system and economic situation in a country. In the literature, a wide range of estimates for society's willingness to pay have been published. A study that determined estimates for society's willingness to pay by converting value-of-life estimates available from various fields to dollars per QALY demonstrated a range of $25,000 to $450,000 per QALY (1998 US dollars, rounded) (32). However, in the medical literature, the generally reported range varies between $10,000 and $100,000 per QALY (33).

In the current analysis, we evaluated MR angiography, duplex US, and DSA, three imaging modalities that are currently widely used for the diagnostic workup of PAD. However, not every center has all three modalities at its disposition and, therefore, the comparison of MR angiography and duplex US may be irrelevant for these centers. The choice to use MR angiography or duplex US may depend on parameters other than those considered in our analysis, such as the expertise of the radiologists or the availability of equipment. The development of new radiologic techniques is ongoing and multidetector spiral CT angiography might be a new alternative for the workup of PAD (34–36). It is often used for the diagnostic workup of abdominal aortic aneurysms and has been shown to have excellent diagnostic accuracy with relatively low costs ($300 in 1997 dollars) (37). In the future, the currently developed decision model may be useful in comparing CT angiography with the existing imaging modalities as more information becomes available regarding sensitivity and specificity and the effect on the treatment plan, prognosis, quality of life, and costs.

Although we attempted to incorporate all the relevant costs and effects of the diagnostic imaging workup for patients with intermittent claudication in this CE analysis, this analysis has limitations, as discussed, and presents only one way of looking at the problem. A decision analysis does not make a clinical study superfluous. In fact, we consider the current study a prelude to, rather than a substitution for, a clinical study. Because the differences in costs and effectiveness across diagnostic imaging strategies were slight, our results suggest that a clinical study should focus on the decision-making process and workflow in clinical practice. An appropriate design for such a comparison would be a pragmatic randomized controlled trial in which patients are randomized among available diagnostic imaging modalities and the outcome measures focus on the clinical decision-making process (38).

In conclusion, the differences among diagnostic imaging strategies for patients with intermittent claudication are slight. This implies that MR angiography or duplex US can replace DSA without substantial loss of effectiveness at a slightly reduced cost, especially if minimally invasive treatment options are considered. In addition, planning an angioplasty procedure in conjunction with diagnostic DSA yields a minimal gain in effectiveness and a slight cost reduction.

Acknowledgments: The authors thank Kai Yu Ho, MD, PhD, for kindly providing data on uninterpretable MR angiography results. This project was supported in part by the Foundation 'Vereniging Trustfonds Erasmus Universiteit Rotterdam' and by the Netherlands Organization for Scientific Research.

References

1. Visser K, Hunink MGM. Peripheral arterial disease: gadolinium-enhanced MR angiography versus color-guided duplex US—a meta-analysis. Radiology 2000; 216:67–77.
2. van der Zaag ES, Legemate DA, Nguyen T, Balm R, Jacobs MJ. Aortoiliac reconstructive surgery based upon the results of duplex scanning. Eur J Vasc Endovasc Surg 1998; 16:383–389.
3. Wain RA, Berdejo GL, Delvalle WN, et al. Can duplex scan arterial mapping replace contrast arteriography as the test of choice before infrainguinal revascularization? J Vasc Surg 1999; 29: 100–107.
4. Elsman BH, Legemate DA, van der Heijden FH, de Vos HJ, Mali WPTM, Eikelboom BC. Impact of ultrasonographic duplex scanning on therapeutic decision making in lower-limb arterial disease. Br J Surg 1995; 82:630–633.
5. Quinn SF, Sheley RC, Semonsen KG, Leonardo VJ, Kojima K, Szumowski J. Aortic and lower-extremity arterial disease: evaluation with MR angiography versus conventional angiography. Radiology 1998; 206:693–701.
6. Baum RA, Rutter CM, Sunshine JH, et al. Multicenter trial to evaluate vascular magnetic resonance angiography of the lower extremity. American College of Radiology Rapid Technology Assessment Group. JAMA 1995; 274: 875–880.
7. Hessel SJ, Adams DF, Abrams HL. Complications of angiography. Radiology 1981; 138:273–281.
8. Egglin TK, O'Moore PV, Feinstein AR, Waltman AC. Complications of peripheral arteriography: a new system to identify patients at increased risk. J Vasc Surg 1995; 22:787–794.
9. de Vries SO, Visser K, de Vries JA, Wong JB, Donaldson MC, Hunink MGM. Intermittent claudication: cost-effectiveness of revascularization versus exercise therapy. Radiology 2002; 222:25–36.
10. Ascher E, Mazzariol F, Hingorani A, Salles-Cunha S, Gade P. The use of duplex ultrasound arterial mapping as an alternative to conventional arteriography for primary and secondary infrapopliteal bypasses. Am J Surg 1999; 178:162–165.
11. Kohler TR, Andros G, Porter JM, et al. Can duplex scanning replace arteriography for lower extremity arterial disease? Ann Vasc Surg 1990; 4:280–287.
12. Waugh JR, Sacharias N. Arteriographic complications in the DSA era. Radiology 1992; 182:243–246.
13. Auditing surgical outcome. 10 Years with the Swedish Vascular Registry—Swedvasc. Eur J Surg Suppl 1998; 581: 1–48.
14. Hunink MGM, Wong JB, Donaldson MC, Meyerovitz MF, Harrington DP. Patency results of percutaneous and surgical revascularization for femoropopliteal arterial disease. Med Decis Making 1994; 14:71–81.
15. de Vries SO, Hunink MGM. Results of aortic bifurcation grafts for aortoiliac occlusive disease: a meta-analysis. J Vasc Surg 1997; 26:558–569.
16. Bosch JL, Hunink MGM. Meta-analysis of the results of percutaneous transluminal angioplasty and stent placement for aortoiliac occlusive disease. Radiology 1997; 204:87–96.
17. Da Silva A, Widmer LK. Arterienprojekt: Peripher arterielle Verschlußkrankheit. In: Widmer LK, Stähelin HB, Nissen C, et al, eds. Venen-, Arterien-Krankheiten, koronare herzkrankheit bei Berufstätigen: Prospektiv-epidemiologische Untersuchung Basler Studie I-III. 1st. Bern, Switzerland: Verlag Hans Huber, 1981; 137–240.
18. de Vries SO, Donaldson MC, Hunink MGM. Contralateral symptoms after unilateral intervention for peripheral occlusive disease. J Vasc Surg 1998; 27: 414–421.
19. de Vries SO, Kuipers WD, Hunink MGM. Intermittent claudication: symptom severity versus health values. J Vasc Surg 1998; 27:422–430.
20. Sculpher M, Michaels J, McKenna M, Minor J. A cost-utility analysis of laser-assisted angioplasty for peripheral arterial occlusions. Int J Technol Assess Health Care 1996; 12:104–125.
21. Torrance GW. Measurement of health state utilities for economic appraisal: a review. J Health Econ 1986; 5:1–30.
22. Tsevat J, Goldman L, Lamas GA, et al. Functional status versus utilities in survivors of myocardial infarction. Med Care 1991; 29:1153–1159.
23. Bosch JL, Haaring C, Meyerovitz MF, Cullen KA, Hunink MGM. Cost-effectiveness of percutaneous treatment of iliac artery occlusive disease in the United States. AJR Am J Roentgenol 2000; 175:517–521.
24. Jansen RM, de Vries SO, Cullen KA, Donaldson MC, Hunink MGM. Cost-identification analysis of revascularization procedures on patients with peripheral arterial occlusive disease. J Vasc Surg 1998; 28:617–623.
25. Bosch JL, Tetteroo E, Mali WP, Hunink MGM. Iliac arterial occlusive disease: cost-effectiveness analysis of stent placement versus percutaneous transluminal angioplasty. Dutch Iliac Stent Trial Study Group. Radiology 1998; 208:641–648.
26. Lipscomb J, Weinstein MC, Torrance GW. Time preference. In: Gold MR, Siegel JE, Russell LB, et al, eds. Cost-effectiveness in Health and Medicine, 1st Edition. New York: Oxford University Press, 1996;233.
27. Weinstein MC, Stason WB. Foundations of cost-effectiveness analysis for health and medical practices. N Engl J Med 1977; 296:716–721.
28. Yin D, Baum RA, Carpenter JP, Langlotz CP, Pentecost MJ. Cost-effectiveness of MR angiography in cases of limb-threatening peripheral vascular disease. Radiology 1995; 194:757–764.
29. Geitung JT, Wikstrom T, Zeuchner J, Gothlin JH. Cost-effectiveness of colour duplex sonography compared with angiography of the pelvis and lower limb. Eur Radiol 1996; 6:481–484.
30. Carpenter JP, Owen RS, Baum RA, et al. Magnetic resonance angiography of peripheral runoff vessels. J Vasc Surg 1992; 16:807–813.
31. Owen RS, Carpenter JP, Baum RA, Perloff LJ, Cope C. Magnetic resonance imaging of angiographically occult runoff vessels in peripheral arterial oc-

clusive disease. N Engl J Med 1992; 326:1577–1581.
32. Hirth RA, Chernew ME, Miller E, Fendrick AM, Weissert WG. Willingness to pay for a quality-adjusted life year: in search of a standard. Med Decis Making 2000; 20:332–342.
33. Graham JD, Corso PS, Morris JM, Segui-Gomez M, Weinstein MC. Evaluating the cost-effectiveness of clinical and public health measures. Annu Rev Public Health 1998; 19:125–152.
34. Kreissig R, Knollmann FD, Steinkamp HJ, Boettcher HD, Ehrenstein T, Felix R. Evaluation of multi-slice helical CT angiography for the assessment of peripheral artery disease. In: Proceedings of the Radiological Society of North America; 2000:593–594.
35. Balzer JO, Herzog C, Thalhammer C, Pira A, Engelmann KS, Vogl TJ. Multidetector CT angiography in the evaluation of peripheral arterial occlusive disease. In: Proceedings of the Radiological Society of North America; 2000: 593.
36. Huber AM, Von Rueckmann B, Bruening RD, Helmberger TK, Schoepf UO, Reiser MF. CTA of the peripheral vascular tree using MDCT. In: Proceedings of the Radiological Society of North America; 2000:593.
37. Rubin GD, Armerding MD, Dake MD, Napel S. Cost identification of abdominal aortic aneurysm imaging by using time and motion analyses. Radiology 2000; 215:63–70.
38. Hunink MGM, Krestin GP. Study design for concurrent development, assessment, and implementation of new diagnostic imaging technology. Radiology 2002; 222:604–614.