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Comparing Cardiac Magnetic Resonance–Guided Versus Angiography-Guided Treatment of Patients With Stable Coronary Artery Disease

Results From a Prospective Randomized Controlled Trial

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ABSTRACT

OBJECTIVES The purpose of this study was the prospective and randomized evaluation of cardiovascular endpoints and quality of life in patients with stable coronary artery disease comparing a cardiac magnetic resonance (CMR)–based management strategy with a coronary angiography–based approach.

BACKGROUND Evidence from trials prospectively evaluating the role of CMR in clinical pathways and decision processes is limited.

METHODS Patients with symptomatic CAD were randomized to diagnostic coronary angiography (group 1) or adenosine stress CMR (group 2). The primary endpoint was the composite of cardiac death and nonfatal myocardial infarction. Quality of life was assessed using the Seattle Angina Questionnaire at baseline and during follow-up.

RESULTS Two hundred patients were enrolled. In group 1, 45 revascularizations (45.9%) were performed. In group 2, 27 patients (28.1%) were referred to revascularization because of ischemia on CMR. At 12-month follow-up, 7 primary events occurred: 3 in group 1 (event rate 3.1%) and 4 in group 2 (event rate 4.2%), with no statistically significant difference ($p = 0.72$). Within the next 2 years, 6 additional events could be observed, giving 4 events in group 1 and 9 events in group 2 (event rate 4.1% vs. 9.4%; $p = 0.25$). Group 2 showed significant quality-of-life improvement after 1 year in comparison to group 1.

CONCLUSIONS A CMR-based management strategy for patients with stable coronary artery disease was safe, reduced revascularization procedures, and resulted in better quality of life at 12-month follow-up, though noninferiority could not be proved. Optimal timing for reassessment remains to be investigated. (Magnetic Resonance Adenosine Perfusion Imaging as Gatekeeper of Invasive Coronary Intervention [MAGnet]; NCT02580851) (J Am Coll Cardiol Img 2018;11:987–96)

Current guidelines recommend proper risk stratification prior to invasive therapy for patients with stable coronary artery disease (CAD) (1–6). Detection or exclusion of moderate to severe myocardial ischemia is a crucial part of the workup process that designates patients with ischemia to the high-risk group (7).

Adenosine perfusion cardiac magnetic resonance (CMR) is a noninvasive imaging modality that can reliably detect reversible myocardial ischemia (8–12). It plays an increasing role in the diagnosis and risk stratification of patients with suspected or known CAD (13). Despite the detection of ischemia, it also offers the advantage of providing comprehensive

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ABBREVIATIONS AND ACRONYMS

CAD = coronary artery disease

CMR = cardiac magnetic resonance

FFR = fractional flow reserve

PCI = percutaneous coronary intervention

SAQ = Seattle Angina Questionnaire

information such as the assessment of myocardial fibrosis and scar (late gadolinium enhancement), which have been proved to further increase its prognostic significance (14–16). Although CMR therefore holds a Class Ia recommendation in the diagnostic workup of patients with symptomatic stable CAD, only a few studies have evaluated a randomized CMR-driven patient management approach.

In this study, a prospective randomized CMR-based management approach for patients with stable CAD was evaluated, with special emphasis on quality of life and occurrence of major cardiac endpoints, in comparison with a conventional approach.

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METHODS

STUDY POPULATION. Patients presenting to the outpatient clinic of our institution for the evaluation of symptoms indicating stable symptomatic CAD (e.g., exercise-related angina pectoris or dyspnea) were considered eligible and consecutively screened for enrollment. Patients had to be at intermediate to high CAD risk. Exclusion criteria were unstable angina pectoris, cardiac or respiratory instability, contraindication to CMR (17), age <18 years, and inability to give written informed consent. The study was approved by the institutional ethics committee.

PROTOCOL. Study protocol and design details have been previously published (18). All patients received thorough history, physical examination, and basic cardiac workup, including rest electrocardiography, treadmill testing, and echocardiography. Risk stratification scores were calculated according to general recommendations (19,20). To assess symptom burden and quality of life, the standardized Seattle Angina Questionnaire (SAQ) was carried out in each subject (21). All patients received guideline-directed medical therapy (1).

After enrollment, patients were randomized to 2 groups in a 1:1 fashion. Randomization was realized by blocked computer-generated random numbers. The allocation sequence was available only to a designated study nurse, who was phoned immediately after the enrollment of an individual patient. In group 1, patients underwent diagnostic coronary angiography after initial assessment. Percutaneous coronary intervention (PCI) was performed according to current guidelines in case of ≥70% stenosis in a coronary vessel with ≥2 mm diameter (1,2) or hemodynamic relevance on fractional flow reserve (FFR) testing. Hence, FFR testing was allowed but not mandated by the study protocol.

In group 2, functional stress testing by adenosine perfusion CMR was performed initially. Functional images were acquired by steady-state free precession images in contiguous short-axis orientation. Adenosine was infused intravenously at a constant rate of 140 μg/kg body weight for 3 min. First-pass perfusion images in 3 short-axis views were acquired using a bolus of gadoterate meglumine 0.05 mmol/kg body weight. The examinations were conducted using a 3.0-T whole-body clinical magnetic resonance scanner using a cardiac 32-channel phased-array receiver coil. Functional evaluation, perfusion imaging, and late gadolinium enhancement assessment were performed according to well-established standard protocols (22–24).

All CMR images were analyzed by 2 readers in consensus. To avoid bias, readers were blinded to initial clinical assessment and the results of other examinations (e.g., treadmill testing). In case myocardial ischemia affecting ≥10% of the myocardium was detected, patients were sent to coronary angiography and subsequent PCI afterward. **Figure 1** depicts an example case of a 58-year-old male patient presenting with typical exercise-related angina pectoris. The study protocol is provided in **Figure 2**.

FOLLOW-UP. Follow-up information was gathered annually after enrollment by outpatient clinic visits and by telephone interviews of patients and their general practitioners. Any reported adverse event was documented and its significance evaluated by the endpoint adjudication committee formed by the investigators. Interim analyses were conducted after each year of follow-up to enable early recognition of safety issues. The primary endpoint was defined as the composite of cardiac death and nonfatal myocardial infarction (25,26). Cardiac death was defined as myocardial infarction leading to death, sudden cardiac death, death related to cardiovascular procedures, and cardiovascular hemorrhage. Any diagnostic or interventional coronary procedure not scheduled at time of initial diagnostic workup was recorded as an unplanned procedure. Decisions for these procedures were the responsibility of the treating physicians and were not influenced by the investigators. Symptom burden and quality of life were assessed using the SAQ each year.

STATISTICAL ANALYSIS AND SAMPLE SIZE CALCULATION. To test the relationship between categorical classification factors, the Fisher exact test was applied. Continuous variables were tested for normal distribution using the D'Agostino-Pearson test. In case of normal distribution, variables are reported as mean ± SD, and a 2-tailed Student's *t*-test