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Long-Term Clinical Impact of Coronary CT Angiography in Patients With Recent Acute-Onset Chest Pain

The Randomized Controlled CATCH Trial

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ABSTRACT

OBJECTIVES The aim of the CATCH (CArdiac cT in the treatment of acute CHest pain) trial was to investigate the long-term clinical impact of a coronary computed tomographic angiography (CTA)-guided treatment strategy in patients with recent acute-onset chest pain compared to standard care.

BACKGROUND The prognostic implications of a coronary CTA-guided treatment strategy have not been compared in a randomized fashion to standard care in patients referred for acute-onset chest pain.

METHODS Patients with acute chest pain but normal electrocardiograms and troponin values were randomized to treatment guided by either coronary CTA or standard care (bicycle exercise electrocardiogram or myocardial perfusion imaging). In the coronary CTA-guided group, a functional test was included in cases of nondiagnostic coronary CTA images or coronary stenoses of borderline severity. The primary endpoint was a composite of cardiac death, myocardial infarction (MI), hospitalization for unstable angina pectoris (UAP), late symptom-driven revascularizations, and readmission for chest pain.

RESULTS We randomized 299 patients to coronary CTA-guided strategy and 301 to standard care. After inclusion, 24 patients withdrew their consent. The median (interquartile range) follow-up duration was 18.7 (range 16.8 to 20.1) months. In the coronary CTA-guided group, 30 patients (11%) had a primary endpoint versus 47 patients (16%) in the standard care group ($p = 0.04$; hazard ratio [HR]: 0.62 [95% confidence interval: 0.40 to 0.98]). A major adverse cardiac event (cardiac death, MI, hospitalization for UAP, and late symptom-driven revascularization) was observed in 5 patients (2 MIs, 3 UAPs) in the coronary CTA-guided group versus 14 patients (1 cardiac death, 7 MIs, 5 UAPs, 1 late symptom-driven revascularization) in the standard care group ($p = 0.04$; HR: 0.36 [95% CI: 0.16 to 0.95]). Differences in cardiac death and MI (8 vs. 2) were insignificant ($p = 0.06$).

CONCLUSIONS A coronary CTA-guided treatment strategy appears to improve clinical outcome in patients with recent acute-onset chest pain and normal electrocardiograms and troponin values compared to standard care with a functional test. (Cardiac-CT in the Treatment of Acute Chest Pain [CATCH]; NCT01534000) (J Am Coll Cardiol Img 2015;8:1404–13)

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Patients presenting with acute chest pain may suffer from vasospastic or structural coronary pathology as the main cause of their symptoms (1). However, a large proportion of patients have noncardiac causes of chest pain, which makes it difficult to identify those with coronary artery disease (CAD) and, hence, the need for revascularization or intensive medical treatment (2–4). Patients with acute chest pain appear to have increased risk of future cardiovascular events even if electrocardiograms (ECG) and cardiac biomarkers are normal (5,6). For several decades, functional tests, including exercise ECG or single-photon emission computed tomography (SPECT) have been cornerstones of the initial diagnostic strategy used to select patients for invasive coronary angiography (ICA). However, because ICA has a relatively low diagnostic yield of 30% to 40%, an improved evaluation strategy seems necessary (7). Coronary computed tomographic angiography (CTA) provides

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detailed anatomical information about coronary pathology with high diagnostic accuracy to exclude CAD (8,9). In current American and European guidelines concerning diagnosis and management of patients with stable CAD or low-risk unstable angina, exercise ECG and SPECT are established as first line noninvasive tests in patients with a broad range of pretest probabilities, whereas the role of coronary CTA is considered mainly a second line approach (10,11). Randomized trials and a meta-analysis have demonstrated that the addition of coronary CTA in the early triage of unselected patients with chest pain is safe and reduces costs and lengths of stay in the emergency department (12–16). However, the impact of coronary CTA performed after discharge on the clinical outcome has not been investigated in patients initially referred for acute coronary syndrome (ACS).

The intent of the CATCH (CArdiac cT in the treatment of acute CHest pain) trial was to evaluate whether a post-discharge coronary CTA-guided diagnostic strategy improved long-term clinical outcome in patients referred for ACS, who had normal ECGs and troponin values.

METHODS

DESIGN AND STUDY POPULATION. The CATCH trial was a randomized, controlled, parallel group trial designed to investigate the clinical value of a coronary CTA-guided diagnostic strategy compared to standard care with a functional test (NCT01534000). Baseline results from the CATCH trial concerning the effect of a coronary CTA-guided strategy on the referral rate for ICA, the positive predictive value for the identification of significant CAD, and subsequent coronary revascularization have previously been published (17). Patients referred for ACS, who turned out to have normal or nondiagnostic ECGs and 2 normal measures of troponin concentrations and who could be discharged after approximately 24 h of in-hospital clinical observation without reoccurrence of chest pain, were considered for enrollment in the trial in case the treating cardiologist found indication for further outpatient evaluation of the patient. Using these criteria, we aimed to include a study population with a low to intermediate pre-test probability of CAD (18). Exclusion criteria were age of <18 years, women of childbearing potential not using approved contraception, patients with geographical residence or mental or physical conditions that would impair follow-up, plasma creatinine concentrations >130 mg/l, known allergy to iodinated contrast agents, abnormal chest radiography, and previous coronary artery bypass graft surgery. Patients were consecutively included in the study within 7 days after hospital admission, and noninvasive tests were performed within 2 weeks from randomization. The study protocol was approved by the local ethics committee and complied with the Declaration of Helsinki.

RANDOMIZATION AND BLINDING. After informed consent was obtained, patients were randomized in a 1:1 ratio to either coronary CTA-guided investigation or standard care based on functional testing. Details of the randomization process were previously published (17). To secure blinding of patients with regard to group allocation, all treatments were planned so

ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome

CAD = coronary artery disease

CTA = computed tomographic angiography

ECG = electrocardiogram

ICA = invasive coronary angiography

MACE = major adverse cardiovascular events

MI = myocardial infarction

SPECT = single-photon emission computed tomography

UAP = unstable angina pectoris

CORE320 trial, which was supported in part by Toshiba Medical Corporation; is a member of the speakers bureau of Toshiba Medical Systems, and the advisory board for Vital Images, Inc.; and has received research grants from AP Møller og hustru Chastine McKinney, Møllers Fond, The John and Birthe Meyer Foundation, Research Council of Rigshopitalet, The University of Copenhagen, The Danish Heart Foundation, The Lundbeck Foundation, and The Danish Agency for Science, Technology and Innovation by The Danish Council for Strategic Research. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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that patients would undergo both post-discharge coronary CTA evaluation and functional testing. In the coronary CTA-guided group, the result of the coronary CTA was sent to the referring physician, who determined the subsequent strategy according to the protocol detailed below. In the standard care group, the coronary CTA was not reconstructed or analyzed, and results remained blinded to the patient and to the referring physician throughout the study.

INDEX DIAGNOSTIC TESTING. Coronary CTA was performed at Rigshospitalet, Copenhagen, using a 320 model multidetector CT scanner (Aquilion One, Toshiba, Irvine, California). In the absence of contraindications, an oral beta-blocker (50 to 150 mg of metoprolol) was given in advance whenever the heart rate was >60 beats/min. The coronary CTA images were interpreted independently by 2 experienced coronary CTA readers (J.D.H. and K.F.K.) in accordance with guidelines published by the Society of Cardiovascular Computed Tomography (19). In the case of disagreement, a final conclusion was made in consensus. Patients with a coronary diameter stenosis >50% in the left main artery or ≥70% in one of the major coronary artery branches with a lumen diameter >2 mm were referred for ICA. In patients with a borderline coronary artery diameter stenosis between 50% and 70% or a nondiagnostic coronary CTA due to motion or other artifacts, excessive calcifications, or nonevaluable coronary stents, the coronary CTA report sent to the referring physician included a recommendation to add functional testing to the clinical decision. In these cases, results of the stress test were made available for the treating physician. A coronary diameter stenosis <50% was considered nonsignificant.

The exercise ECG test was performed in accordance with European guidelines (20). Patients with insufficient physical capacity and patients with nondiagnostic exercise ECG tests were scheduled for SPECT conducted according to established guidelines (21). In the standard care group, patients with a positive exercise ECG test result or a positive or nondiagnostic SPECT result were referred for ICA.

Decision to perform coronary intervention was left to the interventional cardiologist, who was not part of the study team. Fractional flow reserve measurement was performed in patients with borderline coronary stenoses on ICA.

OUTCOME MEASURES. The primary endpoint was the composite of cardiac death, myocardial infarction (MI), hospitalization for unstable angina pectoris (UAP), late symptom-driven revascularization, and readmission for chest pain. Secondary endpoints were major adverse cardiac events (MACE), defined as the composite of all components of the primary endpoint excluding readmission for chest pain, and the individual components of the primary endpoint. The first occurring event for each patient was used in both of the outcome analyses. Specifically, patients readmitted for chest pain who later also experienced MACE were classified as "readmission for chest pain" in the primary endpoint outcome analysis, whereas the subsequent major event was applied in the MACE outcome analysis. Information of post-index diagnostic tests in the follow-up period, including exercise ECG, SPECT, coronary CTA, and ICA was obtained, and information of medical treatment was recorded at baseline and after the index diagnostic evaluation. Medical treatment and decision to refer for new diagnostic testing after index evaluation was left to the treating physicians. Quality of life was assessed at the time of follow-up, using the International Quality of Life Assessment SF-36 questionnaire (22). In the coronary CTA-guided group, extra-cardiac findings meriting further investigation and treatment were recorded.

STUDY ENDPOINTS. Follow-up initiated after at least 1 year with registration of clinical endpoints was conducted by 2 dedicated project nurses. Patients were contacted by letter with a suggested time for a phone interview, and electronic records covering all hospital admissions in the eastern part of Denmark were reviewed for confirmation of exact dates and diagnoses. Failure to reach the patient by phone was followed by a second and, thereafter, a third letter with a new suggested date for the interview. If contact was not achieved following this protocol, hospital records were reviewed at the timepoint for the third suggested interview with recording of clinical endpoints. After completion of data acquisition, blinded adjudication of clinical endpoints was performed independently by 2 experienced cardiologists. A detailed description of the adjudication process including definitions of study endpoints is available in the Online Appendix.

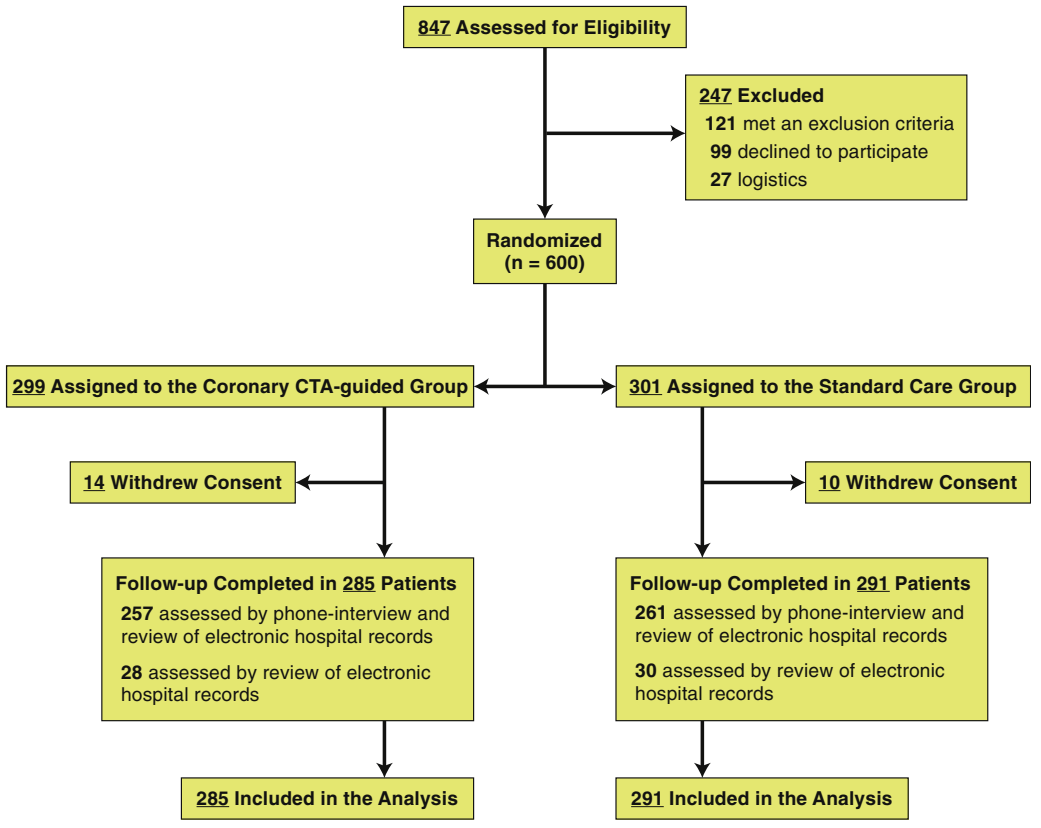
STATISTICAL ANALYSIS. The sample size calculation is available in the Online Appendix. All analyses were performed according to the intention-to-treat principle, except that patients who withdrew their consent were excluded. Continuous data are mean ± SD or median (interquartile range) and were compared using the Student *t* test for unpaired data, Fisher exact test, or the Kruskal-Wallis test as appropriate. A 2-sided p value <0.05 was considered statistically

significant. The primary endpoint and its individual components were compared with log-rank testing, and for the primary endpoint and MACE, the hazard ratios (HRs) were obtained from Cox proportional hazard models. Patients who died of noncardiac causes were censored at the time of death, unless a cardiac event had already been recorded. SAS version 9.1.3 software (SAS, Cary, North Carolina) was used for statistical analyses.

RESULTS

From January 2010 to January 2013, 847 patients were screened for eligibility in the CATCH trial to include 600 patients. Of 299 patients randomized to coronary CTA-guided strategy and 301 patients to standard care strategy, 14 and 10 patients (4% in total) subsequently withdrew their consent before any diagnostic test was performed. Figure 1 shows the patient flow chart. Demographics were comparable between the 2 groups, except for hypertension, which was more common in the coronary CTA-guided group (Table 1). In the coronary CTA-guided group, the treatment strategy during index evaluation was based on coronary CTA in 233 patients (82%), a combination of coronary CTA and functional test in 39 patients (25 patients with borderline coronary CTA stenosis and 14 patients with nondiagnostic coronary CTA; 14% in total), and a functional test alone in 13 patients (5%). Of patients with borderline coronary CTA stenoses or nondiagnostic images, evaluation and treatment strategy were based on exercise ECG in 24 patients (62%), of whom 12 patients were referred for ICA, but none was revascularized, and on SPECT in 15 patients (38%), of whom 5 patients were referred for ICA due to a reversible perfusion defect (1 patient was revascularized). In the standard care group, clinical treatment strategy was based on an exercise ECG test in 221 patients (76%), SPECT in 63 patients (22%), and clinical assessment by a cardiologist without any

FIGURE 1 Study Flow Diagram



Flow diagram shows patient eligibility, randomization, and follow-up. CTA = computed tomographic angiography.

TABLE 1 Baseline Characteristics of Patients Evaluated by Coronary CTA-Guided Strategy Versus Those by Standard Care

	Coronary CTA-Guided Strategy (n = 285)	Standard Care Strategy (n = 291)	p Value
Age, yrs	56 ± 12	55 ± 12	0.14
Women	124 (44)	123 (42)	0.76
BMI, kg/m^2*	28 (24–31)	28 (24–31)	0.60
Hypertension	135 (47)	106 (36)	0.009
Hyperlipidemia	117 (41)	101 (35)	0.12
Diabetes	35 (12)	29 (10)	0.38
Family history of CAD	69 (24)	76 (26)	0.63
Active users of tobacco or ex-smoker	172 (60)	195 (67)	0.10
History of CAD	44 (15)	36 (12)	0.29
Previous PCI	30 (11)	26 (9)	0.31
Symptoms			
Typical angina	35 (12)	34 (12)	0.83
Atypical angina	110 (39)	116 (40)	0.76
Nonanginal chest pain	140 (49)	141 (48)	0.88
Pre-test risk†	36 ± 27	34 ± 26	0.37
Pre-test risk group†			
Low (0%–15%)	59 (21)	60 (21)	1.00
Low to intermediate (15%–50%)	96 (34)	120 (41)	0.07
Intermediate (15%–85%)	161 (56)	173 (59)	0.50
High (>85%)	21 (7)	22 (8)	1.00
TIMI risk score			
0	139 (49)	158 (54)	0.21
1	77 (27)	71 (24)	0.50
2	37 (13)	32 (11)	0.52
≥3	32 (11)	30 (10)	0.79
Median coronary calcium score*	5 (0–154)		
Medication after index evaluation			
Aspirin	134 (47)	106 (36)	0.01
Statin	125 (44)	110 (38)	0.15
Beta-blocker	67 (24)	54 (19)	0.15
Calcium-blockers	52 (18)	33 (11)	0.03
Nitrates	49 (17)	33 (11)	0.06
Diuretics	61 (21)	41 (14)	0.02
ACE-inhibitors/AT2-antagonist	76 (27)	69 (24)	0.44
Platelet inhibitors	40 (14)	18 (6)	0.002

Values are mean ± SD, n (%), or median (IQR). *Interquartile range (25th-75th). †Pre-test risk of having significant coronary artery disease, according to criteria of Diamond and Forrester (18) based on age, sex, and type of chest pain. Patients with a history of CAD were excluded.

ACE = angiotensin-converting-enzyme; AT2 = angiotensin 2; BMI = body mass index (weight [kg]/height^2[m^2]); CAD = coronary artery disease; CTA = computed tomographic angiography; PCI = percutaneous coronary intervention; TIMI = thrombolysis in myocardial infarction.

functional test in 7 patients (2%). In the standard care group, 22 patients with known CAD were evaluated by exercise ECG and 12 by SPECT and by clinical evaluation alone in 2 patients. During index evaluation, 85 patients were referred for ICA, of whom 9 patients underwent fractional flow reserve due to an intermediate diameter stenosis (7 in the coronary CTA-guided group and 2 in the standard care group). In the coronary CTA-guided group, 14 of 49 patients (29%) had normal ICA versus 23 of 36 patients (64%) in the standard care group ($p = 0.002$). In the coronary CTA-guided group, no extra-cardiac findings by full-view CT examination required treatment.

Follow-up with regard to clinical events was completed in all patients. Combined phone interviews and reviews of electronic hospital records were possible for 257 patients (90%) in the coronary CTA-guided group and 261 patients (90%) in the standard care group ($p = 0.89$). For the remaining patients, event registration was obtained by review of electronic hospital records alone. No events recorded in patients completing the planned phone interview were missed by the corresponding electronic hospital records. The median follow-up duration was 18.7 months (interquartile range [IQR]: 16.8 to 20.1 months), with no differences between groups.

POST-INDEX REPEATED ELECTIVE DIAGNOSTIC TESTING AND QUALITY OF LIFE. The frequencies of elective diagnostic tests after index evaluation were similar in the 2 groups, and no differences in any life quality scores were observed between the groups at follow-up (Online Tables 1 and 2).

MEDICAL TREATMENT. After index diagnostic evaluation, more patients were treated with aspirin and other platelet inhibitors in the coronary CTA-guided group (Table 1). In addition, patients in the coronary CTA-guided group were more frequently treated with calcium-blockers and diuretics, but a similar pattern was observed before randomization.

CLINICAL OUTCOME. Frequencies and types of events are presented in Table 2, and occurrence of events over time is presented in Figure 2. In the coronary CTA-guided group 2 patients died from noncardiac causes (liver cirrhosis and pulmonary cancer). However, fewer patients in that group suffered a primary endpoint (cardiac death, MI, UAP, late symptom-driven revascularization and readmission for chest pain) than those in the standard care group (HR: 0.62 [95% confidence interval (CI): 0.40 to 0.98]). In a cox proportional hazard model including baseline hypertension and hyperlipidemia, differences between strategies remained significant (HR: 0.57 [95% CI: 0.36 to 0.91]; $p = 0.02$). A significant risk reduction was also found for the composite of MACE (the composite of all components of the primary endpoint, excluding readmission for chest pain) (HR: 0.36 [95% CI: 0.16 to 0.95]) (Figure 2). Differences in cardiac death and MIs (8 vs. 2, respectively) were insignificant ($p = 0.06$). Of the 9 patients who had MIs, 2 had ST-segment elevation myocardial infarction (both in the standard care group) and

7 had non-ST-segment elevation myocardial infarction. All patients presented with chest pain and had elevated troponin concentrations. Two patients had normal ECGs, and all but 2 patients subsequently underwent coronary revascularization. Of patients readmitted for chest pain, 7 patients (11%) had renewed out-patient diagnostic testing (3 exercise ECG, 3 SPECT, and 1 ICA).

The relationship of index diagnostic evaluation and intervention with cardiovascular events during follow-up is illustrated in Table 3. During index evaluation, revascularization was more frequently performed as a consequence of coronary CTA-guided assessment, compared to standard care with functional testing. Subgroup analyses of patients grouped according to pre-test probability and presence or absence of known CAD are presented in Table 4.

TABLE 2 Clinical Outcome of Patients Evaluated by a Coronary CTA-Guided Strategy Versus Standard Care

	Coronary CTA-Guided Strategy (n = 285)	Standard Care Strategy (n = 291)	p Value
No. at primary endpoint	30 (11)	47 (16)	0.04
First occurring event			
Cardiac death	0 (0)	1 (0)	1.00
Myocardial infarction	1 (0)	7 (2)	0.07
Unstable angina pectoris	3 (1)	2 (1)	0.7
Late symptom-driven revascularization	0 (0)	1 (0)	1.00
Readmission for chest pain	26 (10)	36 (12)	0.23
No. of MACE	5 (2)	14 (5)	0.04
First MACE			
Cardiac death	0 (0)	1 (0)	1.00
Myocardial infarction*	2 (1)	7 (2)	0.18
Unstable angina pectoris*	3 (1)	5 (2)	0.72
Late symptom-driven revascularization	0 (0)	1 (0)	1.00

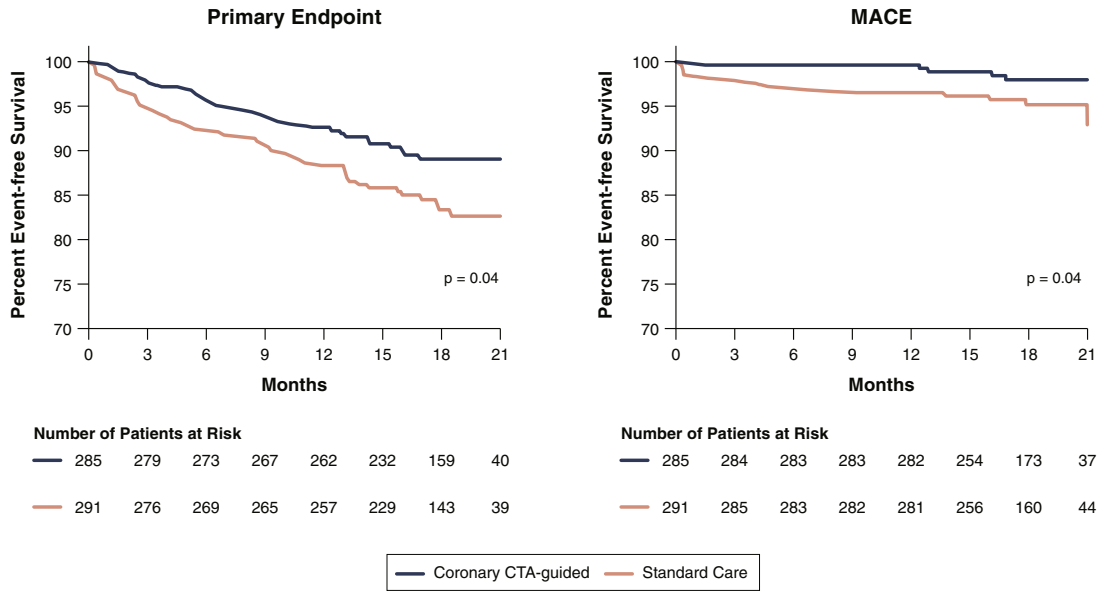
Values are n (%). *For the distribution of the different components of the primary endpoint and the composite of major adverse cardiac events (MACE), only the first occurring type of event is shown. MACE was defined as the composite of all components of the primary endpoint, excluding readmission with chest pain. Comparisons are made by log-rank testing for primary and secondary endpoints.

DISCUSSION

The CATCH trial evaluated in a randomized fashion the long-term clinical value of a coronary CTA-guided treatment strategy in patients referred for acute chest pain, who turned out to have normal ECGs and plasma troponin levels. We found that a coronary CTA-guided treatment strategy reduced the risk of suffering a cardiovascular event compared to standard evaluation with a functional test. This difference remained significant when excluding the soft endpoint of readmission for chest pain.

A coronary CTA-guided strategy identified more patients with significant CAD and resulted in a higher frequency of index revascularizations, compared to standard care. A possible explanation for an improved

FIGURE 2 Long-Term Clinical Outcome



Kaplan-Meier curves show event-free survival of the primary composite endpoint **(left)** and major adverse cardiac events (MACE) **(right)**.

TABLE 3 Index Diagnostic Evaluation, Coronary Intervention, and Cardiovascular Events During Follow-Up

	Coronary CTA-Guided Care Strategy						Standard Care Strategy (Exercise ECG/SPECT)					
	Total	Significant Stenosis	No Significant Stenosis	Borderline Stenosis	Nondiagnostic	No Test or Stress Test Only	Total	Ischemia	No Ischemia	Nondiagnostic	No Test	p Value
Index evaluation/treatment												
Noninvasive test result	285	31	202	25	14	13	291	29	240	15	7	
Referred for ICA	49	31	0	9	7	2	36	28	3	4	1	0.13
Revascularized	29	26	0	1	0	2	12	10	0	2	0	0.006
PCI	25	23	0	1	0	1	8	6	0	2	0	0.002
CABG	4	3	0	0	0	1	4	4	0	0	0	1.00
Follow-up												
Primary endpoint	30	6*	14†	7	3	0	47	10*	29†	5	3	0.04

Values are proportions of patients, and p values are comparisons between total number of patients who underwent coronary CTA-guided care and those who underwent standard care. *p = 0.45 for comparison between the proportions of patients with a primary endpoint events and those with a positive index noninvasive test. †p = 0.03 for comparison between the proportions of patients with a primary endpoint and those with a normal index noninvasive test result. In the standard care group, 192 patients had normal exercise ECG results, and 48 had normal SPECT results.

CABG = coronary artery bypass grafting; CTA = computed tomographic angiography; ECG = electrocardiogram; ICA = invasive coronary angiography; PCI = percutaneous coronary intervention; SPECT = single-photon emission computed tomography.

outcome associated with a coronary CTA-guided strategy therefore seems to be more well-timed and appropriate coronary revascularization of this group. Most events were reported in patients with a normal index diagnostic test and more frequently after standard care testing which indicate that much of the difference found between groups can be explained by false negative stress tests. This is supported by the steep decline of the Kaplan-Meier curve in the standard care group within the first month.

TABLE 4 Subgroup Analyses With Regard to Primary Endpoint and MACE

	Coronary CTA-Guided Strategy (n = 285)	Standard Care Strategy (n = 291)	p Value	Hazard Ratio (95% CI)
History of CAD	44 (15)	36 (12)	0.29	
Primary endpoint	12 (27)	12 (33)	0.49	0.76 (0.34–1.69)
MACE	4 (9)	5 (14)	0.49	0.63 (0.17–2.34)
No History of CAD	241 (85)	255 (88)	0.34	
Primary endpoint	18 (7)	38 (15)	0.02	0.53 (0.31–0.92)
MACE	1 (<1)	9 (4)	0.01	0.12 (0.06–0.73)
Low pre-test probability*	59 (21)	60 (21)	1.00	
Primary endpoint	2 (3)	5 (8)	0.25	0.40 (0.10–1.85)
MACE	0 (0)	0 (0)	1.00	
Intermediate pre-test probability*	161 (56)	173 (59)	0.50	
Primary endpoint	14 (9)	24 (14)	0.13	0.61 (0.32–1.16)
MACE	1 (1)	7 (4)	0.04	0.15 (0.06–0.95)
High pre-test probability*	21 (7)	22 (8)	1.00	
Primary endpoint	2 (10)	6 (27)	0.12	0.30 (0.08–1.34)
MACE	0 (0)	2 (9)	0.14	0.00 (0.01–2.02)

Values are n (%). *Patients with a history of CAD were excluded from subgroup analysis of differentiated pre-test probabilities.

CAD = coronary artery disease; CI = confidence interval; CTA = computed tomographic angiography; MACE = major adverse cardiac events.

A change of medical regimen is another potential contributing factor to the beneficial effect of coronary CTA on clinical patient outcome. After index evaluation, more patients in the coronary CTA-guided group were treated with aspirin and/or other platelet inhibitors, which potentially might have prevented post-index events in some patients.

Previous randomized trials have focused on the application of coronary CTA examination in the emergency department to verify or repudiate ACS. Hoffmann et al. (14) found that inclusion of coronary CTA in the early triage of patients reduced the length of stay in the hospital with no increase in MACE after 28 days and no increase in cost, even though downstream testing was increased. It has also been demonstrated that a normal coronary CTA performed in the emergency department allows patients to be safely discharged with a low 30-day event rate, and 2 studies comparing coronary CTA with SPECT found that coronary CTA reduced the time to make a correct diagnosis and lowered overall cost (12,15,16). None of these randomized trials investigated the mid- or long-term prognostic value of coronary CTA. Two recently published trials investigated the potential role of coronary CTA compared to that of standard care in patients with stable angina pectoris. SCOT-HEART (Scottish COmputed Tomography of the HEART Trial) evaluated the incremental value of coronary CTA on top of standard care and found that additional coronary CTA clarified the diagnosis and enabled targeting of interventions. Further, at 1.7 years coronary CTA was associated with a 38% reduction in fatal and nonfatal MI (26 vs. 42; HR: 0.62; 95% CI: 0.38 to 1.01; p = 0.053), which is consistent with findings in the CATCH trial (23). In the PROMISE trial examination of

patients with either coronary CTA or functional testing (SPECT in 67%) did not result in any difference of the primary composite endpoint (24). The risk of death or nonfatal MI was, however, reduced in the coronary CTA-group at 1 year. In addition coronary CTA resulted in more revascularizations and less redundant ICAs, which was confirmed in our trial where 29% had a normal ICA after coronary CTA, compared to 64% after standard care. Concerning a slightly different patient population the CATCH trial therefore confirms these findings and adds incremental knowledge of the potential clinical benefit of coronary CTA.

CLINICAL IMPLICATIONS. According to the most recent guidelines provided by the American College of Cardiology Foundation/American Heart Association (ACCF/AHA) Task Force and the European Society of Cardiology (ESC), patients with low-risk UAP can be managed safely in an outpatient setting (10,11). Most patients arriving in U.S. emergency department have diagnostic testing performed before discharge from the hospital, which is partly related to concerns about losing the patients to follow-up, which was supported by Poon et al. (25), who found that only 21% of their patients received an out-patient stress test within the follow-up period. In Scandinavian countries, it is a common strategy to perform diagnostic evaluation in an outpatient setting to reduce the costs of acute imaging. Patient compliance for this strategy is usually high, as in our study, where 98% of patients in the standard care group underwent out-patient testing. A primary event occurred before outpatient testing in 3 patients (0.5%), suggesting that this strategy was acceptable with regard to safety. In the ACCF/AHA guidelines, diagnostic evaluation by exercise ECG and SPECT has Class 1 recommendation in patients with intermediate pre-test probability (PTP) and intermediate to high PTP, respectively. In contrast coronary CTA has only Class 2a recommendation. This is also consistent with the recently published ACCF/AHA multimodality appropriate use criteria for the detection and risk assessment of stable CAD in which exercise ECG is appropriate in patients with the ability to exercise and low or intermediate risk, whereas coronary CTA is rated appropriate only in intermediate risk patients with uninterpretable ECG or inability to exercise (26). In the ESC guidelines concerning patients with stable CAD, coronary CTA examination is recommended in patients with a 15% to 50% PTP of CAD, whereas exercise ECG was indicated in patients with a PTP between 15% and 65% and SPECT for the intermediate risk group (PTP of 15% to 85%). In the CATCH trial, most patients had a PTP within the low to intermediate range, and we find it important to underline that in the subgroup of patients with a PTP in the intermediate range (15% to 85%), we found a significant reduction in MACE with a coronary CTA-guided strategy compared to a strategy of standard functional testing. Our findings contribute further to the understanding of how a broader implementation of a coronary CTA-guided strategy in clinical practice could improve patient management.

STUDY LIMITATIONS. The observed clinical event rate in the standard care group was lower than anticipated. Although, it was possible to detect a significant difference in primary outcome, our findings should be confirmed in large-scale randomized trials and meta-analyses. Patients and clinical staff were blinded for group allocation until the index tests were performed, but it was not possible to blind the treating physicians during the follow-up period. Medical treatment and decision to refer patients for post-index noninvasive and/or invasive tests was left to the referring physician and therefore could not be controlled by the investigators. In the coronary CTA-guided group, we used a pragmatic approach in which a functional stress test was included as a diagnostic tool in cases of nondiagnostic coronary CTA images or in cases of borderline coronary artery stenosis. This design excluded the possibility to conclude how coronary CTA alone would influence clinical outcome, and moreover it did not allow direct methodological head to head comparisons between coronary CTA and SPECT.

CONCLUSIONS

This randomized controlled trial concerning patients hospitalized under the suspicion of ACS, who turned out to have normal ECG and plasma troponin values, suggests that a coronary CTA-guided strategy improves long-term clinical outcome, compared to standard care with functional tests.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Among patients hospitalized for acute chest pain, who have normal concentrations of plasma troponins and series of electrocardiograms without signs of ischemia (low-risk unstable angina), an out-patient coronary CTA-guided diagnostic evaluation strategy appears to improve the long-term clinical outcome, compared to standard evaluation with a functional test.

TRANSLATIONAL OUTLOOK: Previous randomized trials on the clinical implementation of coronary CTA have focused on logistical, safety and economic aspects of patient management in the emergency department. The CATCH trial monitored long-term clinical outcome and therefore adds incremental evidence of a beneficial clinical value for patients with chest pain undergoing first line diagnostic evaluation with coronary CTA. However, because the patient population studied in the CATCH trial was evaluated in a post-discharge outpatient setting, the long-term clinical value of early triage with coronary CTA in the ED should be investigated in other randomized studies.

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APPENDIX For supplemental tables and additional references, please see the online version of this article.