The STRATEGY Study (Stress Cardiac Magnetic Resonance Versus Computed Tomography Coronary Angiography for the Management of Symptomatic Revascularized Patients)

Resources and Outcomes Impact

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***Background*—**Computed tomography coronary angiography (cTCA) and stress cardiac magnetic resonance (stress-CMR) are suitable tools for diagnosing obstructive coronary artery disease in symptomatic patients with previous history of revascularization. However, performance appraisal of noninvasive tests must take in account the consequent diagnostic testing, invasive procedures, clinical outcomes, radiation exposure, and cumulative costs rather than their diagnostic accuracy only. We aimed to compare an anatomic (cTCA) versus a functional (stress-CMR) strategy in symptomatic patients with previous myocardial revascularization procedures.

***Methods and Results*—**Six hundred patients with chest pain and previous revascularization included in a prospective observational registry and evaluated by clinically indicated cTCA (n=300, mean age 68.2±9.7 years, male 255) or stress-CMR (n=300, mean age 67.6±9.7 years, male 263) were enrolled and followed-up in terms of subsequent noninvasive tests, invasive coronary angiography, revascularization procedures, cumulative effective radiation dose, major adverse cardiac events, defined as a composite end point of nonfatal myocardial infarction and cardiac death, and medical costs. The mean follow-up for cTCA and stress-CMR groups was similar (773.6±345 versus 752.8±291 days; P=0.21). Compared with stress-CMR, cTCA was associated with a higher rate of subsequent noninvasive tests (28% versus 17%; P=0.0009), invasive coronary angiography (31% versus 20%; P=0.0009), and revascularization procedures (24% versus 16%; P=0.007). Stress-CMR strategy was associated with a significant reduction of radiation exposure and cumulative costs (59% and 24%, respectively; P<0.001). Finally, patients undergoing stress-CMR showed a lower rate of major adverse cardiac events (5% versus 10%; P<0.010) and cost-effectiveness ratio (119.98±250.92 versus 218.12±298.45 Euro/y; P<0.001).

***Conclusions*—**Compared with cTCA, stress-CMR is more cost-effective in symptomatic revascularized patients.

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Key Words: computed tomography ■ coronary artery disease ■ cost ■ cost-effectiveness ■ magnetic resonance ■ outcome ■ radiation exposure ■ revascularization

See Editorial by Hulten and Blankstein
See Clinical Perspective

Patients treated with percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) may have coronary artery disease (CAD) progression, in-stent restenosis (ISR), and graft occlusion. The noninvasive stress tests have limited ability to detect no-flow limiting lesions that may influence patient outcome.[1–3] In contrast, computed tomography coronary angiography (cTCA) emerged as a diagnostic tool with a good negative predictive value but with limited positive predictive value in this setting,[4,5] despite the introduction of high-definition

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scanner.[6,7] Several prospective studies have been performed with the aim of comparing the anatomic approach versus the functional assessment in patients with CAD[8–11] mainly in nonrevascularized patients and using standard 64-slice scanner technology and single photon emission computed tomography (SPECT). Recently, stress-CMR showed reliable diagnostic potential for reversible ischemia assessment[12] with superior diagnostic performance to SPECT,[13] without significant differences between nonrevascularized and revascularized patients.[14] The STRATEGY trial (Stress Cardiac Magnetic Resonance Versus Computed Tomography Coronary Angiography for the Management of Symptomatic Revascularized Patients) is a single-center prospective observational study comparing the cost-effectiveness of functional assessment with stress-CMR versus anatomic evaluation, with cTCA in consecutive symptomatic patients presenting with history of previous myocardial revascularization.

Methods

Six hundred symptomatic patients with a previous history of revascularization by PCI or CABG referred to our hospital between January 2011 and December 2013 to be evaluated by clinically indicated cTCA or stress-CMR were enrolled. Exclusion criteria were unstable angina; cardiac diseases different from CAD, such as heart failure, infiltrative or hypertrophic cardiomyopathy, and myocarditis; estimated glomerular filtration rate ≤30 mL/min; hypersensitivity to iodine-contrast agent; inability to sustain a breath hold; pregnancy; cardiac arrhythmias; body mass index >35 kg/m^2; claustrophobia; presence of a pacemaker or implantable cardioverter device; and contraindication to dipyridamole and gadolinium intravenous administration. All patients gave written informed consent, and the institutional ethical committee approved the study protocol.

Baseline Characteristics

A structured interview was performed and a clinical history was obtained, assessing the following characteristics: hypertension, smoking, hyperlipidemia, diabetes mellitus, family history of CAD, use of cardiovascular drugs, symptoms (atypical or typical angina), number and type of stents, stent material, stent size, number of overlapping stents, number and type of CABG (overall number of graft, right internal mammarian artery, left internal mammary artery, radial artery, and vein graft).

cTCA Protocol

All patients included in the cTCA arm were evaluated with a 64-slice high-definition scanner (Discovery CT 750 HD; GE Healthcare, Milwaukee, WI) with the scan parameters and scan protocol as previously described.[6]

cTCA Interpretation

Data sets of each cTCA were transferred to an image-processing workstation (Advantage Workstation Version 4.5; GE Healthcare, Milwaukee, WI). The analysis was performed by 2 cardioradiologists (G. Pontone and D. Andreini, both with 8 or more years of clinical experience in cTCA performance and analysis) according to the guidelines for reporting.[15] In stented coronary segment, ISR was identified as a darker structure between the metallic struts and the enhanced lumen and quantitatively evaluated as previously described.[7] In CABG patients, surgical grafts were classified based on the supplied native coronary artery (left anterior descending coronary artery, left circumflex coronary artery, or right coronary artery). A coronary territory was deemed unprotected if (1) a nongrafted native coronary artery had a significant stenosis; (2) a significant stenosis was present in a native coronary artery distally to the graft insertion; or (3) significant stenoses were present in both the graft and the grafted native coronary artery. According to cTCA interpretation, each patient was classified as having no significant obstructive disease, de novo obstructive CAD in native coronary arteries, obstructive ISR, both de novo obstructive CAD and ISR, surgical grafts with significant obstructive disease, or as being nonevaluable.

Stress-CMR Protocol

All patients were evaluated in a 1.5-T scanner (Discovery MR450; GE Healthcare, Milwaukee, WI) following a stress protocol in which vasodilatation was induced with 0.84 mg/kg of IV dipyridamole injected over 6 minutes as previously reported.[14]

Stress-CMR Interpretation

CMR data sets were transferred to a dedicated workstation and analyzed with a cardiac software (Report Card 4.0; GE Healthcare, Milwaukee, WI) by 2 cardioradiologists (G. Pontone and D. Andreini, both with 5 or more years of clinical experience in CMR performance and analysis) according to the recommendations of the Society of Cardiovascular Magnetic Resonance and myocardial segmentation of the American Heart Association/American College of Cardiology.[16] According to stress-CMR findings, the patients were classified as having (1) no ischemia; (2) ischemia as a result of perfusion defects alone, defined as a mismatch between hypo-enhancement on first-pass perfusion and enhancement on LGE sequences involving more than 2 myocardial segments; (3) ischemia as a result of a matched perfusion defects plus wall motion abnormalities, defined as a worsening of wall motion between stress and rest condition involving more than 2 myocardial segments; and (4) equivocal results.

Follow-Up Visits

Patient follow-up was performed by trained interviewers who checked medical records or by phone interview collecting the following information:

1. Downstream testing. The results of index test were provided to an independent clinical team of cardiologists of the institution where the study was performed and who went on making clinical decisions based on the integrated evaluation of patient clinical assessment and index test findings. The following downstream testing was recorded from study entry until the end of follow-up: (1) NITs: noninvasive diagnostic tests, including further cTCA or stress testing (exercise or pharmacological stress), with detection of ischemia by ECG, myocardial perfusion, or wall motion abnormalities; and (2) invasive coronary angiography (ICA).
2. Overall radiation exposure. We measured the cumulative effective radiation exposure (ED) over the entire study period by assessing the original average dose for each test performed during the follow-up.[17]
3. Outcomes. Events were defined according to the following definitions:
   - Revascularization by PCI or CABG
   - Nonfatal myocardial infarction (MI): detection of a rise and fall of cardiac biomarker values with at least one value above the 99th percentile upper reference limit, and with at least one of the following: ischemic symptoms, ECG changes of new ischemia (eg, new ST-T interval changes or left bundle branch block), development of pathological Q waves in the ECG, imaging evidence of new loss of viable myocardium, or regional wall motion abnormality. In addition, periprocedural infarctions were defined as >3× the upper limit of normal for serum creatin kinase MB isoenzyme (CK-MB) after PCI and >5× the upper limit of normal after CABG.
   - Cardiac death: any death because of immediate cardiac cause (eg, MI, low-output failure, fatal arrhythmia,) or vascular cause (eg, cerebrovascular disease, pulmonary embolism, ruptured aortic aneurysm, dissecting aneurysm, or other vascular cause). Unwitnessed death and death of unknown cause were classified as cardiovascular death.

   Major adverse cardiac events were defined as a combined end point of nonfatal MI and cardiac death. An independent clinical events adjudication committee reviewed the agreement between all events and the provided definitions.
4. Cost-effectiveness analysis: The analysis was performed as previously described.[18] In detail, the costs of a diagnostic strategy

consist of first-line test costs and subsequent costs, including noninvasive downstream testing and hospitalization for invasive procedure, such as ICA, or revascularization by PCI or CABG according to the reimbursement of public national health system. For each patient, the total costs of a diagnostic algorithm were calculated as the sum of direct costs of first-line test and subsequent costs multiplied by the overall number of noninvasive or hospitalization for invasive procedures performed. Moreover, for each patient, the projected remaining life expectancy was calculated using the observed survival time of patients who died and their projected life expectancy (based on the age–sex matched Italian population) to estimate life-years lost. We assigned 2 life-years lost to every patient who had a MI and survived for the remaining follow-up time. Finally, the cost-effectiveness ratios were calculated according to the following equation:

$$(\text{Index test cost} + \text{downstream diagnostic tests cost}) / \text{projected remaining life expectancy.}$$

Statistical Analysis

Statistical analysis was performed with SPSS software (Version 22.0; SPSS, Chicago, IL). Continuous variables were expressed as mean±standard deviation and discrete variables as absolute numbers and percentages. Considering the not-randomized nature of the study, a propensity score matching analysis was used to estimate the probability of being referred to either stress-CMR or cTCA, fitting a logistic regression model and considering the following covariates: demographics characteristics (age, sex, and body mass index), cardiovascular risk factors, medical therapy (β-blockers, angiotensin-converting enzyme inhibitors, statins), echocardiographic characteristics (left ventricle ejection fraction), cardiac status (typical angina), and PCI characteristics (number of stents per patients, number of stent with diameter <3 mm, and number of overlapping stents). Matching was performed using Matching package in R (Version 3.0.2). The Student's paired *t* test or Wilcoxon signed-rank test were used to evaluate differences of continuous variables with normal and non-normal distribution, respectively. The McNemar chi-squared test was used to study differences in binary data. A *P* value <0.05 was considered statistically significant.

Results

The baseline characteristics are listed in Table 1. No differences were found in terms of cardiovascular risk factors, clinical history, and medical therapy. cTCA and stress-CMR groups were followed for a similar follow-up time (773±345 days versus 752±291days; *P*=0.21). The cTCA results were negative, positive, or not evaluable in 41%, 55%, and 4% of the patients, respectively (Table 2). In detail, we found a de novo coronary artery stenosis >50%, ISR>50%, positive test for both de novo disease and ISR or positive for CABG disease in 27%, 4%, 17, and 7% of patients, respectively (Table 2). Stress-CMR results were negative, positive, or not-evaluable in 69%, 31%, and 3% of patients, respectively. In detail, we found perfusion defects alone or perfusion defects plus wall motion abnormalities in 15% and 15% of patients, respectively (Table 2). Patients who underwent cTCA were more likely to undergo further noninvasive tests (28% versus 17%; *P*=0.0009) and ICA (31% versus 21%; *P*=0.0009) as compared with patients who underwent stress-CMR. They were also more frequently treated with myocardial revascularization (24% versus 16%; *P*=0.007; Table 3). During follow-up, 30 (10%) patients studied with cTCA and 14 (5%) patients who underwent stress-CMR had nonfatal MI, respectively (*P*=0.012; Table 3). Of note, among those with nonfatal MI, 5 (7%) and 2 (4%) patients in the cTCA and CMR group were classified as periprocedural MI, respectively. In addition, 1 (0.3%) patient of the cTCA group and 1 (0.3%) patient of the stress-CMR group died, respectively (*P*=ns; Table 3). A higher rate of major adverse cardiac events was also observed in the cTCA group as compared with the stress-CMR group (10% versus 5%; *P*=0.014).

The cumulative costs after adjustment for baseline clinical characteristics were 2012±2888 Euro and 1516±2464 Euro for the cTCA group and stress-CMR group, respectively, with a 25% higher cost for cTCA patients as compared with stress-CMR patients (*P*<0.001; Table 3).

The mean total ED over the study period was significantly higher for patients who underwent cTCA as compared with those who were studied with stress-CMR (17.4±17.1 mSv versus 7.06±18.2 mSv; *P*<0.001; Table 3). Finally, cTCA showed a higher cost-effectiveness ratio as compared with stress CMR (218.±298 Euro/y versus 119±250 Euro/y; *P*<0.001). The difference between the biased baseline characteristics was not found to be significant between the 2 groups and, therefore, the selection bias was considered insignificant, and therefore, a further propensity score matching analysis was not performed.

Figures 1 and 2 show 2 clinical cases in which cTCA was chosen as the index test. In both cases, cTCA showed obstructive CAD that led to stress-CMR, whose result was negative (Figure 1), and to ICA (Figure 2), which did not confirm cTCA findings. Figure 3 shows a case of a patient in whom stress-CMR was useful to plan the best revascularization strategy.

Discussion

The main results of the STRATEGY study is that the evaluation of chest pain with stress-CMR in patients with previous revascularization procedures is associated with lower downstream noninvasive and invasive testing, CAD-related spending, and ED as compared with cTCA. Although no diagnostic tests are usually required within 2 years after PCI and 5 years after CABG in patients without symptoms, noninvasive stress tests are advised in case patients complain of symptoms after revascularization. In this regard, cTCA has emerged as a highly diagnostic and prognostic tool in low-to-intermediate risk patients[19–21] but also in ISR and CABG disease,[4–6] despite the positive predictive value remains still limited. As regards the functional evaluation of CAD, stress-CMR demonstrated reliable ability for reversible ischemia assessment, with excellent sensitivity and specificity of 90% and 87%, respectively,[12] even in the specific setting of revascularized patients.[14] Neglia et al[9] showed that cTCA is more accurate as compared with functional imaging in patients with suspected CAD. However, whether this better diagnostic performance may translate into any outcome improvement is still under debate. Hlatky et al[8] in a observational prospective registry of 1703 patients with suspected CAD, showed that a functional strategy with SPECT was associated with a 15% and 22% lower cost as compared with cTCA

Table 1. Baseline and Descriptive Characteristics at Time of Index Testing

	Cardiac Computed Tomography Angiography (n=300)	Stress Cardiac Magnetic Resonance (n=300)	*P* Value
Baseline demographics			
Age, y, mean±SD	68.2±9.7	67.6±9.7	0.38
Male, absolute value (%)	255 (85)	263 (88)	0.34
Body mass index, mean±SD	26.9±3.8	26.7±3.5	0.59
Cardiovascular risk factors			
Family history of CAD, absolute value (%)	49 (16)	61 (20)	0.2
Smoker, absolute value (%)	37 (12)	125 (42)	0.32
Hypertension, absolute value (%)	184 (61)	185 (62)	0.93
Hyperlipidemia, absolute value (%)	170 (57)	185 (62)	0.21
Diabetes mellitus, absolute value (%)	63 (21)	70 (23)	0.49
Medical therapy			
β-Blockers, absolute value (%)	199 (66)	207 (69)	0.48
ACE inhibitors, absolute value (%)	207 (69)	194 (64)	0.25
Aspirin, absolute value (%)	300 (100)	300 (100)	1
Dual antiplatelets therapy, absolute value (%)	15 (5)	12 (4)	0.55
Nitrates, absolute value (%)	43 (14)	54 (18)	0.22
Statins, absolute value (%)	232 (77)	239 (80)	0.48
Echocardiographic characteristics			
Left ventricle end-diastolic volume, mL/m², mean±SD	57.9±24.3	56.1±19.1	0.36
Left ventricle end-systolic volume, mL/m², mean±SD	29.8±20.7	27.7±16.6	0.22
Left ventricle ejection fraction, %, mean±SD	53±14	54±14	0.49
Cardiac status			
Atypical angina, absolute value (%)	234 (78)	238 (79)	0.69
Typical angina, absolute value (%)	66 (22)	62 (21)	0.69
Patients with previous revascularization			
Stent, absolute value (%)	181 (60)	199 (66)	0.13
Coronary artery bypass graft, absolute value (%)	67 (22)	53 (18)	0.15
Stent and coronary artery bypass graft, absolute value (%)	52 (17)	48 (16)	0.66
Stent details			
Average number of stents per patients, mean±SD	2.48±1.95	2.49±1.72	0.92
Bare metal stent, absolute value (%)	147 (25)	151 (23)	0.52
Drug-eluting stent, absolute value (%)	441 (75)	493 (77)	0.52
Stent diameter <3 mm, absolute value (%)	88 (15)	96 (14)	0.97
Overlapping stents, absolute value (%)	199 (66)	222 (74)	0.81
Coronary artery bypass graft (CABG) details			
Number, absolute value	324	272	…
Right internal mammarian artery, absolute value (%)	13 (4)	15 (5)	0.38
Left internal mammarian artery, absolute value (%)	123 (38)	110 (37)	0.53
Radial artery, absolute value (%)	6 (2)	7 (2)	0.54
Vein graft, absolute value (%)	182 (56)	140 (47)	0.25
Follow-up (days), mean±SD	773.6±345	752.8±291	0.21

ACE indicates angiotensin-converting enzyme; and CAD, coronary artery disease.

Table 2. Findings of Index Testing

	Number (%)
Computed tomography coronary angiography	
Coronary artery disease ≤50%	125 (41)*
Coronary artery disease >50%	167 (55)*
De-novo coronary artery disease >50% in native coronary arteries	82 (27)
In-stent restenosis >50%	12 (4)
Coronary artery bypass graft disease >50%	22 (7)
In-stent restenoses >50% plus coronary artery bypass graft disease >50%	51 (17)
Not evaluable	8 (4)
Stress cardiac magnetic resonance	
No ischemia	199 (66)
Ischemia	91 (31)
Ischemia because of perfusion defect alone	45 (15)
Ischemia because of perfusion defect plus wall motion abnormality	46 (15)
Not evaluable	10 (3)

*P<0.0001 computed tomography coronary angiography versus stress cardiac magnetic resonance.

(P<0.01) or positron emission tomography (P<0.0001), respectively, with a comparable number of major adverse cardiac events (1.6% versus 0.7% versus 5.5%, respectively) suggesting that the SPECT strategy was economically attractive. More recently, Douglas et al[10] showed that cTCA, as compared with a functional strategy approach, is associated with a lower rate of nonobstructive CAD at ICA evaluation (3.4% versus 4.3%; P=0.02) at the cost of a trend of a higher number of patients referred to catheterization (12.2% versus 8.0%) and revascularization procedures (6.2% versus 3.2%) and higher overall cumulative ED (12 mSv versus 10.1 mSv; P<0.001) without any improvement in the clinical outcomes. Lee et al[22] showed that a one-step strategy with cTCA alone is associated with a higher rate of ICA (75% versus 35%; P<0.001) and combined primary end point of cardiovascular death, nonfatal MI, repeated or delayed revascularization (11.3% versus 4%; P=0.011) as compared with a 2-step strategy, including cTCA followed by confirmatory functional tests. Similarly, SCOT-HEART investigators[11] verified the capability of cTCA to reclassify the diagnosis of CAD in patients evaluated by a functional approach in 27% of the study population, observing a 38% reduction in fatal and nonfatal MI. However, studies including patients with a prior history of revascularization are limited.[23,24] In a registry of 192 009 patients who were evaluated with cTCA as a first test after PCI, Mudrick et al[24] showed a higher rate of further noninvasive testing (10% versus 3%), catheterization (26% versus 15%), and revascularization procedures (13% versus 8%) within 90 days from cTCA (P<0.0001 for all comparisons) as compared with stress testing as an initial evaluation strategy. However, this registry is limited by the fact that it was performed with the use of an old cTCA technology assessing downstream testing and revascularization at short-term (90-day) follow-up and without inclusion of cumulative ED, costs, and outcomes. More recently, Andreini et al[7] showed an improved diagnostic accuracy in the evaluation of ISR when a high-definition cTCA was performed. However, the results of our study showed that in revascularized patients, a functional strategy using stress-CMR is associated with a lower number of further noninvasive diagnostic tests and ICA, revascularization procedures, costs, cumulative ED, and a better cost-effectiveness ratio even if compared with this more efficient cTCA technology.

In terms of noninvasive downstream testing, an interesting result is that most of cTCA-evaluated patients underwent subsequent functional tests (61 out of 86 noninvasive test) as compared with stress-CMR evaluated patients who continued to receive a functional strategy (50 out of 52 noninvasive tests), with the majority of cases still addressed to stress-CMR (25 out of 52 noninvasive tests). These findings could reflect the need of a functional evaluation in the follow-up when a non-evaluable or equivocal/positive cTCA is performed. On the other hand, when a stress-CMR is performed, a binary finding is usually provided recommending to no further test in case of negative stress-CMR or invasive evaluation in case of positive stress-CMR, with the repetition of stress-CMR just in the subset of patients with recurrent symptoms.

Regarding the higher rate of ICA and revascularization procedures in the cTCA group, it may be explained by the strong evidence that downstream testing is influenced by CAD prevalence in the study population, with few cardiac catheterizations performed in patients with normal cTCA and a higher rate of ICA and PCI when an abnormal cTCA is found. Patients with previous coronary stenting and CABG are usually older with a higher risk profile, as compared with the population without prior revascularization, and have a higher prevalence of multiple coronary plaques, calcifications, and stents. All these factors may explain the sizeable number of abnormal or inconclusive cTCA in this clinical setting, often requiring further additional tests.

Moreover, the increased rate of cardiac catheterization may lead to a higher number of revascularization procedures, often because of the well-known phenomenon of the oculostenotic reflex.[25] As a consequence, the higher rate of MI in the cTCA group as compared with the stress-CMR group could be partially explained by the increased rate of periprocedural MI as observed in our population. A second additional explanation could be that a functionally guided revascularization is more effective as compared with an anatomy-based strategy. For example, it could happen in one patient that two 60% to 70% stenoses are treated despite they could be not functionally significant, and a 50% stenosis is not treated despite it could be potentially significant from a functional point of view. As a result, the anatomic approach could be associated with higher number of stents placed but a lower protective effect in terms of outcome as compared with a functional strategy where this kind of scenario is less likely. Our results are in agreement with previous evidence from the FAME trial (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation)[26] in suspected CAD that could be even more valid in the setting of patients with a previous history of revascularization. Finally,

Table 3. Rate of Subsequent Noninvasive Testing, Invasive Coronary Angiography, Revascularization, Cumulative Costs, Radiation Exposure, and Clinical Outcomes

	Cardiac Computed Tomography Angiography (n=300)	Stress Cardiac Magnetic Resonance (n=300)	*P* Value
Noninvasive testing within 1 y since index test			
Number, absolute value, (%)	86 (28)	52 (17)	0.0009
Further functional test, absolute value	61	50	0.2
Exercise ECG, absolute value	33	18	…
Stress Echocardiography, absolute value	13	5	…
Single photon emission computed tomography, absolute value	2	2	…
Stress cardiac magnetic resonance, absolute value	13	25	…
Further computed tomography coronary angiography, absolute value	25	2	0.00001
Invasive procedures within 1 y since index test			
Number of invasive coronary angiography, absolute value (%)	92 (31)	62 (21)	0.0009
Number of percutaneous coronary intervention, absolute value (%)	72 (24)	46 (16)	0.007
Coronary artery bypass graft, absolute value (%)	1 (0.3)	2 (0.6)	0.56
Rate of revascularization/ICA, %	79	77	0.77
Costs			
Cumulative costs including index test, (Euro, mean±SD)	2012±2888	1516.±2464	<0.001
Cumulative effective radiation dose (mSv, mean±SD)	17.4±17.1	7.06±18.2	<0.001
Clinical outcomes			
Nonfatal myocardium infarction, absolute value (%)	30 (10)	14 (5)	0.012
Cardiac death, absolute value (%)	1 (0.3)	1 (0.3)	1
Major adverse cardiac events (combined end point of nonfatal myocardial infarction and cardiac death), absolute value (%)	31 (10)	15 (5)	0.014

ICA indicates invasive coronary angiography.

Borges et al[27] showed that patients with a previous PCI have an independent 2.1-fold increase in the odds of CAD progression in comparison to those with same baseline characteristics but without PCI. A potential explanation is that PCI could be responsible for coronary artery inflammation, producing an immediate local and systemic inflammatory response with consequent CAD progression. The main strength of stress-CMR in this setting is that it is not influenced by blooming artifacts due to calcified plaques or coronary stents,[14] which are often responsible for disease overestimation with cTCA,[6] and it is not associated with radiation exposure.

Our data could seem to contradict the conclusion of a recent meta-analysis published by Bittencourt et al,[28] showing that a cTCA strategy has a positive impact on major adverse cardiac events as compared with a functional strategy. However, our study population is completely different for several reasons that influence the prevalence of CAD and, therefore, the cost-effectiveness of an anatomic strategy versus a functional strategy. First, our population is older than patients from the Bittencourt et al study.[28] Second, in this meta-analysis, the authors have included patients symptomatic for noncardiac chest pain as well with a CAD prevalence ranging between 11% and 64% while we have included only patients symptomatic for angina. Third, the functional strategy used in this meta-analysis was mainly based on SPECT for the PROMISE trial (Prospective Multicenter Imaging Study for Evaluation of Chest Pain) and Min et al studies and exercise ECG for the CAPP trial (Cardiac CT for the Assessment of Chest Pain and Plaque) and SCOT HEART (Scottish Computed Tomography of the HEART Trial). In our study, the functional strategy was stress-CMR, which has been proven to be more accurate, thanks to the higher specificity and positive predictive value as compared with other imaging modalities.[13] Fourth, as a result, the prevalence of CAD in this meta-analysis ranges between 10.7% in the anatomic strategy arm of the PROMISE trial and 42% of the SCOT HEART study, which is lower as compared with that of our study population. Last but not least, in a population with no previous history of revascularization, there are more chances that the early detection of no-flow limiting coronary atherosclerosis by cTCA could positively influence the downstream medical management. Indeed, the percentage of patients who received aspirin or statin at baseline in the Bittencourt et al study was lower than 50%, and the increase of their prescription after cTCA as index test could be one of the reason of improved outcome in this arm. On the contrary, in our study population, 100% and 77% to 80% of patients already received aspirin and statin at baseline, respectively. Thus, potential positive influence of anatomic detection of subclinical coronary atherosclerosis in our study population could be negligible. Therefore, the 2 settings of patients are not comparable.

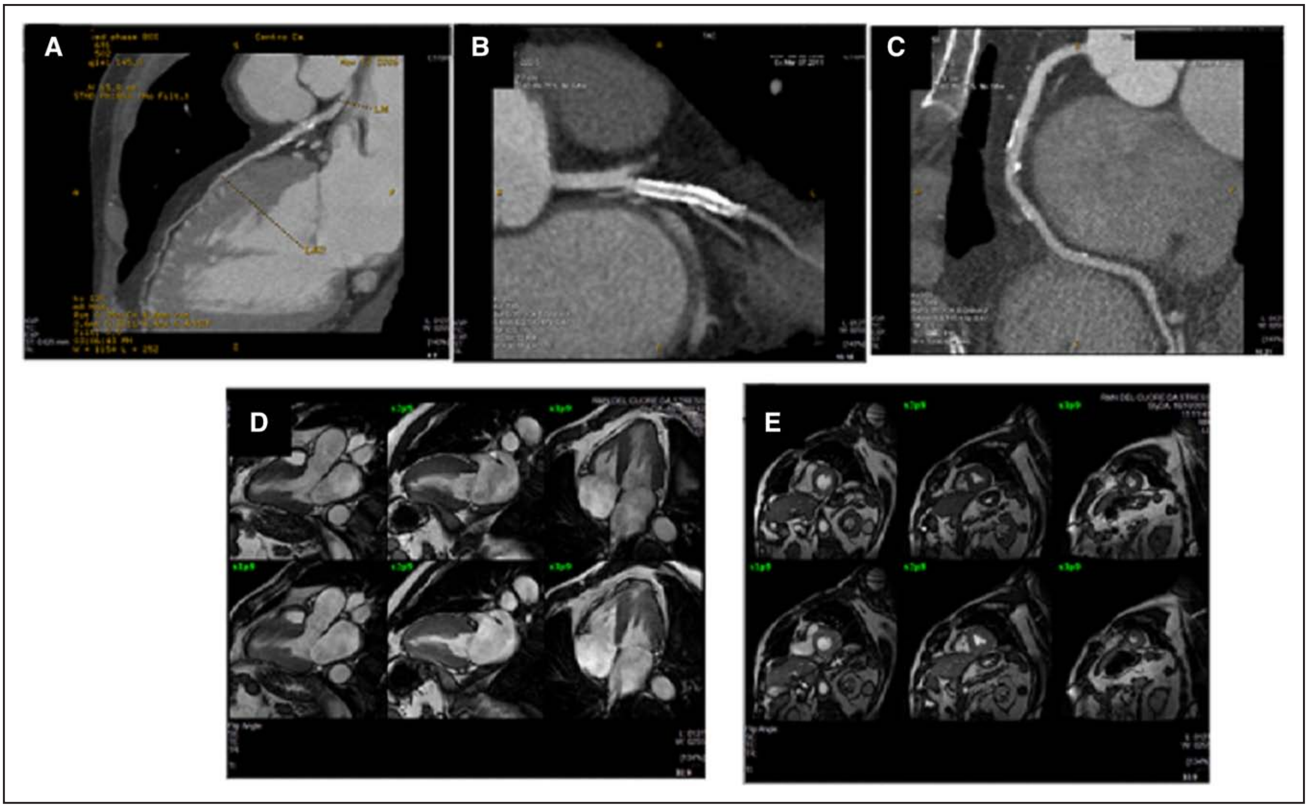

Figure 1. Clinical case of a 59-year- old man with history of previous myocardial infarction who underwent PCI with coronary stenting of the intermediate coronary artery. Atypical chest pain prompted cTCA as first-line test that showed 55% stenosis of proximal left anterior descending coronary artery (**A**), stent patency (**B**), and 65% stenosis of mid right coronary artery (**C**). Further evaluation with stress-CMR did not show any reversible perfusion defect and wall motion abnormalities (**D** and **E**). During the follow-up, no MACE occurred. CAD indicates coronary artery disease; CMR, cardiac magnetic resonance; cTCA, computed tomography coronary angiography; MACE, major adverse cardiac events; and PCI, percutaneous coronay intervention.

Study Limitations

The major limitation is that this is an observational study, and therefore, its results are subject to potential selection biases in comparison to the results from randomized controlled trials. Despite we did everything possible to minimize this limitation by using propensity score analysis, some important additional cofounders, such as decompensated heart failure, obstructive lung disease, cardiac rhythm disorder, or advanced renal insufficiency, could be still present. Most of them have been considered as exclusion criteria, and therefore, it is less likely that they could have influenced the outcomes. However, additional cofounders could be undercoded, and therefore, a risk of residual selection bias needs to be taken into account. Second, this is a single-center study from an Institute with extensive experience in performing

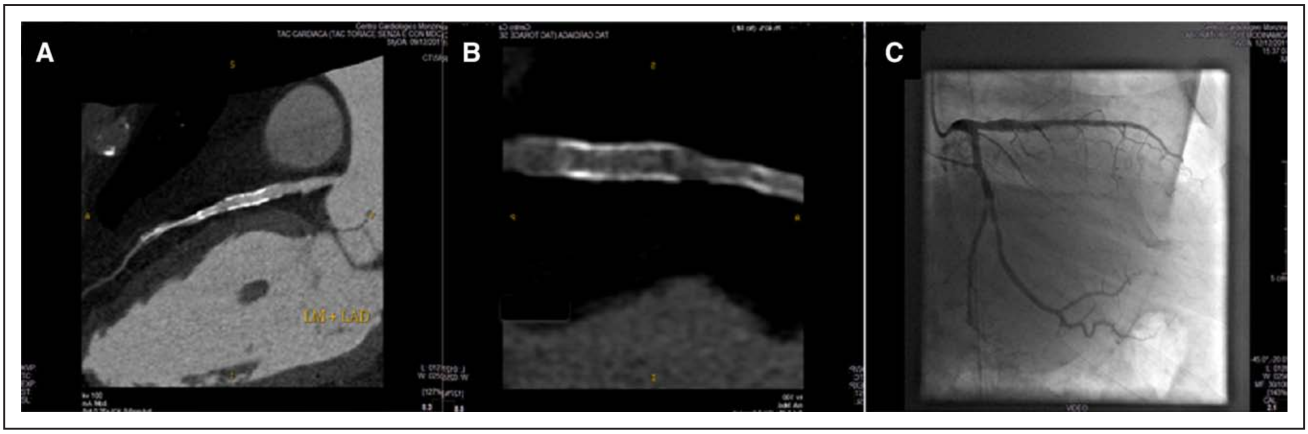

Figure 2. A 62-year-old man with known CAD and previous PCI (first diagonal branch and left anterior descending coronary artery stenting). Because of new onset substernal chest tightness, he underwent cTCA as first-line test that showed significant restenosis at the distal edge of the left anterior descending stent (**A** and **B**). Invasive coronary angiography did not confirm cTCA findings (**C**). CAD indicates coronary artery disease; cTCA, computed tomography coronary angiography; and PCI, percutaneous coronay intervention.

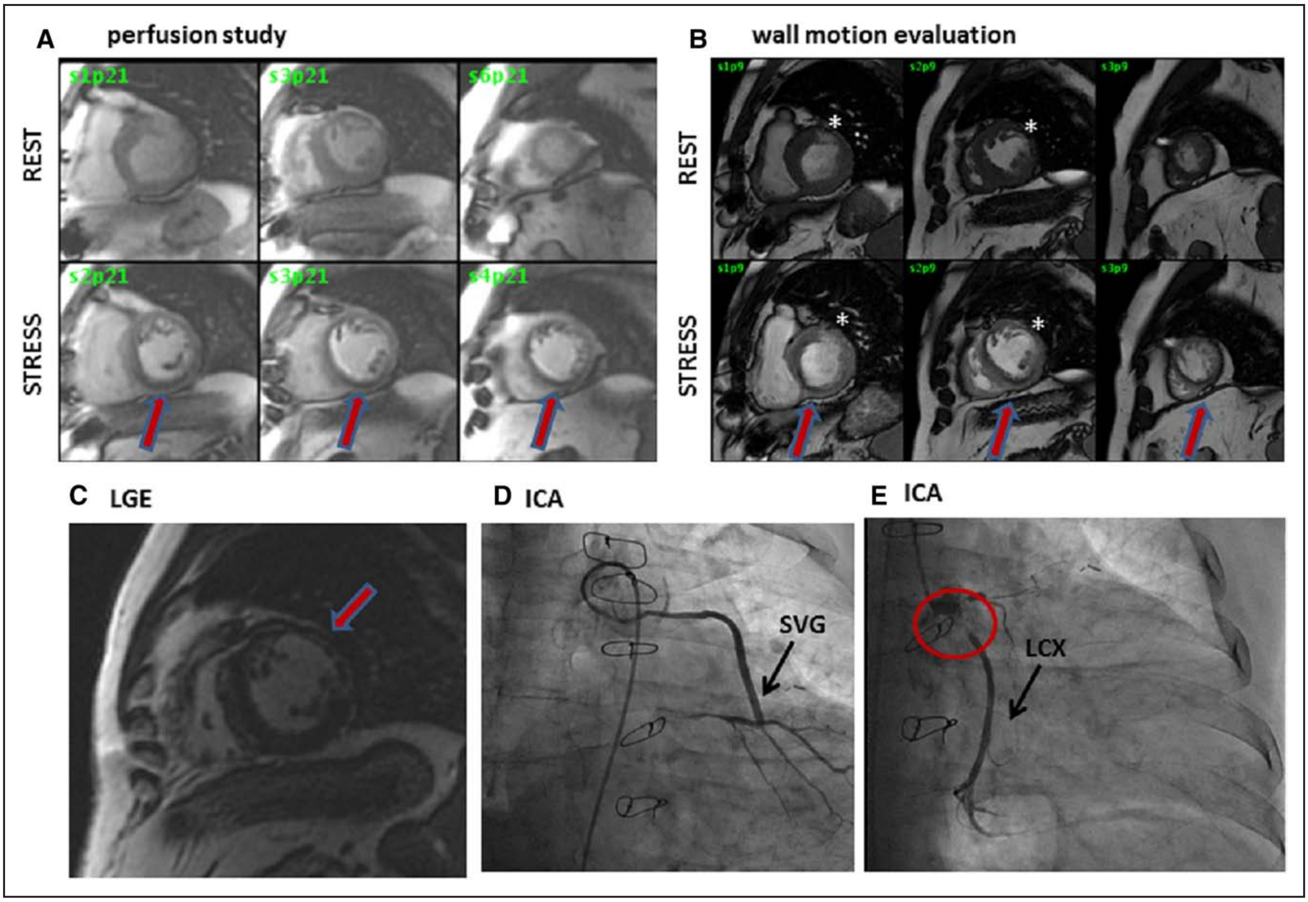

Figure 3. Clinical case of a 66-year-old male patient with history of previous revascularization with LIMA to LAD and SVG to marginal branch and recent onset of angina. Stress-CMR was performed as first-line test showing a reversible perfusion defect in LV inferior wall (**A**, arrows) with associated reversible hypokinesis under stress (**B**, arrows) and akinesis at rest and stress of the LV anterior wall (**B**, asterisks). The LGE study showed the presence of a scar at the level of LV anterior wall (**C**, arrow). The patient underwent ICA that showed occlusion of LIMA to LAD and patency of SVG to the marginal branch (**D**) with subocclusion of a dominant LCX (**E**, circle). This patient underwent PCI with stenting of the LCX ostium and his symptoms diasappeared. CMR indicates cardiac magnetic resonance; LAD, left anterior descending artery; LCX, left circumflex coronary artery; LIMA, left internal mammary artery; LGE, late gadolinium enhancement; LV, left ventricle; PCI, percutaneous coronary intervention; and SVG, saphenous vein graft.

cTCA and stress-CMR examinations. Therefore, our findings could not be directly transferred to the real clinical world. However, on the other hand, when patients are enrolled from multiple different centers, despite the use of a common protocol and data standards, differences in clinical practice patterns among centers might affect the clinical and economic outcomes assessed. In other words, the single-center design could be more rigorous from this perspective. Third, the sample size was small, and therefore, the cost-effectiveness analysis may be limited. Fourth, our study did not compare the index tests at baseline with a reference standard technique. However, considering that we are comparing an anatomic versus a functional strategy, a common reference diagnostic tool cannot be found, and therefore, the use of outcomes as reference for the clinical utility of the 2 strategies may be valid. Fifth, the unit costs for all cardiac tests fed into the model may vary between different geographical regions, and therefore, the results cannot be directly transferred in different healthcare systems. Moreover, the costs related to office visits and medical therapy changes have not been included because of the difficulty to collect and to standardize them. However, we think that the overall cost of downstream noninvasive testing and the cost of hospitalization for invasive procedures reflect the hard costs for this population. Sixth, the higher prevalence of male patients in our study population does not allow to generalize our findings in female patients. Finally, cTCA was performed with a standard single-source 64-slice scanner. Recent technologies could change the balance between cTCA and stress-CMR mainly in terms of cumulative ED, thanks to the capability to scan all patients with <2 mSV. Finally, the intermediate duration follow-up time is not long term. However, it is consistent with the mean follow-up of similar studies, such as the SPARC (Economic outcomes in the Study of Myocardial Perfusion and Coronary Anatomy Imaging Roles in Coronary Artery Disease registry)[8] and PROMISE trials.[10]Nonetheless, larger prospective randomized studies with longer follow-up would be required to further investigate the findings and confirm the hypothesis.

Conclusions

The use of stress-CMR was associated with lower resource utilization, better outcomes, and lower costs as compared with cTCA in the evaluation of symptomatic patients with a previous history of revascularization. Future research should further explore the diagnostic benefit of integrating anatomy imaging and functional testing in this clinical setting.

Disclosures

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CLINICAL PERSPECTIVE

The STRATEGY study (Stress Cardiac Magnetic Resonance Versus Computed Tomography Coronary Angiography for the Management of Symptomatic Revascularized Patients) is a single-center prospective observational study comparing the cost-effectiveness of functional assessment with stress cardiac magnetic resonance versus anatomic evaluation with computed tomography coronary angiography in consecutive symptomatic patients presenting with history of previous myocardial revascularization. In 600 patients with chest pain and previous revascularization included in a prospective observational registry and evaluated by clinically indicated computed tomography coronary angiography (n: 300) or stress cardiac magnetic resonance (n: 300), we found that the functional strategy is associated with lower downstream noninvasive and invasive testing, coronary artery disease–related spending, radiation exposure, and cost-effectiveness ratio as compared with computed tomography coronary angiography. The main limitations of computed tomography coronary angiography, such as blooming artifacts, due to calcified plaques or coronary stents and radiation exposure are not present in case of stress cardiac magnetic resonance. Our data support the use of stress cardiac magnetic resonance in this setting of patients where specific recommendations about which test should be used are not available.

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The STRATEGY Study (Stress Cardiac Magnetic Resonance Versus Computed Tomography Coronary Angiography for the Management of Symptomatic Revascularized Patients): Resources and Outcomes Impact

Gianluca Pontone, Daniele Andreini, Andrea I. Guaricci, Cristina Rota, Marco Guglielmo, Saima Mushtaq, Andrea Baggiano, Virginia Beltrama, Laura Fusini, Anna Solbiati, Chiara Segurini, Edoardo Conte, Paola Gripari, Andrea Annoni, Alberto Formenti, Maria Petulla', Federico Lombardi, Giuseppe Muscogiuri, Antonio L. Bartorelli and Mauro Pepi

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