Radiology

CT Coronary Angiography in Patients Suspected of Having Coronary Artery Disease: Decision Making from Various Perspectives in the Face of Uncertainty[1]

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Purpose: To determine the cost-effectiveness of computed tomographic (CT) coronary angiography as a triage test, performed prior to conventional coronary angiography, by using a Markov model.

Materials and Methods: A Markov model was used to analyze the cost-effectiveness of CT coronary angiography performed as a triage test prior to conventional coronary angiography from the perspective of the patient, physician, hospital, health care system, and society by using recommendations from the United Kingdom, the United States, and the Netherlands for cost-effectiveness analyses. For CT coronary angiography, a range of sensitivities (79%–100%) and specificities (63%–94%) were used to help diagnose significant coronary artery disease (CAD). Optimization criteria (ie, outcomes considered) were: revised posttest probability of CAD, life-years, quality-adjusted life-years (QALYs), costs, and incremental cost-effectiveness ratios (ICERs). Extensive sensitivity analysis was performed.

Results: For a prior probability of CAD of less than 40%, the probability of CAD after CT coronary angiography with negative results was less than 1%. The Markov model calculations from the patient/physician perspective suggest that CT coronary angiography maximizes life-years respectively in 60-year-old men and women at a prior probability of less than 38% and 24% and maximizes QALYs at a prior probability of less than 17% and 11%. From the hospital/health care perspective, CT coronary angiography helps reduce health care and direct nonhealth care–related costs (according to UK/U.S. recommendations), regardless of prior probability, and lowers all costs, including production losses (Netherlands recommendations) at a prior probability of less than 87%–92%. Analysis performed from a societal perspective by using a willingness-to-pay threshold level of €80 000/QALY suggests that CT coronary angiography is cost-effective when the prior probability is lower than 44% and 37% in men and women, respectively. Sensitivity analyses showed that results changed across the reported range of sensitivity of CT coronary angiography.

Conclusion: The optimal diagnostic work-up depends on the optimization criterion, prior probability of CAD, and the diagnostic performance of CT coronary angiography.

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Patients with chest pain who are suspected of having coronary artery disease (CAD) usually undergo conventional coronary angiography to help diagnose CAD. These patients may be imaged noninvasively with computed tomographic (CT) coronary angiography and avoid invasive conventional coronary angiography. Systematic reviews and meta-analyses have shown that CT coronary angiography is accurate in helping diagnose CAD with a patient-level sensitivity of 96%–99% and a specificity of 74%–94% (1–3). Although CT coronary angiography is rapidly being introduced in clinical practice as a triage test performed prior to conventional coronary angiography, its effect on patient outcome and cost-effectiveness has not yet been determined.

Every year, approximately 4.5 people per 1000 visit a doctor with chest pain (4); more than 2 million conventional coronary angiograms are performed in Europe (5) and approximately 1.7 million are performed in the United States (6). The use of CT coronary angiography as an initial triage test could reduce costs and minimize discomfort for patients. However, a tradeoff must be made between the benefits and disadvantages of CT coronary angiography.

Current guidelines recommend the use of CT coronary angiography in patients with a low to intermediate prior probability of CAD who are unable to exercise or who have inconclusive functional test results (7). However, what constitutes a low to intermediate prior probability remains to be elucidated. The purpose of this study was to determine the cost-effectiveness of CT coronary angiography performed as a triage test prior to conventional coronary angiography in patients with suspected CAD.

Materials and Methods

One author (J.J.B.) is the recipient of research grants from Edwards Lifesciences (Nyon, Switzerland), Biotronik (Tilburg, the Netherlands), GE Healthcare (Brussels, Belgium), BMS Medical Imaging (North Billerica, Mass), St Jude (St Paul, Minn), and Medtronic (Maastricht, the Netherlands). All other authors had full control over the inclusion of any data and information that might have represented a conflict of interest.

Decision Model

We developed a decision model (in DATA Pro, 2009 Suite; TreeAge Software, Williamstown, Mass) to evaluate the use of 64-section CT coronary angiography (new strategy) as an initial imaging test, followed by conventional coronary angiography if CT coronary angiographic results were positive when compared with conventional coronary angiography only (current practice) (Fig 1). Short-term outcomes related to the diagnostic imaging tests were modeled with a decision tree and a Markov model (cycle length, 1 year) was used to model long-term outcomes. We modeled whether a patient was alive or dead and whether a cardiovascular event occurred. Quality of life was modeled on the chance of successful relief from angina by means of treatment. Costs were estimated for diagnostic tests, treatment (percutaneous coronary intervention [PCI], coronary artery bypass graft [CABG], medication), and events during follow-up. The decision was analyzed from the perspectives of the physician, patient, hospital, health care system, and society by using various optimization criteria (8) and by taking into account the uncertainty involved.

Data Sources and Assumptions

We searched the literature for input data and for data to be used in sensitivity analyses (Appendix E1, *[http://radiology.rsna.org/lookup/suppl/doi:10.1148/radiol.2533090507/-/DC1]*). All variables were entered in the model as distributions. Recent studies and meta-analyses were used to derive a range of per-patient specificities for CT coronary angiography (64%–93%) (1,3,10). To account for the inverse relationship between sensitivity and specificity, we modeled the sensitivity (79%–100%) as a function of specificity and the diagnostic

Advances in Knowledge

- According to cost-effectiveness model analyses, our results suggest that CT coronary angiography performed as a triage test prior to conventional coronary angiography is cost-saving and cost-effective in men with a prior probability of coronary artery disease (CAD) of less than 44% and in women with a prior probability of CAD of less than 37%.
- The optimal diagnostic strategy depends on the optimization criterion, prior probability of CAD, and the diagnostic performance of CT coronary angiography.

Implications for Patient Care

- CT coronary angiography performed as triage test prior to conventional coronary angiography is likely to be cost-saving in most situations.
- Patients with a low prior (pretest) probability of CAD should undergo CT coronary angiography as a triage test prior to conventional coronary angiography.
- Patients with a moderate or high prior (pretest) probability of CAD should not undergo CT coronary angiography as a triage test prior to conventional coronary angiography.

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Abbreviations:
CABG = coronary artery bypass graft
EVPI = expected value of perfect information
ICER = incremental cost-effectiveness ratio
PCI = percutaneous coronary intervention
QALY = quality-adjusted life-year
WTP = willingness to pay

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Guarantors of integrity of entire study, T.S.S.G., M.G.M.H.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; literature research, M.F.L.M., N.R.M., M.J.C., M.G.M.H.; clinical studies, W.B.M., M.F.L.M., J.D.S., N.R.M., A.C.W., F.P., J.J.B., M.J.C., G.P.K., P.J.d.F., M.G.M.H.; statistical analysis, T.S.S.G., W.B.M., M.G.M.H.; and manuscript editing, T.S.S.G., W.B.M., M.F.L.M., N.R.M., M.J.C., G.P.K., M.G.M.H.

See Materials and Methods for pertinent disclosures.

odds ratio and its reported range (1). Specificity and the diagnostic odds ratio were assumed to be independent of age, sex, risk factors, and presentation. Significant CAD was defined as a reduction of lumen diameter of 50% or more, which is appropriate in the setting of selecting patients for some form of treatment or further diagnostic testing. The mortality rate for CT coronary angiography was assumed to be equivalent to that for intravenous contrast materials (11). Conventional coronary angiography was used as the reference standard, assuming 100% sensitivity and specificity. Sex-specific probabilities of 60-year-old patients for having CAD were determined by using the method of Diamond and Forrester (9), which, although published in 1979, is still commonly used to estimate the prior probability of CAD on the basis of age, sex, and type of chest pain. A wide range was used to account for the uncertainty in the prior probability of CAD (mean, 79% for men and 65% for women). Cardiovascular event rates in patients without CAD (patients with true-negative or false-positive test results) were assumed to be equivalent to first cardiovascular event rates in the general population and were calculated with a recently published prediction model by D'Agostino et al (15) on the basis of the Framingham Heart Study, which was the most representative study population available. To account for the higher risk in our target population, event rates were modeled for the average risk factor profiles of patients as observed in a cohort of patients presenting to our institution with chest pain. Cardiovascular events included coronary death, myocardial infarction, coronary insufficiency, angina, stroke, cardiac arrest, peripheral arterial disease, and heart failure. We estimated that symptomatic patients diagnosed with CAD who are subsequently treated (those with true-positive test results) will have a 1.5-fold (95% confidence interval: 1.3, 1.7) cardiovascular event rate compared with patients without symptomatic CAD on the basis of a multivariable Cox model reported from the EUROPA study (16). Following a first cardiovascular event, the cardiovascular recurrence rate will be 1.44-fold (95% confidence interval: 1.25, 1.66) higher than that for a patient with CAD and no previous cardiovascular event (16). We assumed that the cardiovascular event rate is reduced by means of treatment (hazard rate ratio, 0.63; range 0.44–0.88) (17,18), modeled with a combined weighted average effectiveness of CABG, PCI, and treatment with medication (28,29). Missed CAD patients (those with false negative results) forego the benefit of treatment, implying reduced quality of life and a 2.4-fold (range, 1.5–3.2) cardiovascular event rate compared with a patient without CAD (17,18). After a cardiovascular event during the follow-up in patients with an initial negative test result, CAD is diagnosed and treated and the patient will be subject to a higher recurrence rate from then on. Cardiovascular disease−related 1-year mortality (including in-hospital mortality) following a cardiovascular event was assumed to be 17% (range, 10%–25%) (18,19,20). Age- and sex-specific risks of radiation-induced fatal cancer associated with performing CT or conventional coronary angiography were based on reported estimates of lifetime-attributable cancer incidence (21) and adjusted to reflect mortality given the BEIR VII report (22). Age- and sex-specific noncardiovascular mortality rates were obtained from the Dutch Cen-

Figure 1

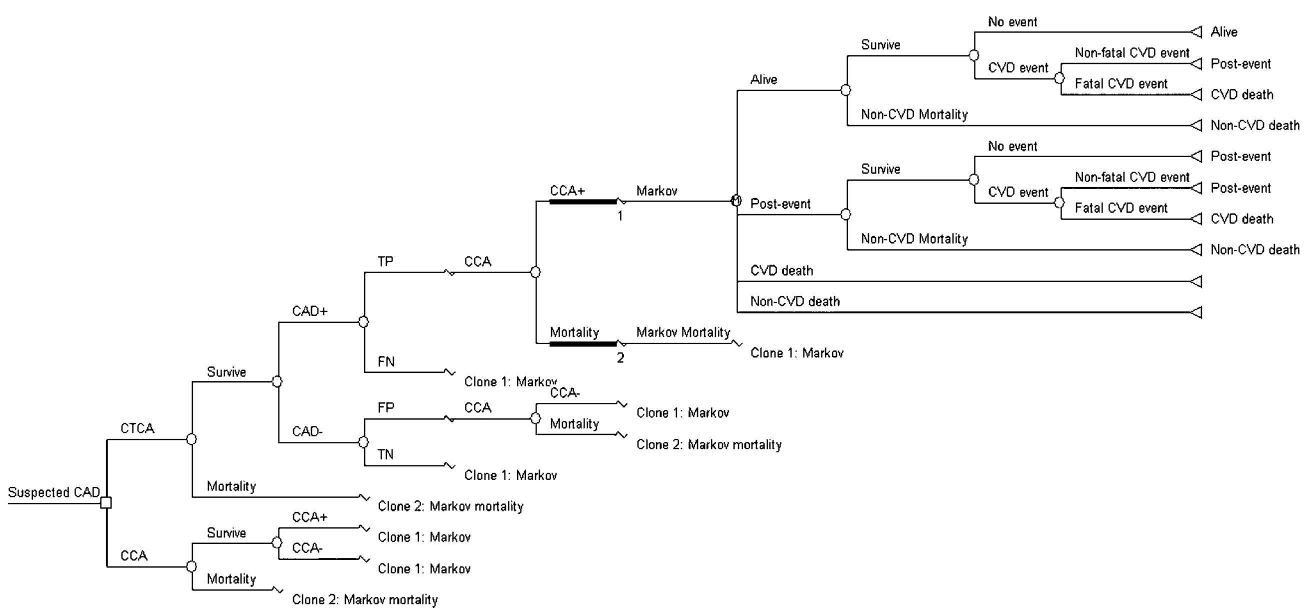

Figure 1: Decision tree for treatment shows decision node (□), chance nodes (○), and Markov nodes (M). Conventional coronary angiography *(CCA)* performed after CT coronary angiography *(CTCA)* reveals positive results. *Clone* indicates structure identical to another subtree, which is marked with black line and corresponding number. CVD = cardiovascular disease, FN = false negative, FP = false positive, TN = true negative, TP = true positive.

tral Bureau for Statistics (11). Technical details and assumptions are clarified in the Appendix (*http://radiology.rsna.org/lookup/suppl/doi:10.1148/radiol.2533090507/-/DC1*).

Quality of Life

Quality of life estimates following treatment were a pooled weighted average taking into account that 51% of patients diagnosed with symptomatic CAD undergo PCI, 25% undergo CABG, and 24% will be on medication only (36). Five years after treatment, 15% of CABG-treated patients and 16% of PCI-treated patients still have angina (23); the quality of life weight for angina is 0.74 (range, 0.71–0.77) and without angina is 0.87 (range, 0.86–0.88) (23). Patients in whom the diagnosis was missed (those with false-negative test results) were all assumed to have angina during follow-up until a cardiovascular event occurred, after which they would be diagnosed and treated (23). A disutility of 0.04 (range, 0.02–0.07) QALYs was modeled for a cardiovascular event (such as myocardial infarction) during follow-up (24).

Costs

Costs for both CT and conventional coronary angiography were determined with a cost analysis and included direct health care costs (personnel, materials, equipment), indirect health care costs (housing, overhead), direct nonhealth care–related costs (patient travel and time costs), and indirect nonhealth care–related costs (production losses). Costs for CABG and PCI were determined on the basis of estimates from the National Health Care Authority (27). Annual costs for medical therapy for diagnosed CAD patients were determined on the basis of treatment with aspirin, nitrates, statins, and angiotensin-converting enzyme inhibitors and included one follow-up visit per year (25). Costs for cardiovascular events were estimated to range from €8000–€18 000 (mean, €13 000), which is consistent with previously published data (38). Costs for reinterventions were taken into account by using weighted averages of reintervention rates for the treatment options. Noncardiovascular disease–related health care costs arising from increased longevity (inducing costs associated with increased life expectancy) were not taken into account to avoid a financial advantage of reduced longevity (33–35). All costs were converted to year 2007 rates, given Dutch consumer price indices, and reported in euros (14). In 2007, €1.00 was equivalent to U.S. $1.37. All costs were represented by gamma distributions.

Data Analysis

To analyze the decision from various perspectives, we used several optimization criteria (ie, the revised posttest probability of CAD, life-years, quality-adjusted life-years (QALYs), costs, and incremental cost-effectiveness ratios (ICERs).

Patient and physician perspectives.—To reflect the physician and patient perspectives, we determined the revised (posttest) probability for positive and negative CT coronary angiographic results depending on the prior (pretest) probability. The probability of having CAD after a CT coronary angiogram with positive results is equivalent to the positive predictive value. The probability of CAD after a CT coronary angiogram with negative results is equivalent to 1 minus the negative predictive value. Posttest probabilities were calculated by using the per-patient sensitivities and specificities as reported in the literature (1,3,10). Next, we determined the strategy that maximized life-years and QALYs and calculated the prior probability threshold level below which CT coronary angiography would be preferred.

Hospital and health care perspectives.—In an analysis from the hospital perspective, we calculated the diagnostic costs and determined the prior probability threshold level below which CT coronary angiography would reduce cost. The analysis from the health care perspective considered QALYs and health care costs and was performed according to UK recommendations, discounting both future costs and effectiveness at 3.5% (31,32).

Societal perspective.—A cost-effectiveness analysis from the societal perspective was performed according to U.S. recommendations, which considered QALYs, health care costs, and direct nonhealth care–related costs (patient time and travel costs), and discounted both future costs and effectiveness at 3% (33–35). Subsequently, an analysis from the societal perspective was performed according to Dutch recommendations, which, in addition to the above, also took productivity losses (friction costs) into account and discounted future costs and effectiveness at 4% and 1.5%, respectively (26). A willingness-to-pay (WTP) threshold level of €80 000/QALY, as recommended by the Dutch Council for Public Health (39), was used to assess cost-effectiveness. If the ICER (difference in costs divided by the difference in effectiveness, of strategy A compared with strategy B) is lower than the societal WTP threshold level, we conclude that strategy A is a cost-effective alternative to strategy B.

By using one- and two-way sensitivity analyses, we assessed the effect of varying each parameter across its distribution. Probabilistic sensitivity analysis was performed by drawing from all variable distributions (Table E1 *[http://radiology.rsna.org/lookup/suppl/doi:10.1148/radiol.2533090507/-/DC1]*) by using a cohort Monte Carlo simulation of 100 000 samples (one-level). We calculated the probability that performing CT coronary angiography as the initial test was cost-effective compared with conventional coronary angiography for varying WTP threshold levels and present acceptability curves. Expected value of perfect information (EVPI; simulation with 100 000 samples) was calculated to assess the value of performing further research and partial EVPI calculations (two-level simulation performed with 1000 × 1000 samples) identified the parameters that were the major sources of uncertainty (40–42).

Specific Scenario: Cohort Study

To determine the cost-effectiveness of CT coronary angiography at our own institution, we modeled a specific scenario in which we reanalyzed the model on the basis of a study that evaluated 64-section CT coronary angiography (10) in our institution by using the per-patient sensitivity and specificity and the observed sex-specific prior probabilities of disease from this study. The study population in this cohort comprised 233 stable patients suspected of having CAD who presented with chest pain suggestive of angina. In this study, all patients were referred for conventional coronary angiography on the basis of their history or functional test results that suggested the presence of cardiac ischemia, and all patients underwent CT coronary angiography prior to conventional coronary angiography. This study was approved by the institutional review board and all patients signed informed consent. All cost-effectiveness analyses were recalculated for the specific scenario.

Results

Cohort Study

Data from 156 men and 77 women with stable angina in the cohort were analyzed. Of these, 113 (72.4%) men and 33 (42.9%) women had significant CAD seen at conventional coronary angiography. Mean patient age was 60 years (range, 49—74 years), 151 (64.8%) presented with typical chest pain, 75 (32.2%) smoked, 149 (63.9%) had hypertension, 47 (20.2%) had diabetes mellitus, and 36 (15.5%) had experienced prior myocardial infarction. Given these risk factors, the average annual hazard rate for a cardiovascular event was calculated by using the Framingham Heart Study, resulting in a rate of 0.024 (range, 0.014–0.077) for men and 0.014 (0.008–0.053) for women (15). Details are provided in the Appendix (*http://radiology.rsna.org/lookup/suppl/doi:10.1148/radiol.2533090507/-/DC1*).

Reference Case Analysis

Patient and physician perspectives.—In the setting of a prior probability of disease of less than 40%, the revised probability of CAD after CT coronary angiography with negative results is less than 1% (Fig 2), regardless of whether the test characteristics were based on the meta-analysis or the cohort study. In contrast, the probability of CAD after CT coronary angiography with positive results varies over a wide range, depending on the prior probability (Fig 2).

The analysis of life-years demonstrated that below a prior probability threshold level of 38% in men and 24% in women, patients would, on average, benefit from CT coronary angiography performed as the initial imaging test (Fig 3). CT coronary angiography maximizes QALYs at a prior probability of less than 17% in men and less than 11% in women (Fig 3).

Hospital and health care perspectives.—CT coronary angiography lowered diagnostic costs below a prior probability of disease of 84% in men and women when compared with conventional coronary angiography. By using the UK recommendations for cost-effectiveness analysis, CT coronary angiography lowered health care costs across all prior probabilities (Fig 3). For men, there was a small gain in QALYs of 0.037 with conventional coronary angiography, a small increment in cost of €589, and an ICER of €15 915/QALY gained when compared with CT coronary angiography. For women, there was a QALY gain of 0.036, a cost increment of €714, and an ICER of €19 913/QALY (Table). In both men and women, performing conventional coronary angiography alone increased the net health benefit compared with performing CT followed by conventional coronary angiography by 0.03 QALY equivalents (Table).

Societal perspective.—By using the U.S. recommendations for cost-effectiveness analysis, CT coronary angiography increases savings for health care and direct nonhealth care–related costs regardless of the prior probability (Fig 3). For men, there was a small gain in QALYs of 0.039, with a small increment in cost of €643, and an ICER of €16 509/QALY gained for conventional compared with CT coronary angiography. For women, there was a gain in QALYs of 0.038, a cost increment of €775, and a €20 360/QALY gained (Table). Performing conventional coronary angiography without prior CT coronary angiography increased net health benefit compared with initial CT coronary angiography by 0.03 QALY equivalents (Table).

By using the Dutch recommendations for cost-effectiveness analysis, health care costs and direct nonhealth care–related costs, including production losses, were reduced to a prior disease probability of less than 87% in men and less than 92% in women for CT coronary angiography when compared with conventional coronary angiography (Fig 3). For men, there was a small

Figure 2

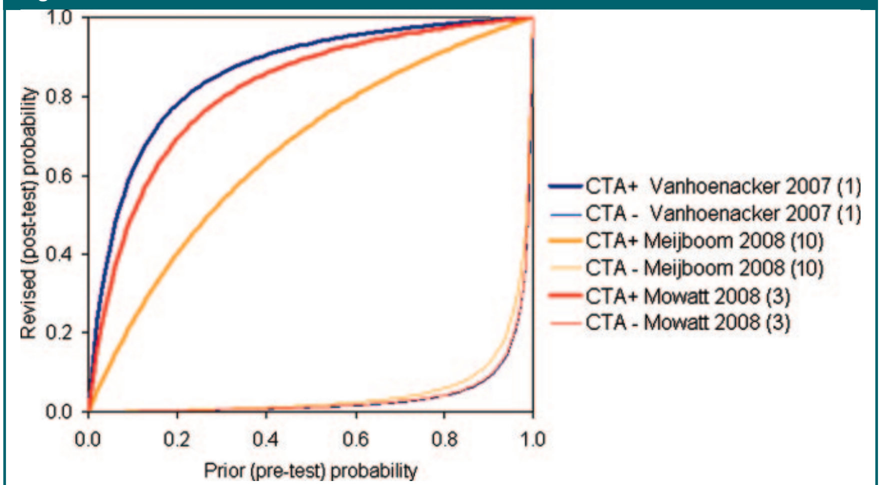

Figure 2: Revised (posttest) probability of CAD, plotted as function of prior (pretest) probability of CAD for positive and negative CT coronary angiography results by using test characteristics found in cohort study and meta-analyses (1,3,10). Note that for low to moderate prior probability of disease (prior probability <40%), CT coronary angiography with negative results virtually excludes CAD (revised probability <1%), regardless of whether cohort study or meta-analysis results are used. CTA = CT coronary angiography.

gain in QALYs of 0.046, with a small increment in cost of €182, and an ICER of €4095/QALY gained for conventional compared with CT coronary angiography. For women, there was a QALY gain of 0.047, a cost increment of €485, and an ICER of €10 383/QALY (Table). Performing conventional coronary angiography increased net health benefit by 0.04 QALY equivalents when compared with initial CT coronary angiography (Table).

Sensitivity Analyses

The prior probability threshold levels were not sensitive to changes across plausible ranges of all parameter inputs, with one exception. Varying the sensitivity of CT coronary angiography (independently from specificity) from 80% to 100%, the prior probability threshold level below which CT coronary angiography maximizes QALYs for women ranged from 2% to 44% and cost-effectiveness (UK recommendations) was optimized at 8% to 72%. Varying specificity (independently of sensitivity) of CT coronary angiography and test costs had little effect (Fig. 4). Varying the disutility incurred by a cardiovascular event and the fatality rate associated with a cardiovascular event did not alter the results.

For probabilistic sensitivity analyses, the probability that CT coronary angiography is cost-effective when compared with conventional coronary angiography was 2% in men and 13% in women for a threshold level WTP of €80 000/QALY (Fig. 5). Value of information analysis showed an EVPI for further research of €3 per man and €46 per woman, which, for the European Union population (500 million, annual incidence 4.5 per 1000) over a period of 5 years (discounted at 3.5%) amounts to approximately €0.38 billion, and for the U.S. population (300 million) over a period of 5 years (discounted at 3%) amounts to €0.23 billion. Partial EVPI calculations demonstrated that the expected value of information for women was mainly a result of uncertainty in the prior probability of CAD, radiation risk, and test characteristics (combined EVPI, €44). For both men and women, the uncertainty in the parameters related to long-term outcome, quality of life, and costs had a negligible partial EVPI.

Specific Scenario

The Table shows the results from the cost-effectiveness analyses for the specific scenario. Conventional coronary angiography was the preferred strategy in all cases, except for women analyzed according to the UK and US recommendations.

The prior probabilities observed in our cohort study were consistent with the estimates derived from Diamond and Forrester (9) for all patients, except for women with typical angina. The prior probability of CAD for women in the co-

Figure 3

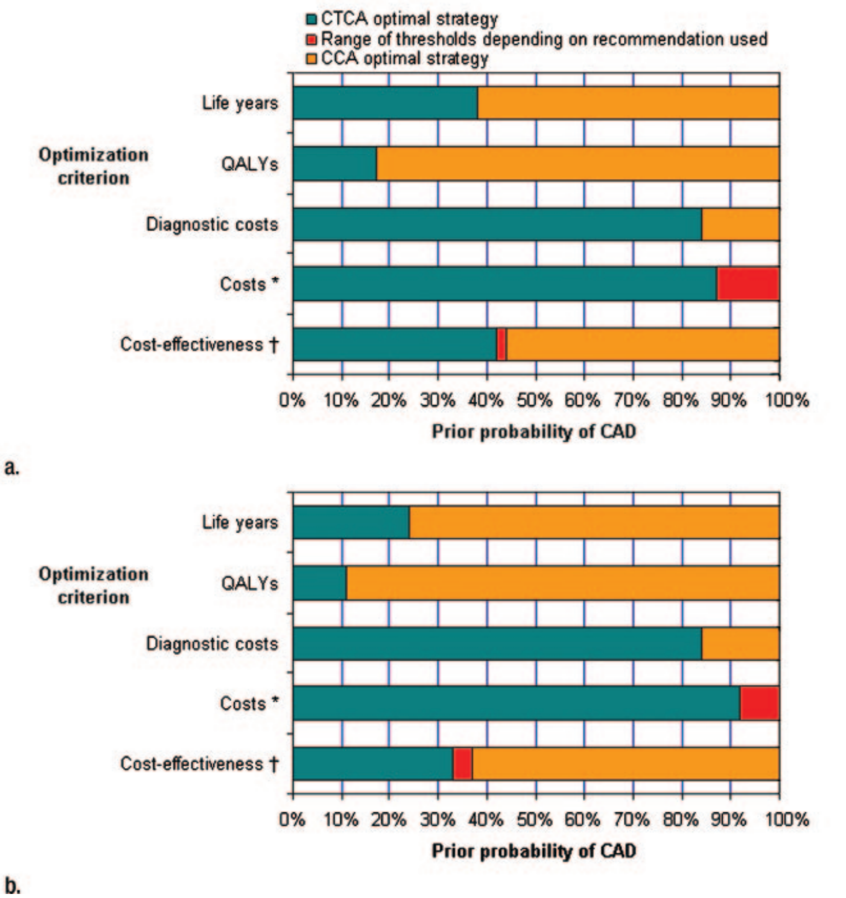

Figure 3: Sensitivity analysis for prior probability of CAD in 60-year-old men (upper) and women (lower). Threshold level for prior probability of CAD below which CT coronary angiography (*CTCA*, followed by conventional coronary angiography *[CCA]* in case of positive results) is preferred to CCA only, from perspectives of patient, physician, hospital, health care system, and society. Above this threshold level, CCA optimizes criterion used. **(a)** For 60-year-old men, cost-effectiveness analysis was performed by using recommendations from UK (health care perspective), U.S. (societal perspective), and Dutch (societal perspective) recommendations by using WTP threshold level of €80 000/QALY. *Based on recommendations used, threshold level below which CTCA is optimal strategy (for costs) varies from 87% to 100%. †Given recommendations used (U.S., UK, NL), threshold level below which CTCA is cost-effective varies from 42% to 44%. **(b)** For 60-year-old women, cost-effectiveness analysis was performed by using recommendations from UK (health care perspective), U.S. (societal perspective), and Dutch (societal perspective) recommendations by using WTP threshold level of €80 000/QALY. *Based on recommendations used, threshold level below which CTCA is optimal strategy (when optimizing costs) varies from 92% to 100%. †Depending on recommendations used, threshold level below which CTCA is cost-effective varies from 33% to 37%.

hort study with typical angina was 43%, whereas this probability would be estimated as 85%, according to Diamond and Forrester. However, this discrepancy does not alter the decision given our threshold levels for cost-effectiveness.

Discussion

In this study, we evaluated the comparative effectiveness, costs, and cost-effectiveness of CT coronary angiography performed as an initial test (followed by conventional coronary angiography if positive results were obtained) compared with conventional coronary angiography alone in patients with stable angina and functional test results suggestive of ischemia. Our results demonstrate that in the setting of a low to moderate prior probability of disease, CT coronary angiography with negative results virtually excludes CAD. In contrast, the revised probability of CAD after CT coronary angiography with positive results probability varies over a wide range, implying that a positive CT coronary angiogram needs to be confirmed with conventional coronary angiography. Although CT coronary angiography is less costly and less invasive compared with conventional coronary angiography, the radiation risk is higher by using both studies, and false-negative CT coronary angiography results can occur, in which case patients forego the benefit of treatment. We showed that CT coronary angiography can be a cost-saving technique in that it helps avoid unnecessary angiograms but comes with the disadvantage of a slight decrement in patient outcomes. Optimization criteria developed on the basis of QALYs favors the use of conventional coronary angiography because it will identify all patients with CAD and the potential long-term benefit of treating CAD outweighs the small risk involved. When considering costs only, CT coronary angiography is preferred because it is less expensive and can help avoid performing unnecessary angiograms in a substantial proportion of patients. When considering disadvantages, benefits, and costs together, our results suggest that the use of CT coronary angiography as an initial test is cost-effective below an average prior probability

Cost-effectiveness Analysis of CT Followed by Conventional Coronary Angiography Compared with Conventional Coronary Angrography Only

Strategy	Cost (€)	Effectiveness (QALY)	ICER (€ per QALY)	Incremental NHB of CCA vs CTCA
Reference case analysis				
Men (prior probability of CAD: 79%)				
UK				
CTCA	31 506	11.578		
CCA	32 095	11.615	15 915	0.0296
United States				
CTCA	34 154	12.180		
CCA	34 797	12.219	16 509	0.0309
The Netherlands				
CTCA	386 640	14.36		
CCA	386 822	14.406	4095	0.0435
Women (prior probability of CAD: 65%)				
UK				
CTCA	26 020	13.263		
CCA	26 734	13.299	19 913	0.0269
United States				
CTCA	28 307	14.05		
CCA	29 082	14.088	20 360	0.0284
The Netherlands				
CTCA	252 455	16.941		
CCA	252 940	16.988	10 383	0.0407
Cohort study				
Men (prior probability of CAD: 72%)				
UK				
CTCA	30 377	11.62		
CCA	30 531	11.626	25 014	0.0042
United States				
CTCA	32 843	12.228		
CCA	32 998	12.234	23 681	0.0046
The Netherlands				
CTCA	383 971	14.415		
CCA	384 063	14.423	11 413	0.0069
Women (prior probability of CAD: 43%)				
UK				
CTCA	21 007	13.409		
CCA	21 384	13.413	95 602	−0.0008
United States				
CTCA	22 788	14.206		
CCA	23 183	14.21	87 804	−0.0004
The Netherlands				
CTCA	245 313	17.132		
CCA	245 691	17.139	56 117	0.002

Note.—This analysis was performed according to recommendations in the UK, the United States, and the Netherlands for 60-year-old men and women. The results indicate that at a willingness-to-pay threshold level of €80 000/QALY, conventional coronary angiography is optimal in men and women. In our cohort study, CT coronary angiography is optimal in women only if UK or U.S. recommendations are used. A strategy is dominated if another strategy is equally as effective or more effective and less costly. The incremental net health benefit (NHB) is calculated as $NHB_{CCA} - NHB_{CTCA}$ with NHB = QALY − (cost/€80 000) and expressed in units of QALY equivalents. CCA = conventional coronary angiography, CTCA = 64-detector CT coronary angiography.

Figure 4

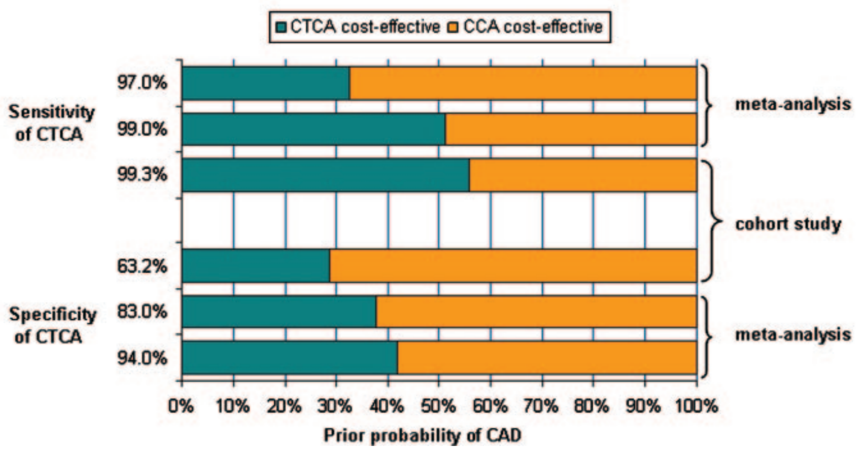

Figure 4: Two-way sensitivity analyses for test characteristics and prior probability of CAD in women. Graph shows influence of varying test characteristics (independently from each other) on prior probability threshold level above which conventional coronary angiography *(CCA)* would be more cost-effective. Upper and lower bars are range in sensitivity and specificity, respectively, as observed in the Mowatt et al (3) and Vanhoenacker et al (1). Other bars are sensitivity and specificity as observed in cohort study (Appendix *[http://radiology.rsnajnls.org/cgi/content/full/2533090507/DC1]*). Note that effect of varying sensitivity on prior probability threshold level is substantial. Varying specificity does not alter prior probability threshold level as much as does varying sensitivity. Analysis performed by using UK recommendations for cost-effectiveness analysis (health care perspective). Changes in probability threshold level were similar in men: by varying sensitivity from 97%–99.3%, threshold level for cost-effectiveness ranged from 39%–66%. Varying specificity resulted in threshold levels ranging from 40%–52%. CTCA = CT coronary angiography.

Figure 5

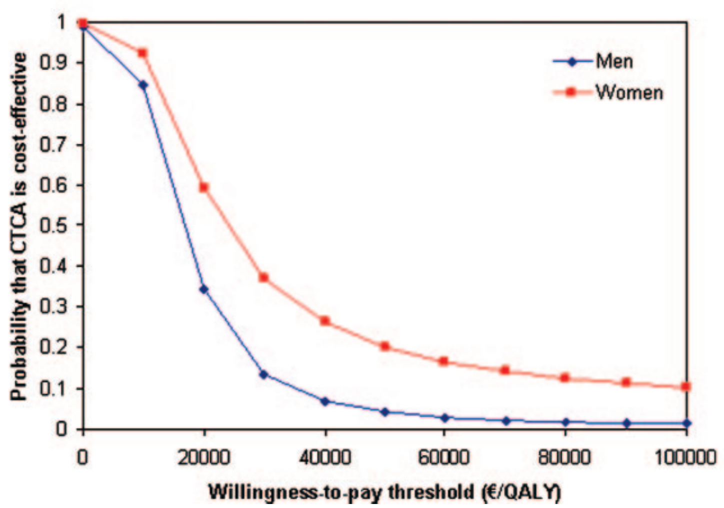

Figure 5: Acceptability curves for CT coronary angiography *(CTCA)* strategy plots probability that strategy is cost-effective given particular WTP threshold level. We ran 100 000 Monte Carlo probabilistic simulations that used random draws from distributions that represent uncertainty around parameter estimates. For men and women, UK recommendations were used for cost-effectiveness analysis (health care perspective) and WTP threshold level of €80 000/QALY. In 2% and 13% of simulations for men and women, respectively, CTCA was cost-effective compared with conventional coronary angiography, which corresponds to 2% and 13% probability of cost-effectiveness.

threshold level of 40%. Above this threshold level, conventional coronary angiography remains the preferred strategy. The use of UK, U.S., and Dutch recommendations for cost-effectiveness analyses did not substantially influence the results.

It is important to note that a lower threshold level exists, one that is not addressed in our study. Below this threshold level, the net gain of performing CT coronary angiography is too small and it would therefore not be cost-effective when compared with either not testing or performing another less-invasive, less-costly test. However, including additional strategies was beyond the scope of this paper.

In our cohort study, CT coronary angiography was a cost-effective strategy for women in the UK and U.S. analyses. The difference in cost-effectiveness between the reference case analysis and ours is driven by the difference in prior probability (women had a lower prior probability in the study) and test characteristics.

In our cost-effectiveness analysis, we used a WTP threshold level of €80 000/QALY (39). Had we used a WTP threshold level of €50 000/QALY, our conclusions would be the same because all ICERs for conventional coronary angiography were less than €50 000 in the reference case analysis. For our cohort study, the results only changed for women who were analyzed according to the Dutch recommendations for whom CT coronary angiography would be cost-effective at the €50 000 threshold level, whereas conventional coronary angiography would be cost-effective at the €80 000 threshold level.

In our study, a stenosis of 50% or more in at least one vessel was considered as significant, whereas a stenosis of 70% or more is commonly considered as hemodynamically significant. Only hemodynamically significant stenoses are eligible for revascularization, which makes a threshold level of 70% or more relevant. However, our aim was to select patients that require some form of treatment. We modeled medication-based therapy, PCI, and CABG as treatment strategies, which is why we used a threshold level of a stenosis of 50% or more for significant CAD.

One could argue that physicians are primarily interested in diagnosing severe CAD, as these patients would be eligible for revascularization, whereas others can be adequately treated by using medication alone. Although the model uses a dichotomized definition of CAD, the model does allow for differences in treatment effects incurred by differences in disease location and severity. This was carried out by including weighted averages of treatment effects, quality-adjusted life estimates, and costs. Additionally, the uncertainty in such parameters was taken into account by using distributions.

The additional information that is provided by CT coronary angiography (eg, assessment of plaque burden) could potentially improve the management of CAD patients. Currently however, too little evidence is available. Future studies should investigate the added value of assessing plaque burden and the effectiveness of decision-making on the basis of such findings.

Our analysis focused on a 64-section CT scanner, which implies that our results are only applicable to patients undergoing 64-section CT. However, with the rapid rate of advancement in technology, newer generations of CT scanners are expected to be more accurate in helping diagnose significant CAD, owing to a higher temporal and spatial resolution. In addition, new techniques are being developed to minimize radiation dose. Such improvements will increase the cost-effective application of CT coronary angiography.

Our methods were different from a previously published cost-effectiveness analysis by Dewey and Hamm (43), who used costs per correctly identified CAD patient as a measure of cost-effectiveness, did not consider costs of subsequent treatment and ignored the benefit of correct exclusion of CAD. They found a threshold level of 60% prior probability of CAD below which CT coronary angiography is indicated. Kuntz et al (44) examined the cost-effectiveness of several noninvasive functional (imaging and nonimaging) tests. When compared with exercise single photon emission CT and exercise echocardiography, conventional coronary angiography had an ICER of $32 600 and $35 200 respectively, for 50–59-year-old men with mild chest pain. This is slightly higher compared with what we found for conventional coronary angiography compared with CT coronary angiography for men by using the U.S. recommendations.

More recently, Khare et al (45) and Ladapo et al (46) studied the cost effectiveness of CT coronary angiography in low-risk patients with acute chest pain. Our analysis focused on patients with stable chest pain and much higher disease prevalence. Therefore, our analysis adds new information to the current knowledge about cost-effective applications of CT coronary angiography.

One limitation of our study was the use of meta-analyses for the diagnostic performance of CT coronary angiography that were published in 2007 and 2008. Alternative data sources for diagnostic performance, such as Miller et al (47), recently studied the diagnostic accuracy of CT coronary angiography. Miller et al reported a per-patient sensitivity and specificity for diagnosing significant (≥50% stenosis) CAD of 85% and 90%, respectively. They excluded patients with Agatston coronary calcium scores of 600 or higher, which makes their results relevant to a diagnostic strategy by using CT coronary calcium scoring as a triage test prior to performing CT coronary angiography. However, such a diagnostic strategy was not considered in our study. Although their study population was different from our target population, the ranges of sensitivity and specificity we used also included the results reported by Miller et al.

Our aim was to design a lucid decision model that would be easy to interpret and that can help guide decision making. Consequently, we had to make several assumptions. First, parameter estimates were obtained from the literature by using the best available published evidence. Second, for the purpose of estimating costs and disutility of a cardiovascular event, we assumed that cardiovascular events were mainly myocardial infarctions and that costs and disutility of other cardiovascular events were similar to that of myocardial infarctions. Third, the quality-of-life estimates were derived from Hlatky et al (23), which was a study on multivessel CAD. This may be an underestimate of the quality of life of patients with single-vessel disease, which therefore may have overestimated the gain in effectiveness with treatment, which, in turn, would have created bias in favor of conventional coronary angiography. Fourth, work-up for chest pain following a CT coronary angiogram with negative results was not modeled and may have created bias in favor of CT coronary angiography. Fifth, we assumed the sensitivity and diagnostic odds ratio to be independent of age, sex, risk factors, and presentation. Sixth, we did not consider other noninvasive tests but rather considered only patients referred for conventional coronary angiography for whom either the history or functional test results have suggested the presence of cardiac ischemia.

Furthermore, it is important to realize that all costs were based on European estimates. In the cost-effectiveness analysis, we were interested in evaluating how the different perspectives (health care system vs societal) and the different (UK vs U.S. vs Dutch) recommendations would affect the results and therefore chose to use the same cost estimates for these comparisons. Reported costs for CT and conventional coronary angiography in the United States range from $630–$3000 and $1750–$5176, respectively (45,46). In addition, a U.S. health care cost database provides an estimate of $10 000 for performing conventional coronary angiography (48). Because the costs for conventional coronary angiography in the United States are relatively high compared with the costs for CT coronary angiography, CT coronary angiography might be a more cost-effective approach in the US. However, all costs in the US are generally higher, as is the WTP threshold level, which could lead to different results and merits further study.

Finally, it is important to note that the differences between the two strategies in terms of costs, QALYs, and net health benefits were rather small, which is why we performed extensive (probabilistic) sensitivity analysis and value-of-information analysis. We used modern techniques to evaluate whether further research is necessary and to inform the choice of a future study. Value-of-information analysis showed a rather high expected value of further research for both Europe and the United States and indicated that future research should focus on test characteristics, the risk of radiation, and prediction rules for the diagnosis of CAD.

In conclusion, the optimal diagnostic strategy depends on the optimization criterion, prior probability of CAD, and test characteristics. Analysis of our cost-effectiveness model suggests that CT coronary angiography performed as a triage test prior to conventional coronary angiography is cost-effective in men with a prior probability of CAD of less than 44% and in women with a prior probability of CAD of less than 37%. Above this threshold level, conventional coronary angiography remains the most cost-effective strategy. To maximize patient outcomes, a lower threshold level applies and to lower costs, a higher threshold level should be used.

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