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ORIGINAL RESEARCH

Cost-Effectiveness Analysis of Stress Cardiovascular Magnetic Resonance Imaging for Stable Chest Pain Syndromes

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ABSTRACT

OBJECTIVES The aim of this study was to compare, using results from the multicenter SPINS (Stress CMR Perfusion Imaging in the United States) study, the incremental cost-effectiveness of a stress cardiovascular magnetic resonance (CMR)–first strategy against 4 other clinical strategies for patients with stable symptoms suspicious for myocardial ischemia: 1) immediate x-ray coronary angiography (XCA) with selective fractional flow reserve for all patients; 2) single-photon emission computed tomography; 3) coronary computed tomographic angiography with selective computed tomographic fractional flow reserve; and 4) no imaging.

BACKGROUND Stress CMR perfusion imaging has established excellent diagnostic utility and prognostic value in coronary artery disease (CAD), but its cost-effectiveness in current clinical practice has not been well studied in the United States.

METHODS A decision analytic model was developed to project health care costs and lifetime quality-adjusted life years (QALYs) for symptomatic patients at presentation with a 32.4% prevalence of obstructive CAD. Rates of clinical events, costs, and quality-of-life values were estimated from SPINS and other published research. The analysis was conducted from a U.S. health care system perspective, with health and cost outcomes discounted annually at 3%.

RESULTS Using hard cardiovascular events (cardiovascular death or acute myocardial infarction) as the endpoint, total costs per person were lowest for the no-imaging strategy ($16,936) and highest for the immediate XCA strategy ($20,929). Lifetime QALYs were lowest for the no-imaging strategy (12.72050) and highest for the immediate XCA strategy (12.76535). The incremental cost-effectiveness ratio for the CMR-based strategy compared with the no-imaging strategy was $52,000/QALY, whereas the incremental cost-effectiveness ratio for the immediate XCA strategy was $12 million/QALY compared with CMR. Results were sensitive to variations in model inputs for prevalence of disease, hazard rate ratio for treatment of CAD, and annual discount rate.

CONCLUSIONS Prior to invasive XCA, stress CMR can be a cost-effective gatekeeping tool in patients at risk for obstructive CAD in the United States. (Stress CMR Perfusion Imaging in the United States [SPINS] Study; NCT03192891 (J Am Coll Cardiol Img 2020;13:1505–17) © 2020 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

APC = ambulatory payment classification

CAD = coronary artery disease

CCTA = coronary computed tomographic angiography

CMR = cardiovascular magnetic resonance

CPT = Current Procedural Terminology

CT = computed tomographic

FFR = fractional flow reserve

ICER = incremental cost-effectiveness ratio

MACE = major adverse cardiovascular event(s)

MI = myocardial infarction

PSA = probabilistic sensitivity analysis

QALY = quality-adjusted life year

SPECT = single-photon emission computed tomography

XCA = x-ray coronary angiography

Coronary artery disease (CAD) remains a major cause of patient mortality and morbidity and accounts for more than $200 billion in health care expenditures in the United States annually (1). Although more than 1 million diagnostic coronary angiographic studies are performed annually in the United States (1), it has been estimated that as many as two-thirds of elective studies do not show any obstructive disease and may be unnecessary (2,3), suggesting that better noninvasive strategies are needed to triage patients according to their risk and to curb health care expenses. Stress cardiovascular magnetic resonance (CMR) perfusion imaging is a robust clinical tool with excellent diagnostic accuracy (4–7) and prognostic value (8,9). Cost-effectiveness analyses have suggested that stress CMR as an initial assessment for patients with stable chest pain syndrome is cost effective compared with other stress modalities in practice or with direct x-ray coronary angiography (XCA) (10–13), but data on comparative cost-effectiveness from the U.S. health care system are limited.

The SPINS (Stress CMR Perfusion Imaging in the United States) study was recently performed using a registry developed by the Society for Cardiovascular Magnetic Resonance to assess the diagnostic and prognostic values of stress CMR and the downstream costs of care in patients presenting with chest pain syndromes in a multicenter cohort in the United States (9). In the present study, using a base-case decision tree model, we compared the lifetime health benefits, health care costs, and incremental cost-effectiveness of 5 competing diagnostic strategies for stable, symptomatic patients at intermediate pre-test likelihood of obstructive coronary disease using data from the SPINS registry and contemporary published research: 1) immediate XCA for all patients, with a select number undergoing measurement of fractional flow reserve (FFR); 2) CMR-based management, in which those with abnormal test results undergo XCA; 3) single-photon emission computed tomography (SPECT)-based management; 4) coronary computed tomographic angiography (CCTA) with performance of computed tomographic (CT) FFR for a select number of patients; and 5) no initial imaging, with subsequent testing only for patients with persistent symptoms (**Central Illustration**).

METHODS

THE SPINS STUDY. The methods and results of the SPINS study were recently published (9). In brief, SPINS retrospectively included consecutive patients with chest pain syndromes suspicious for obstructive CAD who underwent stress CMR between January 1, 2008, and December 31, 2013, from 13 U.S. sites (9). Stress CMR perfusion protocols were based on product pulse sequences available at the sites, and study interpretations were based on sites' reporting of ischemia and infarction according to the 16-segment American Heart Association nomenclature for perfusion and 17-segment model for late gadolinium

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Cardiovascular Imaging* author instructions page.

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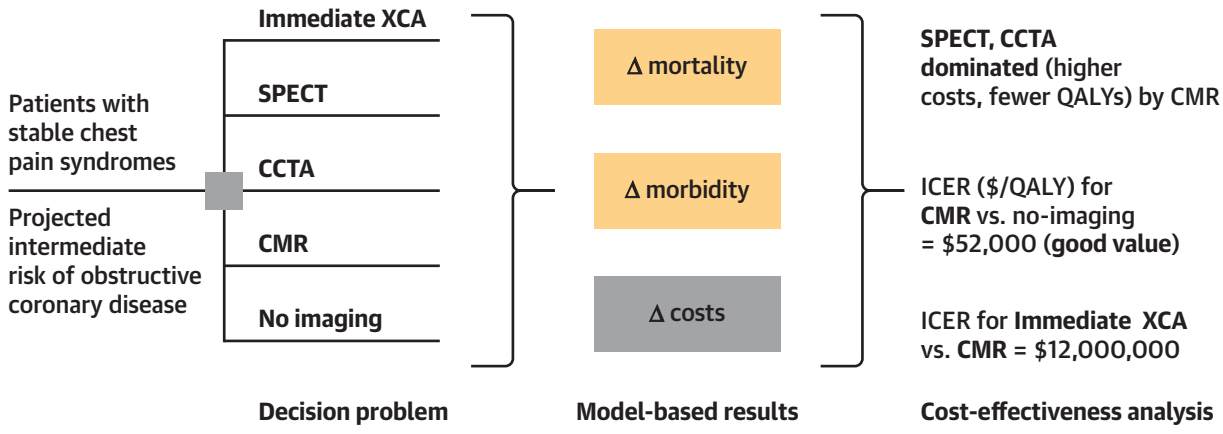
CENTRAL ILLUSTRATION **Conceptual Diagram of the Cost-Effectiveness Analysis**



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Patients enter the simulation model and are assigned to 1 of 5 diagnostic strategies. The model estimates the impact of strategy choice on mortality, morbidity, and coronary disease–related cost outcomes. The trade-offs between quality-adjusted life years (QALYs) and costs are evaluated using incremental cost-effectiveness analysis methods.

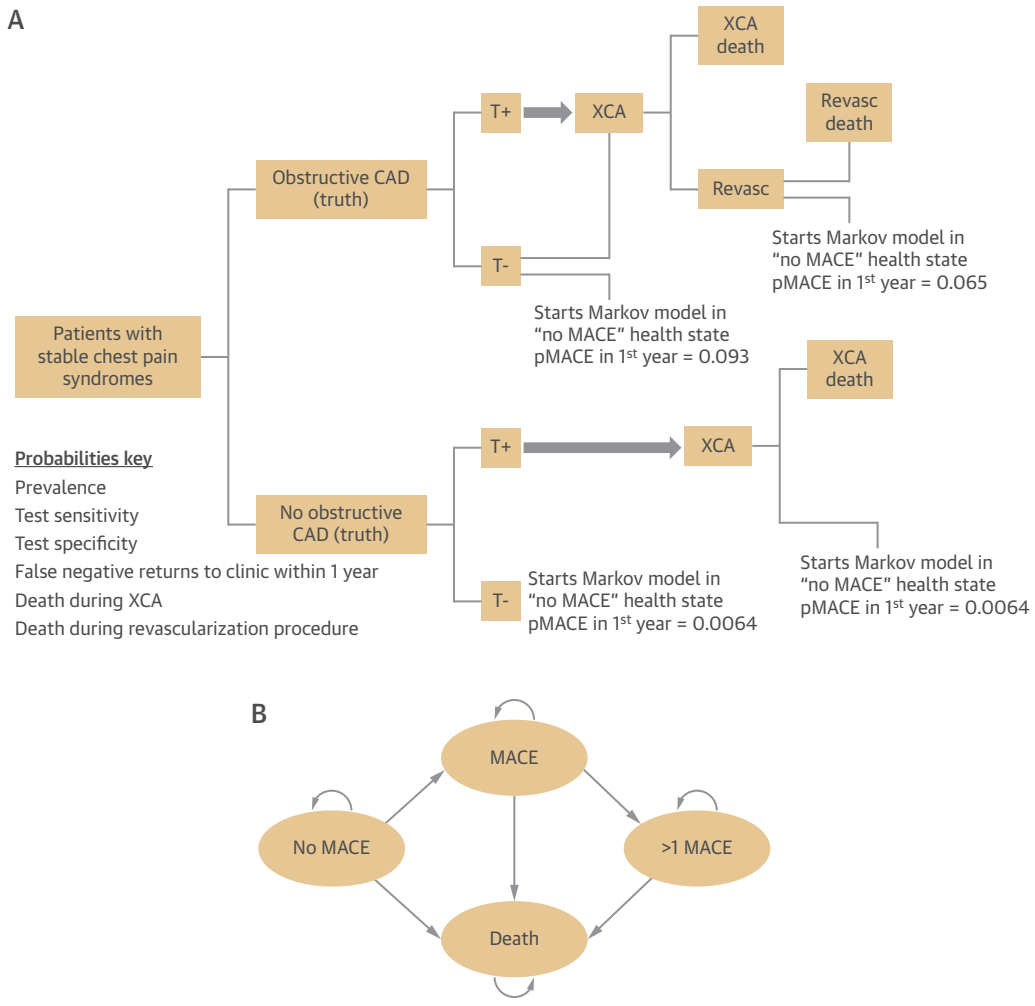
enhancement imaging, respectively. Inducible ischemia was defined as the presence of at least 1 segment with a stress perfusion defect in the absence of matching myocardial infarction (MI) by late gadolinium enhancement in a typical endocardial pattern within 1 of the coronary artery territories. Follow-up for clinical cardiovascular events occurred for a target of at least 4 years after the index stress CMR study. Major adverse cardiovascular events (MACE) included cardiovascular death, acute nonfatal MI, hospitalization for unstable angina or congestive heart failure, and late coronary artery bypass grafting >6 months following index CMR. Before the study began, definitions of all clinical variables were standardized across the sites by training webinars, instructional documents, and online postings. We obtained local Institutional Review Board approval at each participating site, with a waiver of the requirement to obtain written informed consent.

MODEL OVERVIEW. We performed a computer-simulated state-transition model that projected MACE, life expectancy, quality-adjusted life years (QALYs), and lifetime health care costs for a symptomatic patient cohort at risk for obstructive coronary disease at initial clinical presentation (Figure 1). The annual risk for clinical events depended on CAD status, initiation of therapy (medical and revascularization), and risk for XCA and revascularization procedures. Death could occur as result of cardiovascular events, noncardiovascular events, or complications arising from invasive diagnostic or therapeutic options. Depending on the clinical management strategy, patients in the model received optimal therapy (including medical and revascularization procedures) immediately, later in life on the basis of disease progression, or never. Base-case model inputs and sensitivity analysis ranges are reported in Table 1.

For each management strategy, health care costs and QALYs were projected to derive incremental cost-effectiveness ratios (ICERs). We used $100,000/QALY as a threshold for willingness to pay for health (14). The analyses were conducted from a health system perspective over a lifetime horizon, with all costs projected to 2017 dollars, and future health care costs and QALYs discounted at 3% annually (15). The model was programmed in TreeAge Pro 2012 (TreeAge Software, Williamstown, Massachusetts).

CLINICAL STRATEGIES EVALUATED. In the immediate XCA strategy, all patients underwent invasive angiographic procedures at the time of clinical presentation. Given that most recent guidelines recommend performance of FFR in vessel stenosis from 50% to 90% (16,17), we extrapolated that 41% of patients would undergo this procedure, on the basis of historic data on the prevalence of lesions angiographically >50% (2). We conducted a sensitivity analysis, varying the rates of FFR use between 0% and 100%. Invasive XCA carried a 0.07% chance of fatal complications in the base-case analysis (18). Patients identified to have obstructive CAD were assumed to undergo optimal medical therapy and revascularizations procedures, of which 69.2% were attributed to percutaneous coronary intervention

FIGURE 1 Model Structure



Model structure for the cardiovascular magnetic resonance, single-photon emission computed tomography, and coronary computed tomographic angiography test strategies leading up to the first year **(A)** and the Markov model used to simulate lifetime outcomes **(B)**. CAD = coronary artery disease; MACE = major adverse cardiovascular event(s); pMACE = probability of having MACE; Revasc = revascularization; T+ = positive test; T− = negative test; XCA = x-ray coronary angiography.

and 30.8% to coronary artery bypass grafting according to the ratio in the SPINS study. Complication rates for revascularization procedures are summarized in Table 1. In the computed tomography-based strategy, all patients underwent CCTA, and 41% underwent CT FFR to additionally characterize intermediate lesions. We conducted a sensitivity analysis, varying the rates of CT FFR use between 0% and 100%. In the CMR and SPECT strategies, patients underwent XCA only if noninvasive imaging demonstrated abnormal findings. Those with true positives were assumed to undergo both medical and revascularization therapies, and this combination led to overall improved outcomes. Patients with normal findings were presumed to be free of obstructive CAD and were managed accordingly. In the no-imaging strategy, patients were initially managed without any investigations. However, we included a provision that because of escalating symptoms, 58% of patients with obstructive CAD would return within the first year, and each year thereafter, for investigations and undergo XCA directly, and we varied this proportion in sensitivity analyses (11). Similarly, in patients who initially underwent any of the imaging strategies, we assumed that each year, 58% of those with false-negative results would present with escalating symptoms and undergo XCA directly.

TABLE 1 Key Model Variables With Base-Case Values and Ranges Used in 1-Way Sensitivity Analysis

	Base-Case Value	Sensitivity Analysis Range	Source/Ref. #
Age, yrs	62.5	55 to 75	SPINS
Proportion male	0.53	0.4 to 0.6	SPINS
Discount rate	0.03	0 to 0.05	(35)
Probability of patient's having treatable CAD	0.324	0.1 to 0.6	SPINS
Sensitivity of CMR	0.89	0.85 to 0.92	(20)
Specificity of CMR	0.87	0.83 to 0.91	(20)
Sensitivity of SPECT	0.73	0.62 to 0.82	(20)
Specificity of SPECT	0.83	0.71 to 0.90	(20)
Sensitivity of CCTA with selective CT FFR	0.90	0.85 to 0.93	(19)
Specificity of CCTA with selective CT FFR	0.71	0.65 to 0.75	(19)
Probability patient with false-negative result returns for XCA within 1 yr	0.5759	0 to 1	(11)
Annual rate of having a new MACE for patients without CAD	0.0064	0.0173*	SPINS
First-year rate of having a MACE for patients with CAD who underwent revascularization	0.065	0.312*	SPINS
Post-first-year rate of having a MACE for patients with CAD who underwent revascularization	0.0217	0.0452*	SPINS
Hazard rate ratio for patients who received medical therapy and underwent revascularization	0.7	0.6 to 0.9	(21,36,37)
Probability of dying during XCA	0.0007	0.0004 to 0.001	(18)
Proportion of revascularizations that are PCI (vs. CABG)	0.692	0 to 1	SPINS
Probability of dying during PCI	0.00128	0.0009 to 0.0017	(38)
Probability of dying during CABG	0.00791	0.0066 to 0.0094	(39)
Post-MACE all-cause mortality multiplier (male)	1.6	1.28 to 1.92	(22)
Post-MACE all-cause mortality multiplier >1 event (male)	3.4	2.72 to 4.08	(22)
Post-MACE all-cause mortality multiplier (female)	2.1	1.68 to 2.52	(22)
Post-MACE all-cause mortality multiplier >1 event (female)	2.5	2.00 to 3.00	(22)
Cost of CMR	$807	$646 to $968	CMS
Cost of SPECT	$1,219	$975 to $1,463	CMS
Cost of CCTA without CT FFR	$386	$309 to $463	CMS
Cost of CCTA with CT FFR	$1,836	$1,469 to $2,203	CMS
Proportion of patients undergoing CCTA who also undergo CT FFR	0.41	0 to 1	(2)
Cost of XCA without FFR	$3,084	$3,153 to $4,730	CMS
Cost of XCA with FFR	$5,175	$4,140 to $6,210	CMS
Proportion of patients undergoing XCA who also undergo FFR	0.41	0 to 1	(2)
Cost of PCI	$36,556	$29,245 to $43,867	(23)
Cost of CABG	$38,797	$31,038 to $46,556	(23)
Acute (first-year) cost of nonfatal MACE	$11,124	$8,899 to $13,349	(40)
Acute (first-year) cost of fatal MACE	$18,206	$14,565 to $21,847	(23)
Chronic (post-first-year) cost of MACE	$3,368	$2,694 to $4,042	(23)
Utility of no-MACE state for men	0.851	0.68 to 1.00	(24)
Utility of no-MACE state for women	0.824	0.66 to 1.00	(24)
Utility of MACE health state	0.778	0.622 to 0.934	(25)
Disutility from acute nonfatal MACE	−0.041	−0.0328 to −0.0492	(25)

*Includes cardiac hospitalization and CABG in definition of MACE (beyond acute MI and CV death).

CABG = coronary artery bypass grafting; CAD = coronary artery disease; CMR = cardiovascular magnetic resonance; CMS = Centers for Medicare and Medicaid Services; CT = computed tomographic; CCTA = coronary computed tomographic angiography; CV = cardiovascular; FFR = fractional flow reserve; MACE = major adverse cardiovascular events; MI = myocardial infarction; PCI = percutaneous coronary intervention; SPECT = single-photon emission computed tomography; SPINS = Stress CMR Perfusion Imaging in the United States; XCA = x-ray coronary angiography.

CAD STATUS AND CARDIOVASCULAR RISK. The demographics of the SPINS cohort were used to simulate the patient population; specifically, the model population was 53% male, with an average age of 63 years and a 32.4% probability of obstructive CAD (9). Sensitivity and specificity for the detection of angiographic significant CAD for stress CMR, SPECT, and CCTA with CT FFR were 89% and 87%, 73% and 83%, and 90% and 71%, respectively, per prior publications (19,20). As the diagnostic gold standard of angiographically significant CAD, XCA with FFR was assumed to have sensitivity and specificity of 100%. We conducted 2 cost-effectiveness analyses, using hard MACE (cardiovascular death and acute MI) in one analysis and all composite MACE (cardiovascular death, acute MI, cardiovascular hospitalizations for unstable angina and congestive heart failure, and late coronary artery bypass grafting) in the other analysis. For patients with obstructive CAD who remained untreated (false-negative results) because of

TABLE 2 Lifetime Per Person Utilization Outcomes, QALYs, Costs, and ICERs for Base-Case Analysis

Strategy	Any XCA	Any Coronary Revascularization	Life Years	QALYs*	Costs*	ICER
Hard MACE defined as acute MI and CV death						
No imaging	29.4%	29.4%	22.13730	12.72050	$16,936	Ref.
CMR	41.1%	32.3%	22.21665	12.76522	$19,273	$52,000/QALY
SPECT	43.2%	31.8%	22.20168	12.75678	$19,578	Strongly dominated
CCTA	51.5%	32.3%	22.21579	12.76472	$19,886	Strongly dominated
Immediate XCA	100%	32.4%	22.21699	12.76535	$20,929	$12 million/QALY†
All MACE defined as acute MI, CV death, cardiac hospitalization, and late CABG						
No imaging	23.6%	23.6%	18.81560	11.06833	$20,605	Ref.
CMR	41.0%	31.8%	18.94289	11.14408	$24,961	$58,000/QALY
SPECT	41.9%	30.2%	18.91937	11.13009	$24,904	Weakly dominated‡
CCTA	51.4%	31.9%	18.94274	11.14401	$25,596	Strongly dominated
Immediate XCA	100%	32.4%	18.95012	11.14849	$26,865	$430,000/QALY†

*Discounted at 3%. †Compared with CMR strategy. ‡The SPECT strategy had a higher ICER than the CCTA strategy, which is more effective, therefore the SPECT strategy is weakly dominated and the immediate XCA ICER is compared with the CMR strategy, per the accepted methods of incremental cost-effectiveness analysis. In other words, SPECT is not on the efficient frontier in this incremental cost-effectiveness analysis.

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life-year; other abbreviations as in Table 1.

underdetection, we applied a hazard rate ratio of 1.43 to adjust event rates (21). For patients who experienced 1 or more cardiovascular events, we used subsequent mortality multipliers of 1.6 and 3.4 for men and 2.1 and 2.5 for women, respectively (22).

COSTS AND HEALTH-RELATED QUALITY OF LIFE. Costs associated with fatal and nonfatal cardiovascular events and revascularization procedures were estimated from a recent analysis of a large managed care population in the United States and from the Agency for Healthcare Research and Quality (21,23). Costs of medical therapy were not explicitly calculated but were presumed to form the cost of a chronic CAD state. All patients diagnosed with CAD were assumed to receive the same drug regimens. Costs of SPECT, stress CMR, XCA, and CCTA were derived from publicly available 2017 Medicare rates, combining Current Procedural Terminology (CPT) codes to reflect professional costs, as well as ambulatory payment classification (APC) codes to reflect average technical fee. We used estimated costs as follows: SPECT (CPT code 78452 + APC code 5593) cost $1,219, stress CMR (CPT code 75563 + APC code 5573) cost $807, XCA (CPT code 93454 + APC code 5191) cost $3,084, XCA with FFR (CPT code 93454 + CPT code 93571 + APC code 5192) cost $5,175, CCTA (CPT code 75574 + APC code 5571) cost $386, and CT FFR (CPT code 0503T) cost $1,450. Health-related quality of life was assigned to all health states in the model and was represented by utility values between 0 (death) and 1 (perfect health). Baseline state was assigned a utility value of 0.851 for men and 0.824 for women (24), which dropped to 0.778 after a nonfatal cardiovascular event. In addition, we applied a disutility of −0.041 for the first year following a nonfatal event (25).

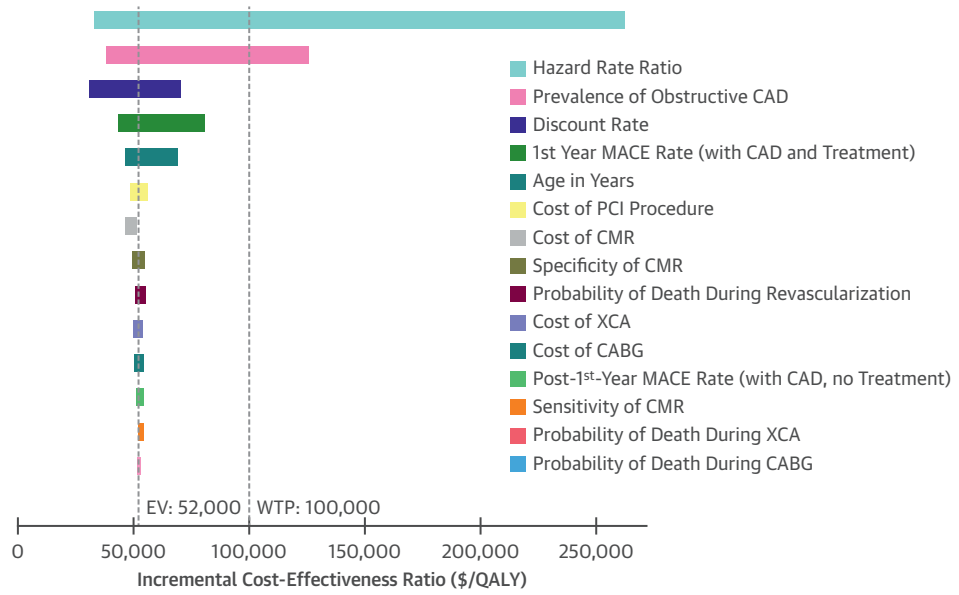
SENSITIVITY ANALYSES. One-way sensitivity analyses were performed to evaluate the sensitivity of results to plausible variations in parameters for model inputs (Table 1). A 2-way sensitivity analysis was performed for the prevalence of obstructive CAD and probability that a patient with a false-negative result would return for investigation each year because of escalating symptoms. Other 2-way sensitivity analyses were performed for sensitivity and specificity of stress CMR, SPECT, and CCTA with selective CT FFR. We also performed sensitivity analyses for rate of use of both FFR and CT FFR. Overall model uncertainty was evaluated in a probabilistic sensitivity analysis (PSA) by simultaneously conducting 10,000 random draws from probability distributions (Supplemental Table 1) for selected key variables and recalculating the cost-effectiveness of each strategy.

RESULTS

In the base-case analysis, obstructive CAD was detected in the first year in 18.7% of patients with the no-imaging strategy, 30.9% with the stress CMR strategy, 28.7% with the SPECT strategy, 31% with the CCTA strategy, and 32.4% with the immediate XCA strategy. The no-imaging strategy resulted in the lowest total lifetime discounted costs but also the lowest QALYs. The immediate XCA strategy had the highest lifetime discounted costs among the 5 strategies but also the highest lifetime discounted QALYs (Table 2).

Table 2 shows the cost-effectiveness results for populations with a prevalence of obstructive CAD of 32.4%. When considering hard MACE, the stress CMR–based decision-making strategy had an ICER of

FIGURE 2 One-Way Sensitivity Analysis Results (ICERs for CMR vs. No Imaging)



CABG = coronary artery bypass grafting; CMR = cardiovascular magnetic resonance; EV = expected value; ICER = incremental cost-effectiveness ratio; PCI = percutaneous coronary intervention; QALY = quality-adjusted life-year; WTP = willingness to pay; other abbreviations as in Figure 1.

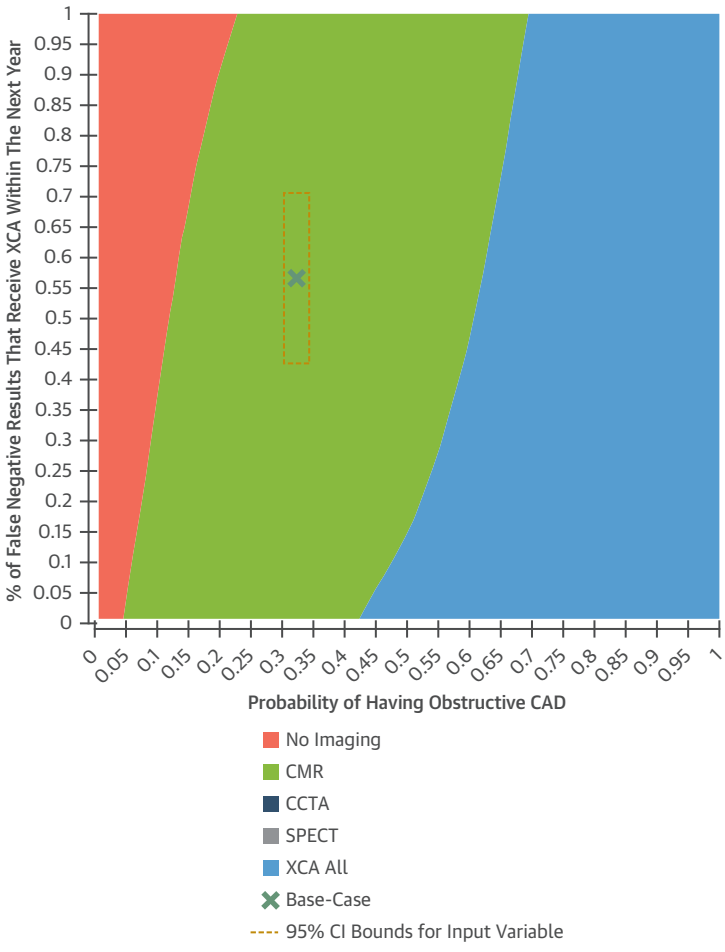
$52,000/QALY compared with the no-imaging strategy. The CMR strategy strongly dominated (i.e., had more QALYs and lower costs) the SPECT and CCTA strategies, whereas the immediate XCA strategy had an ICER of $12 million/QALY compared with the CMR-based strategy. Table 2 also shows results for the scenario analysis when considering all MACE rather than hard events alone. In this scenario, at a threshold of $100,000/QALY, the CMR-based strategy remained the preferred strategy in the base case, with an ICER of $58,000/QALY compared with the no-imaging strategy, whereas the immediate XCA strategy had an ICER of $430,000/QALY compared with the CMR-based strategy.

Under an alternative scenario in which a positive result on stress CMR was defined as the presence of at least 2 abnormal myocardial segments, the stress CMR-based decision making strategy had an ICER of $60,000/QALY compared with the no-imaging strategy, when considering hard MACE. The CMR strategy strongly dominated the SPECT, CCTA, and immediate XCA strategies.

Figure 2 shows ICER results for the CMR-based decision-making strategy compared with the no-imaging strategy for the 15 most influential variables evaluated in 1-way sensitivity analyses. Using a cost-effectiveness threshold of $100,000/QALY in the United States, the ICER for the CMR-based decision-making strategy compared with the no-imaging strategy was below this threshold in most 1-way sensitivity analyses. The cost-effectiveness results were most sensitive to uncertainty in the hazard rate ratio for treatment of CAD, prevalence of obstructive CAD, and annual discount rate. At hazard rate ratios >0.809, an initial strategy of no imaging was optimal using a cost-effectiveness threshold of $100,000/QALY; the immediate XCA strategy was optimal with hazard rate ratios <0.372. Model results were not sensitive to the proportion of patients undergoing CT FFR assessment with the CCTA strategy (Supplemental Figure 1); despite lower CCTA imaging costs, the CMR strategy strongly dominated the CCTA strategy even when this proportion was set to zero, driven by the CMR strategy resulting in fewer coronary angiographic examinations (41.1%) compared with the CCTA strategy (51.5%). Similarly, model results were not sensitive to the proportion of patients undergoing FFR assessment with the immediate XCA strategy (Supplemental Figure 1).

Figure 3 shows the 2-way sensitivity analysis results, varying the prevalence of obstructive CAD and the probability that a patient with a false negative result would return for investigation within 1 year because of escalating symptoms. Combinations of low

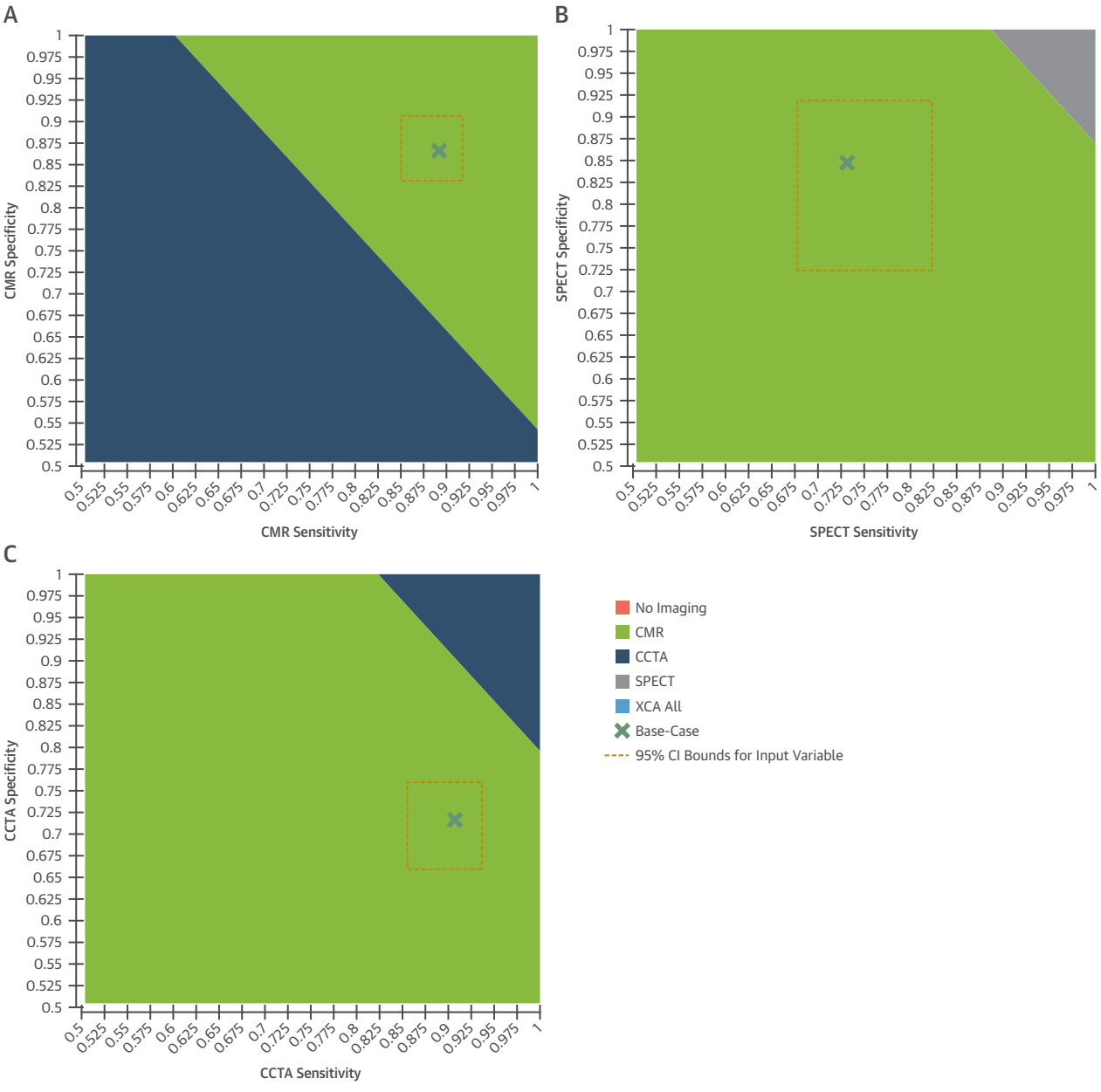
FIGURE 3 2-Way Sensitivity Analysis Results



Probability of having treatable CAD and percentage of patients with false-negative results who undergo XCA within the next year, assuming willingness to pay for health of $100,000/QALY. CCTA = coronary computed tomographic angiography; CI = confidence interval; SPECT = single-photon emission computed tomography; other abbreviations as in Figures 1 and 2.

disease prevalence and high likelihood of return favored the no-imaging strategy; high disease prevalence and low likelihood of return favored the immediate XCA strategy. For example, a prevalence of 10% for obstructive CAD and a 90% likelihood of return would result in the no-imaging strategy being optimal, whereas values of 70% and 10%, respectively, would result in the immediate XCA strategy being optimal. Figure 4 shows the 2-way sensitivity analysis results, varying test sensitivity and specificity of CMR (Figure 4A), SPECT (Figure 4B), and CCTA (Figure 4C). Either SPECT or CCTA is favored over CMR when performance goes beyond the 95% confidence interval from the input data sources (e.g., when both sensitivity and specificity are >90%). Figure 5 shows the cost-effectiveness acceptability curve results for the PSA. The CMR-based decision-making strategy was most likely to be optimal in the PSA using a cost-effectiveness threshold of $100,000/QALY. The CMR-based strategy was optimal in 84% of PSA iterations; no imaging was optimal in 16%; and SPECT, CCTA, and immediate XCA were optimal in 0%. Using a cost-effectiveness threshold of $50,000/QALY, no imaging was optimal in 79% of PSA iterations, while CMR was optimal in 21%. Using a cost-effectiveness threshold of $150,000/QALY, CMR was optimal in 95% of PSA iterations, and no imaging was optimal in 4% of PSA iterations.

FIGURE 4 **Two-Way Sensitivity Analysis Results**



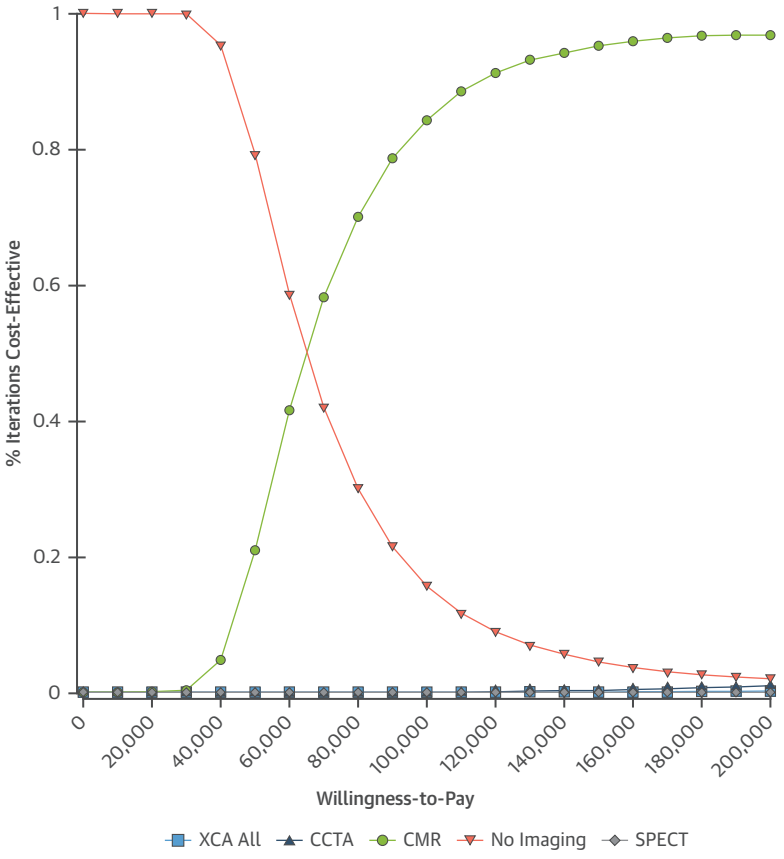
Probability of CMR **(A)**, SPECT **(B)**, and CCTA **(C)** sensitivity and specificity, assuming willingness to pay for health of $100,000/QALY. Abbreviations as in Figures 2 and 3.

DISCUSSION

Stress CMR has been shown in multiple large-scale studies over recent years to be a robust modality for diagnosis and risk stratification of patients suspected of having CAD (6,9) and determining the physiological significance of coronary stenosis (26). Compared with clinical standard of care, stress CMR has also been shown to reduce the rate of unnecessary angiographic examinations (27). Despite the robust body of published research and society recommendations supporting its use (28), contemporary data on its cost-effectiveness compared with other state-of-the-art noninvasive modalities remain limited.

In the present study, we used data from the SPINS registry, a contemporary stress CMR multicenter U.S. cohort of patients with stable chest pain syndromes, to develop a decision analytic model to evaluate

FIGURE 5 Cost-Effectiveness Acceptability Curve From Probabilistic Sensitivity Analysis



Abbreviations as in Figures 2 and 3.

clinical management strategies. We used updated meta-analyses for noninvasive test sensitivity and specificity, with XCA with selective FFR as the gold standard to diagnose significant CAD (19,20). This was chosen given studies showing that anatomic assessment alone of lesion severity has significant limitations (29,30). In this model cohort, we found that CMR-based assessment was optimal on the basis of a $100,000/QALY cost-effectiveness threshold for the United States. The no-imaging strategy resulted in the lowest lifetime costs and lowest rate of diagnosis of obstructive CAD but also the lowest life expectancy and lifetime QALYs. The SPECT, CCTA, and immediate XCA strategies all had higher costs (driven by imaging costs, the cost of follow-up diagnostics and procedures, and downstream CAD events); SPECT and CCTA had fewer QALYs compared with the CMR strategy.

Our findings were robust to plausible variation in the diagnostic performance and cost of stress CMR. Our cost-effectiveness results were also robust to plausible variations in cohort age, rates of cardiac events, and costs of diagnostic and revascularization procedures. Our cost-effectiveness results were most sensitive to hazard rate ratio for treatment of CAD, prevalence of CAD, and discount rate. Using base-case model inputs, the CMR-based strategy was optimal for combinations of intermediate disease prevalence and lower likelihood that a patient with a false-negative result would return for angiography within 1 year. These scenario results are clinically intuitive; a high prevalence of disease favors immediate XCA, whereas a high likelihood of return after false-negative findings favors no imaging (i.e., minimizes the consequence of a false negative).

Most (10–13) but not all (21) previous studies that have examined stress CMR compared with direct XCA with and without FFR and other stress modalities have found it to be a cost-effective alternative. Boldt et al. (10) performed a cost analysis from the German

health care system and determined that stress CMR was more cost effective than SPECT in patients with low to intermediate probability of obstructive CAD. Similar to our results, XCA became the preferred approach when disease prevalence exceeded 60% (10). Moschetti et al. compared a stress CMR-guided strategy with direct XCA with FFR and concluded that the former is more cost effective with disease prevalence <82% (12). The investigators subsequently used data from the EuroCMR registry and extrapolated a cost saving of 24% in a U.S. system, when comparing stress CMR to angiography plus FFR (13). In a United Kingdom model of health care, Walker et al. (11) examined various combinations of 4 diagnostic modalities, namely, exercise treadmill testing, SPECT, stress CMR, and XCA (11). Using a base-case analysis with disease prevalence of 40%, the 2 most cost-effective strategies involved the use of stress CMR, either alone or following abnormal results on exercise treadmill testing, with a cost of £20,000 to £30,000 per QALY. Our results expand on those of previous studies in important ways. We extrapolated the cost-effectiveness of stress CMR using baseline data from the SPINS registry, which represents a large, multicenter cohort of U.S. patients. In these patients, we found that stress CMR is a cost-effective alternative compared with other imaging modalities, including SPECT, which remains the most widely used gatekeeper for invasive angiography in the United States, and CCTA with CT FFR, which is an emerging noninvasive technique for imaging of coronary anatomy and physiology. Furthermore, our results indicate that direct XCA is cost effective in the U.S. health care system only when disease prevalence exceeds 60%, which is an unlikely scenario given that most national registries report a disease rate of only approximately 50% in patients who undergo elective diagnostic angiography (2,3,31).

STUDY LIMITATIONS. First, our reliance on simulation required the combination of inputs from various sources to perform the cost-effectiveness analyses. Despite this inevitable limitation, our sensitivity analyses showed that our cost-effectiveness results were robust across plausible changes in model inputs.

Second, our decision model did not include stress echocardiography or exercise treadmill testing, given the limited number of patients and studies available to reliably derive respective sensitivities and specificities with XCA with FFR as the gold standard.

Third, XCA with selective FFR is considered the gold standard for epicardial coronary stenosis, but not microvascular disease, which can be detected on stress testing and is associated with worse long-term prognosis (32).

Fourth, SPINS included experienced CMR centers and enrolled patients at intermediate risk for obstructive CAD. Therefore, uncertainty exists as to whether the present results can generalize to lower risk patients, such as those represented in the CE-MARC trial. By design, we collected information on downstream but not upstream cardiac testing.

Finally, the clinical benefit assigned to diagnosis of obstructive CAD in our model was based on a combination of medical and revascularization therapy. The value of the latter, particularly in stable coronary disease, is controversial (33) and is currently under investigation in an ongoing large randomized trial (34).

CONCLUSIONS

Stress CMR is an emerging noninvasive technique capable of detecting obstructive CAD with excellent diagnostic accuracy. Our model-based analyses showed that a stress CMR-based strategy to diagnose patients at intermediate risk met conventional standards of cost-effectiveness in the U.S. health care system. Future randomized studies of stress CMR against comparative strategies are required to address both clinical outcomes and cost from a societal perspective.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: In patients presenting with stable chest pain syndromes and at intermediate risk for having obstructive CAD, a decision analytic model projects stress CMR to be a cost-effective modality in the United States, compared with other common noninvasive imaging strategies or invasive XCA as the first-line investigation.

TRANSLATIONAL OUTLOOK: Stress CMR met conventional standards of cost-effectiveness for the evaluation of stable chest pain syndromes in the United States and should be considered for future clinical trials.

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APPENDIX For a supplemental table and figure, please see the online version of this paper.