ORIGINAL ARTICLE

Magnetic Resonance Perfusion or Fractional Flow Reserve in Coronary Disease

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ABSTRACT

BACKGROUND

In patients with stable angina, two strategies are often used to guide revascularization: one involves myocardial-perfusion cardiovascular magnetic resonance imaging (MRI), and the other involves invasive angiography and measurement of fractional flow reserve (FFR). Whether a cardiovascular MRI–based strategy is noninferior to an FFR-based strategy with respect to major adverse cardiac events has not been established.

METHODS

We performed an unblinded, multicenter, clinical-effectiveness trial by randomly assigning 918 patients with typical angina and either two or more cardiovascular risk factors or a positive exercise treadmill test to a cardiovascular MRI–based strategy or an FFR-based strategy. Revascularization was recommended for patients in the cardiovascular-MRI group with ischemia in at least 6% of the myocardium or in the FFR group with an FFR of 0.8 or less. The composite primary outcome was death, nonfatal myocardial infarction, or target-vessel revascularization within 1 year. The noninferiority margin was a risk difference of 6 percentage points.

RESULTS

A total of 184 of 454 patients (40.5%) in the cardiovascular-MRI group and 213 of 464 patients (45.9%) in the FFR group met criteria to recommend revascularization (P=0.11). Fewer patients in the cardiovascular-MRI group than in the FFR group underwent index revascularization (162 [35.7%] vs. 209 [45.0%], P=0.005). The primary outcome occurred in 15 of 421 patients (3.6%) in the cardiovascular-MRI group and 16 of 430 patients (3.7%) in the FFR group (risk difference, −0.2 percentage points; 95% confidence interval, −2.7 to 2.4), findings that met the noninferiority threshold. The percentage of patients free from angina at 12 months did not differ significantly between the two groups (49.2% in the cardiovascular-MRI group and 43.8% in the FFR group, P=0.21).

CONCLUSIONS

Among patients with stable angina and risk factors for coronary artery disease, myocardial-perfusion cardiovascular MRI was associated with a lower incidence of coronary revascularization than FFR and was noninferior to FFR with respect to major adverse cardiac events. (Funded by the Guy's and St. Thomas' Biomedical Research Centre of the National Institute for Health Research and others; MR-INFORM ClinicalTrials.gov number, NCT01236807.)

Management of the care of patients with stable coronary artery disease is based on reduction of risk factors, guideline-directed medical therapy, and revascularization in those with persistent symptoms or proven ischemia.[1,2] In symptomatic patients with risk factors for coronary artery disease, two strategies are predominantly used to establish the diagnosis and guide management of care. The first uses invasive angiography visualizing the presence and distribution of coronary artery disease, supported by assessment of fractional flow reserve (FFR) to guide the need for subsequent revascularization.[3,4] The second uses noninvasive functional stress testing, followed by invasive angiography and revascularization in patients with a positive test. International guidelines differ in their recommendations for noninvasive testing.[1,2] However, there is consensus that revascularization should be guided by ischemia testing[5] unless the left main coronary artery is involved.[6]

Myocardial-perfusion cardiovascular magnetic resonance imaging (MRI) is a noninvasive test for the detection of coronary artery disease that has a high concordance with FFR for ischemia detection.[7-9] Cardiovascular MRI has been associated with a lower incidence of invasive angiography than testing based on clinical risk assessment.[10] However, data are lacking on the effectiveness of a cardiovascular MRI–based strategy to guide coronary revascularization as compared with an invasive angiography–based strategy. We hypothesized that an initial management strategy based on myocardial-perfusion cardiovascular MRI would be noninferior to a strategy guided by invasive angiography and FFR in terms of major adverse cardiac events.

Methods

Trial Design and Oversight

The Myocardial Perfusion CMR versus Angiography and FFR to Guide the Management of Patients with Stable Coronary Artery Disease (MR-INFORM) trial was an unblinded, investigator-led, international, multicenter, comparative-effectiveness, noninferiority trial involving patients with symptoms of stable angina and risk factors for coronary artery disease. The trial design and methods have been published previously.[11] The trial was approved by the United Kingdom National Research Ethics Service and local institutional review boards. Oversight of trial conduct was provided by the Joint Research Office of Guy's and St. Thomas' Hospital and King's College London.

Trial investigators and committees are presented in the Supplementary Appendix, available with the full text of this article at NEJM.org. An independent data and safety monitoring board monitored the progress of all aspects of the trial. An independent clinical-research organization (Pharmtrace, Berlin) oversaw the data management and quality, as well as the safety and efficacy outcomes. After database closure, an independent trial statistician analyzed the data. All procedures were carried out in accordance with Good Clinical Practice guidelines and the principles of the Declaration of Helsinki.

Funding was provided by the Guy's and St. Thomas' Biomedical Research Centre of the National Institute for Health Research, United Kingdom, and the German Center for Cardiovascular Research, with supplemental corporate support from Bayer, Germany, as an unrestricted grant payable to King's College London. Funders had no role in the design of the trial; the collection, analysis or interpretation of the data; or the writing and review of the manuscript. The authors vouch for the completeness and accuracy of the data and for the fidelity of the trial to the protocol (available at NEJM.org).

Trial Population

Patients were enrolled at 16 sites in the United Kingdom, Portugal, Germany, and Australia (Table S1 in the Supplementary Appendix). Patients 18 years of age or older with typical angina symptoms (Canadian Cardiovascular Society [CCS] class II or III angina, with classes ranging from I to IV and higher classes indicating greater limitations on physical activity due to angina) and either two or more cardiovascular risk factors (smoking, diabetes, hypertension, hyperlipidemia, or a family history of coronary artery disease) or a positive exercise treadmill test were included. No systematic effort was made to maximize medical therapy for angina before screening for enrollment. Exclusion criteria were contraindications to adenosine myocardial-perfusion cardiovascular MRI,[11] cardiac arrhythmias (atrial fibrillation or frequent ectopic beats of >20 per minute), a known left ventricular ejec-

tion fraction of less than 30%, New York Heart Association class III or IV heart failure (with classes ranging from I to IV and higher classes indicating greater disability), previous coronary-artery bypass grafting (CABG), percutaneous coronary intervention (PCI) within 6 months, or an estimated glomerular filtration rate of less than 30 ml per minute per 1.73 m^2 of body-surface area. All the patients provided written informed consent.

MANAGEMENT STRATEGY

Patients were randomly assigned in a 1:1 ratio to the cardiovascular-MRI group (guideline-directed medical therapy and revascularization guided by myocardial-perfusion cardiovascular MRI) or the FFR group (guideline-directed medical therapy and revascularization guided by invasive angiography with measurement of FFR). Randomization was performed with fixed block sizes, stratified according to center and sex within center. All the randomly assigned diagnostic tests were performed and interpreted by senior local physicians, who made all subsequent clinical management decisions.

Patients assigned to the FFR group underwent invasive coronary angiography and FFR testing in all coronary arteries with a caliber of 2.5 mm or more and a stenosis severity of 40% or more, if technically feasible. Total occlusions were deemed to be FFR-positive. Details of the FFR procedure have been described previously.[11] Revascularization was recommended in all vessels with an FFR of 0.8 or less. The decision to proceed to PCI or CABG was made in line with practice guidelines.[1] Patients in this group also underwent a cardiovascular MRI study (including assessment of myocardial perfusion) before the invasive study. This scan was not reported, and all results were blinded.

In the cardiovascular-MRI group, myocardial-perfusion cardiovascular MRI was performed with the use of scanners that had a magnetic field strength of 1.5 Tesla; the scanner vendors at each site are listed in Table S1 in the Supplementary Appendix. The cardiovascular MRI protocol has been described previously.[11] In brief, myocardial perfusion was assessed with the first pass of gadobutrol (in the form of Gadovist, from Bayer, Leverkusen, Germany) at a dose of 0.075 mmol per kilogram of body weight during adenosine infusion at a rate of 140 to 210 μg per kilogram per minute for up to 6 minutes, followed by assessment of resting perfusion after 10 minutes and scar imaging. Clinically significant inducible ischemia was defined as involving any of the following: two or more neighboring segments, two adjacent slices, or a single transmural segment (approximately 6% of the myocardium).[11] Ischemic burden was calculated semiquantitatively, as described in the Supplementary Appendix. Patients with clinically significant inducible ischemia underwent invasive angiography, and revascularization was recommended, guided by the localization of the ischemic territory. The final decision on need for and type of revascularization and the target vessel or vessels was left to the performing interventional cardiologist. FFR was not permitted in this group.

All the patients undergoing coronary revascularization received dual antiplatelet therapy. All the patients and their health care providers received protocol-directed guidance on guideline-directed medical therapy, treatment targets, and lifestyle advice (see the Supplementary Appendix). In the case of persistent chest pain, antianginal therapy was increased. Subsequent invasive angiography was performed at the discretion of the responsible physician for patients with refractory symptoms.

The quality of the cardiovascular-MRI and FFR studies was assessed in a randomly selected 10% of cases by the first author (for cardiovascular MRI) or the Glasgow Coronary Physiology Core (for FFR). The quality and completeness of data entry were monitored with a combination of site visits and remote monitoring. A subgroup of patients received a second cardiovascular-MRI examination, including stress perfusion imaging, after 6 months.

CLINICAL OUTCOME

The primary outcome was a composite of major adverse cardiac events (death from any cause, nonfatal myocardial infarction, or target-vessel revascularization) at 12 months.[11] Each component of the primary outcome was analyzed separately as a secondary outcome. The frequency of invasive coronary angiography that was not performed according to the protocol was assessed. Members of an independent clinical-events committee adjudicated all primary and secondary outcome events without knowledge of the randomization assignments and the results of the index test. Definitions of outcomes are provided in the Supplementary Appendix.

Table 1. Patient Characteristics at Baseline, According to Trial Group.*

Characteristic	Cardiovascular-MRI Group (N=454)	FFR Group (N=464)
Age — yr	62±10	62±9
Ejection fraction — %	61±8	60±6
Male sex — no. (%)	329 (72.5)	335 (72.2)
Body-mass index	28.7±4.6	29.4±4.7
Race — no. (%)†		
White	408 (89.9)	421 (90.7)
Other	46 (10.1)	43 (9.3)
Median blood pressure (IQR) — mm Hg		
Systolic	142 (127–154)	143 (129–156)
Diastolic	79 (72–86)	80 (72–87)
Cholesterol — mmol/liter		
Total	4.8±2.0	4.8±1.4
HDL	1.3±0.5	1.4±0.5
LDL	2.7±1.2	2.7±1.2
Triglycerides — mmol/liter	2.2±1.5	2.2±1.5
Random glucose — mmol/liter	6.1±2.4	6.2±2.4
Current smoker — no. (%)	82 (18.1)	76 (16.4)
History — no. (%)		
Diabetes	112 (24.7)	138 (29.7)
Hypertension	317 (69.8)	337 (72.6)
Cerebrovascular disease	25 (5.5)	29 (6.2)
Myocardial infarction	39 (8.6)	33 (7.1)
Previous PCI	57 (12.6)	44 (9.5)
CCS angina class — no. (%)‡		
I	0	0
II	407 (89.6)	415 (89.4)
III	45 (9.9)	48 (10.3)
Missing data	2 (0.4)	1 (0.2)
NYHA heart-failure class — no. (%)§		
I	249 (54.8)	247 (53.2)
II	203 (44.7)	217 (46.8)
III or IV	0	0
Missing data	2 (0.4)	0
Medication — no. (%)		
ACE inhibitor	142 (31.3)	148 (31.9)
ARB	69 (15.2)	57 (12.3)
Statin	296 (65.2)	311 (67.0)
Other lipid-lowering drug	71 (15.6)	52 (11.2)
Platelet inhibitor	329 (72.5)	364 (78.4)
Pretest likelihood of CAD — %¶	75±14	74±13

* Plus–minus values are means ±SD. There were no significant between-group differences at baseline, except for body-mass index (the weight in kilograms divided by the square of the height in meters) (P=0.02), other lipid-lowering drugs (P=0.05), and platelet inhibition (P=0.03). To convert the values for cholesterol to milligrams per deciliter, divide by 0.02586. To convert the values for triglycerides to milligrams per deciliter, divide by 0.01129. To convert the values for glucose to milligrams per deciliter, divide by 0.05551. Percentages may not total 100 because of rounding. ACE denotes angiotensin-converting enzyme, ARB angiotensin-receptor blocker, FFR fractional flow reserve, HDL high-density lipoprotein, IQR interquartile range, LDL low-density lipoprotein, MRI magnetic resonance imaging, and PCI percutaneous coronary intervention.

† Race was reported by the patients.

‡ Canadian Cardiovascular Society (CCS) angina classes range from I to IV, with higher classes indicating greater limitations on physical activity due to angina.

§ New York Heart Association (NYHA) heart-failure classes range from I to IV, with higher classes indicating greater disability.

¶ The pretest likelihood of coronary artery disease (CAD) was calculated according to a modified Diamond and Forrester score.[12]

STATISTICAL ANALYSIS

The sample-size calculation was based on the expected percentage of patients with the primary outcome at 1 year. A 10% incidence in the FFR group and a noninferiority margin of 6 percentage points were assumed on the basis of the Fractional Flow Reserve versus Angiography for Multivessel Evaluation (FAME) trial.[4] With these assumptions, a sample size of 826 would suffice to determine noninferiority of a cardiovascular MRI–guided strategy as compared with an FFR-guided strategy with a power of at least 80% at a one-sided level of significance of 2.5%.[11] With allowance for 10% of the patients withdrawing, a sample size of 918 patients was chosen. No interim analyses were performed.

The primary analysis was a modified intention-to-treat analysis, including only those patients with complete follow-up data on major adverse cardiac events at 12 months (defined to include last follow-up within 28 days before the 12-month time point). An intention-to-treat analysis was done as a sensitivity analysis by imputation of events for patients with no 12-month data. No other imputation was performed. In addition, all efficacy analyses were performed on a per-protocol set that excluded patients with major protocol deviations (see the Supplementary Appendix).

The time-to-first-event analyses were performed with the use of a Cox proportional-hazards model and Kaplan–Meier methods on all randomly assigned patients as time from randomization to first major adverse cardiac event. The primary and all secondary efficacy variables were analyzed descriptively. For the primary outcome, differences in proportions and asymptotic 95% confidence intervals were calculated to test for noninferiority. Fisher's exact test was used for categorical data, and the log-rank test was used for time-to-event data. The pretest likelihood of coronary artery disease was calculated according to a modified Diamond and Forrester score.[12] All analyses were performed with the use of SAS software, version 9.4 (SAS Institute).

Figure 1 (facing page). Randomization and Follow-up of the Patients.

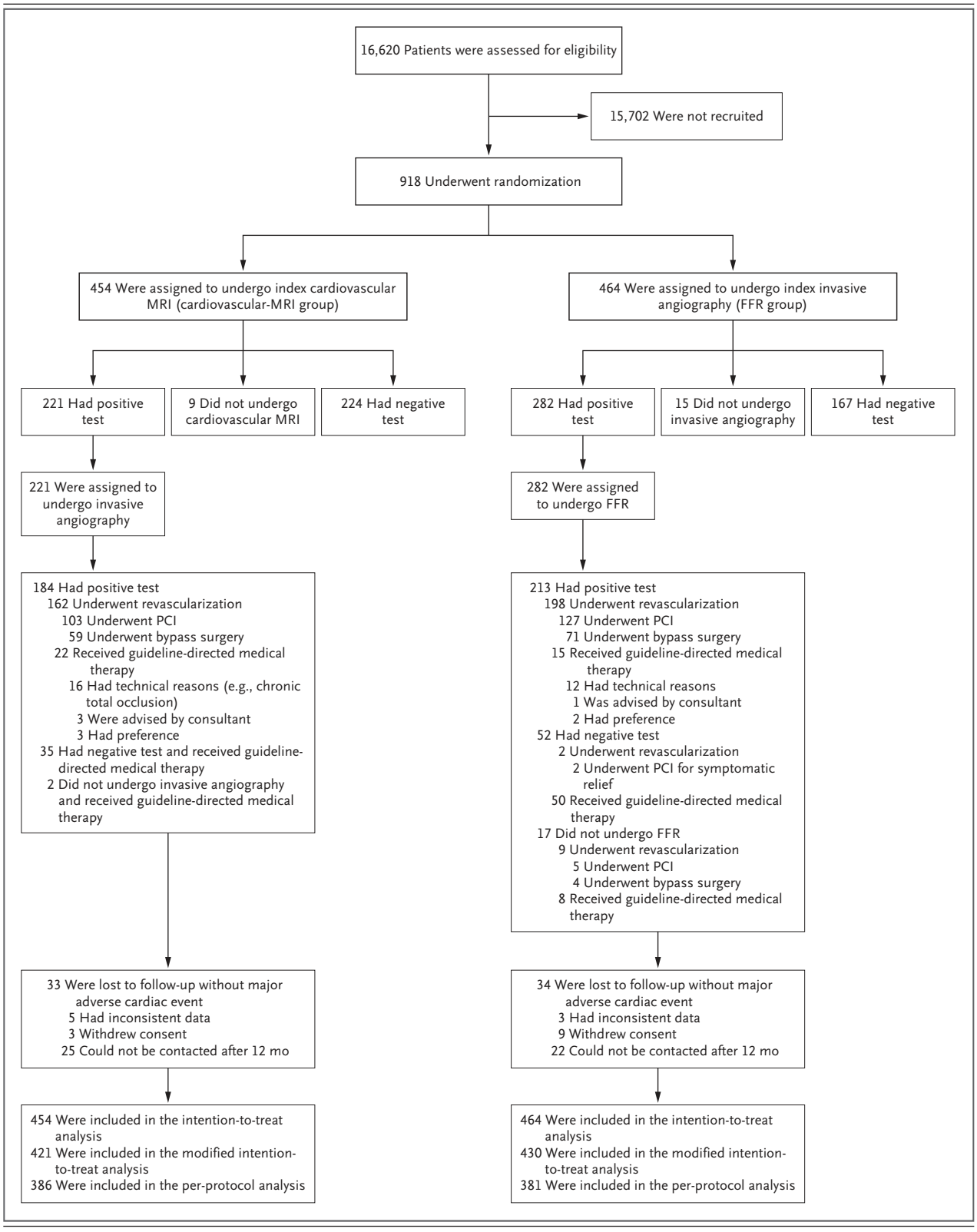
In the group assigned to a diagnostic strategy based on cardiovascular magnetic resonance imaging (MRI), the index cardiovascular MRI was regarded as positive when the stress perfusion scan showed clinically significant inducible ischemia, defined as involving any of the following: two or more neighboring segments, two adjacent slices, or a single transmural segment. The index angiogram in the cardiovascular-MRI group was visually interpreted by the performing consultant as positive or negative. Of the 184 patients with a positive angiogram in the cardiovascular-MRI group, 67 had single-vessel disease, 58 had two-vessel disease, and 59 had triple-vessel disease. In the group assigned to a diagnostic strategy based on fractional flow reserve (FFR), FFR was performed in all coronary arteries with a caliber of 2.5 mm or more and a stenosis severity of 40% or more, if technically feasible. Total occlusions were deemed to be FFR-positive. Revascularization was recommended in all vessels with an FFR of 0.8 or less. Of the 282 patients with a positive angiogram in the FFR group, 52 were classified as not having hemodynamically significant stenoses on the basis of 93 FFR interrogations. Of the remaining 230 patients, 118 had single-vessel disease, 75 had two-vessel disease, and 37 had triple-vessel disease. Inconsistent data were defined as any database entry not logically possible (e.g., revascularization before recruitment or an outcome event before recruitment). PCI denotes percutaneous coronary intervention.

RESULTS

BASELINE CHARACTERISTICS, DIAGNOSTIC PROCEDURES, AND THERAPY

A total of 16,620 patients were assessed for eligibility between December 2, 2010, and August 8, 2015; of these, 918 were deemed to be eligible and enrolled in the trial. Recruitment numbers according to center are presented in Table S1 in the Supplementary Appendix; reasons for the exclusion of ineligible patients are shown in Figure S1 in the Supplementary Appendix. Patient characteristics are summarized in Table 1. The two groups (454 patients in the cardiovascular-MRI group and 464 patients in the FFR group) did not differ significantly with respect to age, sex, or symptoms at presentation. Baseline medications and risk factors also did not differ significantly between the two groups (Table S2 in the Supplementary Appendix).

The results of the diagnostic tests as well as the subsequent management strategies are shown in Figure 1. The percentage of patients in the cardiovascular-MRI group with an abnormal cardiovascular MRI result (≥6% of myocardium ischemic) and positive index angiography did not differ significantly from the percentage in the FFR group with an abnormal FFR result (FFR



≤0.8): 184 patients (40.5%) in the cardiovascular-MRI group and 213 patients (45.9%) in the FFR group (P=0.11). The percentage of patients who underwent index revascularization was lower in the cardiovascular-MRI group than in the FFR group (162 [35.7%] vs. 209 [45.0%], P=0.005). In those patients in the cardiovascular-MRI group who underwent invasive angiography, the median ischemic burden was 18% (interquartile range, 12 to 27).

FOLLOW-UP

The median follow-up was 375 days (interquartile range, 366 to 394). There were marked reductions from baseline in blood-pressure and lipid levels (Table S2 in the Supplementary Appendix), with no significant differences between the two groups. After 1 year, more patients in both groups were receiving angiotensin-converting–enzyme inhibitors or angiotensin-receptor blockers (46.5% in the cardiovascular-MRI group and 44.2% in the FFR group at baseline vs. 53.3% and 56.3%, respectively, at 1 year) and lipid-lowering therapy (78.0% in the cardiovascular-MRI group and 77.2% in the FFR group at baseline vs. 87.4% and 87.8%, respectively, at 1 year). A total of 67 patients (7.3%) were lost to follow-up by 1 year before an outcome event had occurred. Reasons for loss to follow-up are specified in Figure 1.

PRIMARY OUTCOME

The primary outcome of major adverse cardiac events at 1 year occurred in 15 of 421 patients (3.6%) in the cardiovascular-MRI group and in 16 of 430 patients (3.7%) in the FFR group (risk difference, −0.2 percentage points; 95% confidence interval [CI], −2.7 to 2.4; noninferiority margin, 6 percentage points) (Table 2). In the time-to-first-event analysis, the hazard ratio was 0.96 (95% CI, 0.47 to 1.94; P=0.91) in an unstratified analysis and 0.94 (95% CI, 0.46 to 1.92; P=0.87) with stratification according to center

Table 2. Primary and Secondary Outcomes.*

Outcome	Cardiovascular-MRI Group	FFR Group	Risk Difference or Hazard Ratio (95% CI)
Primary outcome: major adverse cardiac event (modified ITT analysis, unstratified)†			
No. of patients with event/total no. (%)	15/421 (3.6)	16/430 (3.7)	−0.2 (−2.7 to 2.4)‡
No. of total events	16§	19§	
Secondary outcomes (ITT population, time-to-first-event analyses, unstratified)			
No. of patients evaluated	454	464	
Major adverse cardiac event — no. of patients	15¶	16¶	0.96 (0.47 to 1.94)
Death			
From any cause	4¶	2¶	2.05 (0.38 to 11.21)
From cardiac cause	2¶	2¶	1.03 (0.15 to 7.29)
Nonfatal myocardial infarction			
No. of patients with event	9¶	10¶	0.84 (0.35 to 2.02)
Total no. of events	9	10	
Target-vessel revascularization			
No. of patients with event	3¶	7¶	0.34 (0.09 to 1.26)
Total no. of events	3	7	

* Major adverse cardiac events were a composite of death, nonfatal myocardial infarction, or target-vessel revascularization. ITT denotes intention to treat.
† The analysis was limited to patients with 12 months of follow-up (lower accepted time window, −28 days).
‡ Shown is the risk difference in percentage points. The other values in this column are hazard ratios.
§ Four patients had multiple events, so the number of total events is higher than the number of patients with events.
¶ No median time to event is provided because the median was not reached.

and sex. The Kaplan–Meier curves for event-free survival are shown in Figure 2. Results of the sensitivity analysis that was performed on an intention-to-treat basis, as well as the per-protocol analysis, were similar to those of the primary analysis (Table S3 in the Supplementary Appendix).

SECONDARY AND EXPLORATORY OUTCOMES

The secondary outcomes for each component of the primary outcome are summarized in Table 2, with a detailed description of the patients who died provided in Table S4 in the Supplementary Appendix. The occurrence of events according to the results of the index test and the performance of revascularization is shown in Figure 3. There was a significant reduction in the average CCS class in both groups from baseline to 1 year (Table S5 in the Supplementary Appendix). The percentage of patients free from angina after 12 months did not differ significantly between the cardiovascular-MRI group (49.2%) and the FFR group (43.8%) (P=0.21).

There were 31 angiograms that were not performed according to the protocol during the follow-up period (19 in the cardiovascular-MRI group [4.2% of patients] and 12 in the FFR group [2.6% of patients], P=0.14), resulting in 8 revascularizations not performed according to the protocol in the cardiovascular-MRI group (3 target-vessel revascularizations and 5 non–target-vessel revascularizations) and 8 in the FFR group (7 target-vessel revascularizations and 1 non–target-vessel revascularization) (Fig. S2 in the Supplementary Appendix). The other protocol-specified secondary outcomes that are not reported in this article are listed in Table S6 in the Supplementary Appendix. Serious adverse events, which occurred in similar numbers of patients in each group, are presented in Table S7 in the Supplementary Appendix.

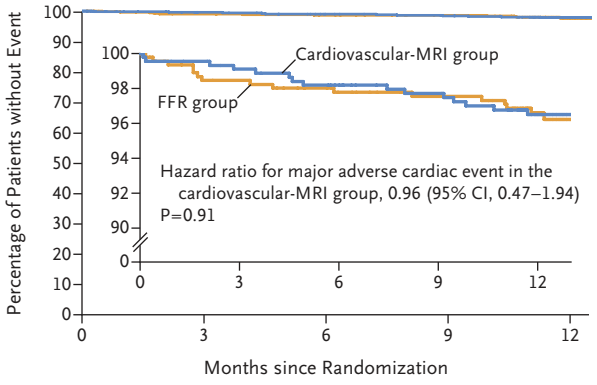


Figure 2. Kaplan–Meier Analysis of Event-free Survival.

The graph shows the unadjusted Kaplan–Meier estimates of patients surviving free from the primary composite outcome (death from any cause, nonfatal myocardial infarction, or target-vessel revascularization). The inset shows the same data on an expanded y axis.

DISCUSSION

In the MR-INFORM trial, we found that, in patients with stable angina and risk factors for coronary artery disease, the use of myocardial-perfusion cardiovascular MRI in guiding initial management of patient care was noninferior to the use of invasive coronary angiography combined with FFR with respect to the primary outcome of major adverse cardiac events at 1 year. The use of cardiovascular MRI was associated with a significantly lower incidence of invasive coronary angiography and coronary revascularization than was the use of FFR. Only 48.2% of the patients in the cardiovascular-MRI group underwent invasive angiography (as compared with 96.8% of those in the FFR group) despite a pretest likelihood for coronary artery disease of 75%. Furthermore, 35.7% of the patients in the cardiovascular-MRI group, as compared with 45.0% of those in the FFR group, underwent index revascularization.

Current guidelines on the management of the care of patients with suspected coronary artery disease separate diagnostic strategies from therapeutic strategies owing to a lack of evidence comparing combined diagnostic and therapeutic pathways.[13] The MR-INFORM trial closes this knowledge gap by comparing two frequently used, well-defined, standardized, and validated[9,14-18] clinical management strategies. The cardiovascular-MRI methods used in this trial are readily available and can be implemented on standard MRI systems.

The benefits of revascularization in patients with angina, clinically significant myocardial

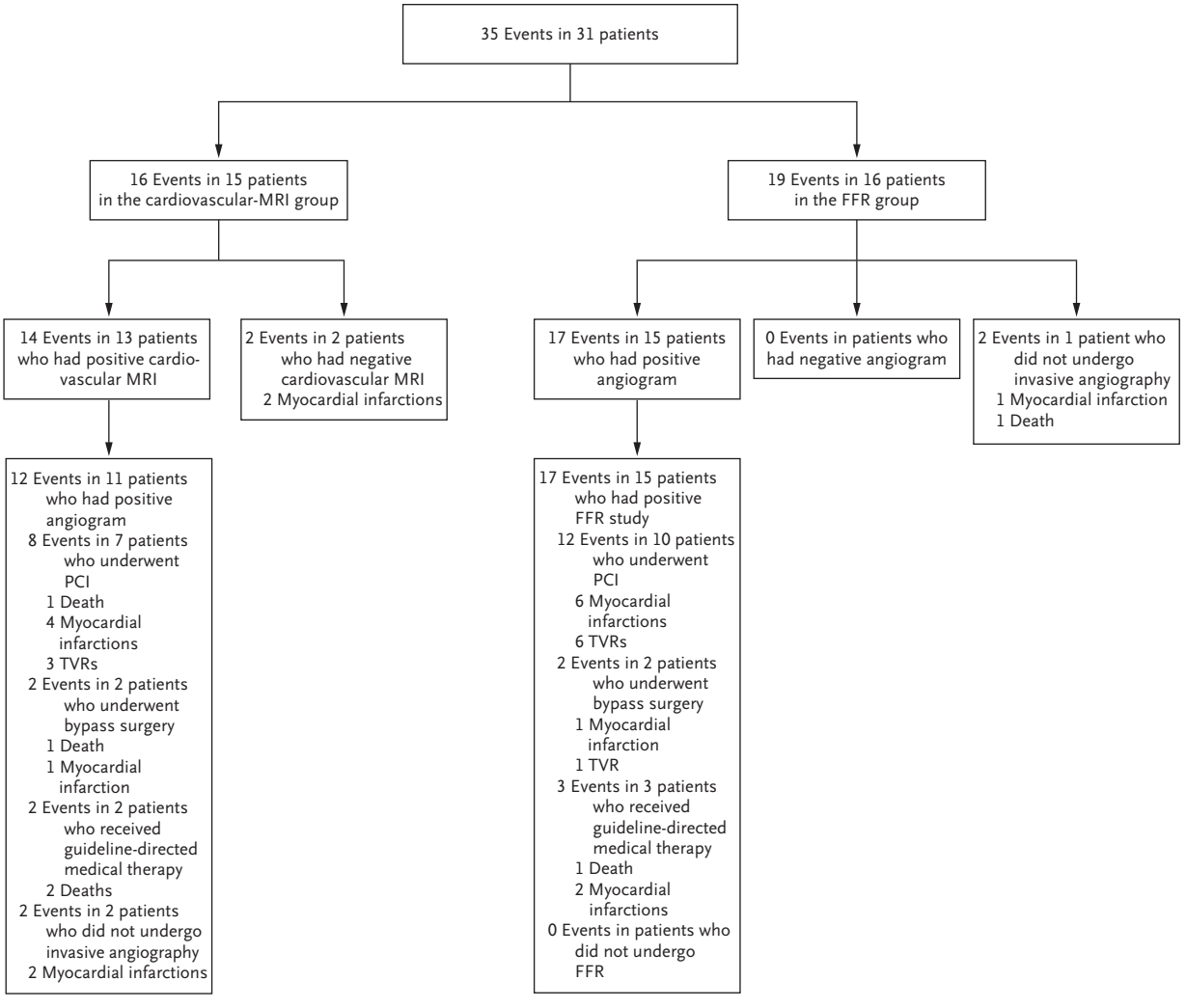


Figure 3. Primary Outcome Events.

The figure shows the group assignment, test results, and subsequent therapy for all events. Five events occurred in patients who received guideline-directed medical therapy despite a positive index test: two in patients in the cardiovascular-MRI group who were on the waiting list for bypass surgery, two in patients in the FFR group who were on the waiting list for bypass surgery, and one in a patient in the FFR group who had a chronic total occlusion that was not amenable to revascularization. TVR denotes target-vessel revascularization.

ischemia, or hemodynamically relevant coronary artery disease are contested.[19-21] Therefore, one limitation of the MR-INFORM trial is the lack of a third group of patients randomly assigned to medical therapy without planned revascularization. The ongoing International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) is designed to answer the question of the need for revascularization in patients with an intermediate-to-severe burden of myocardial ischemia.[22] It is notable that three of four deaths from cardiac causes in the current trial occurred in patients with severe ischemia on the index examination while on the waiting list for bypass surgery, with one death from cardiac causes occurring in a patient who had a myocardial infarction before index angiography.

The most important limitation of the trial is that the incidences of outcome events at 1 year

were lower than expected on the basis of data from the FAME trial (which enrolled only patients with documented multivessel disease).[4] As a result, the noninferiority margin was large relative to the incidence of major adverse cardiac events. Thus, noninferiority of cardiovascular MRI would have been shown even if the incidence was twice as high as that in the FFR group. The actual incidences in the two groups, however, were similar.

No evidence of ischemia was required to proceed to target-vessel revascularization. This may have caused some bias since interventional cardiologists may have had greater confidence in one index examination over the other. Similarly, a bias toward revascularization in the FFR group cannot be fully ruled out, since conversion from a diagnostic to a therapeutic procedure was easier in this group.

Additional limitations should also be considered. Systematic maximization of antianginal therapy was not performed before screening for enrollment, so patients who might have been asymptomatic after medication adjustment may have been enrolled in the trial. The follow-up period of 1 year may mask some longer-term differences between the strategies. The patient population was primarily male and white. The results cannot be extrapolated to other tests for myocardial ischemia or the functional significance of a coronary artery stenosis because of differences in diagnostic performance as compared with myocardial-perfusion cardiovascular MRI.

In conclusion, in patients with stable angina and risk factors for coronary artery disease, an initial management strategy guided by myocardial-perfusion cardiovascular MRI was noninferior to a strategy of invasive angiography and FFR with regard to major adverse cardiac events at 12 months.

The views expressed in this article are those of the authors and not necessarily those of the NHS, the National Institute for Health Research, or the Department of Health, United Kingdom.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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APPENDIX

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