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Prognostic Value of Coronary CT Angiography in Patients With Non–ST-Segment Elevation Acute Coronary Syndromes

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ABSTRACT

BACKGROUND Severity and extent of coronary artery disease (CAD) assessed by invasive coronary angiography (ICA) guide treatment and may predict clinical outcome in patients with non-ST-segment elevation acute coronary syndrome (NSTEACS).

OBJECTIVES This study tested the hypothesis that coronary computed tomography angiography (CTA) is equivalent to ICA for risk assessment in patients with NSTEACS.

METHODS The VERDICT (Very Early Versus Deferred Invasive Evaluation Using Computerized Tomography in Patients With Acute Coronary Syndromes) trial evaluated timing of treatment in relation to outcome in patients with NSTEACS and included a clinically blinded coronary CTA conducted prior to ICA. Severity of CAD was defined as obstructive (coronary stenosis ≥50%) or nonobstructive. Extent of CAD was defined as high risk (obstructive left main or proximal left anterior descending artery stenosis and/or multivessel disease) or non-high risk. The primary endpoint was a composite of all-cause death, nonfatal recurrent myocardial infarction, hospital admission for refractory myocardial ischemia, or heart failure.

RESULTS Coronary CTA and ICA were conducted in 978 patients. During a median follow-up time of 4.2 years (interquartile range: 2.7 to 5.5 years), the primary endpoint occurred in 208 patients (21.3%). The rate of the primary endpoint was up to 1.7-fold higher in patients with obstructive CAD compared with in patients with nonobstructive CAD as defined by coronary CTA (hazard ratio [HR]: 1.74; 95% confidence interval [CI]: 1.22 to 2.49; p = 0.002) or ICA (HR: 1.54; 95% CI: 1.13 to 2.11; p = 0.007). In patients with high-risk CAD, the rate of the primary endpoint was 1.5-fold higher compared with the rate in those with non-high-risk CAD as defined by coronary CTA (HR: 1.56; 95% CI: 1.18 to 2.07; p = 0.002). A similar trend was noted for ICA (HR: 1.28; 95% CI: 0.98 to 1.69; p = 0.07).

CONCLUSIONS Coronary CTA is equivalent to ICA for the assessment of long-term risk in patients with NSTEACS. (Very Early Versus Deferred Invasive Evaluation Using Computerized Tomography in Patients With Acute Coronary Syndromes [VERDICT]; NCT02061891) (J Am Coll Cardiol 2021;77:1044–52) © 2021 by the American College of Cardiology Foundation.

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In patients with non-ST-segment elevation acute coronary syndrome (NSTEACS) the recommendation of the current treatment guidelines is—on top of optimal medical therapy—to undertake an individualized, patient-level assessment of the risks and benefits of invasive coronary investigation and possible revascularization (1–3). Coronary pathology in patients with NSTEACS may range from structurally normal vessels, varying degrees of nonobstructive coronary artery disease (CAD), to extensive obstructive CAD affecting all major branches of the coronary tree. Therefore, the current primary diagnostic pathway for optimal management of patients with clinically confirmed NSTEACS is invasive coronary angiography (ICA). Severity of coronary pathology defined by nonobstructive versus obstructive disease and the extent of CAD in the vascular tree are considered important angiographic guides to the risk-benefit ratio of coronary revascularization and provides assessment of the overall long-term risk of patients with NSTEACS (4–6). Nevertheless, a routine invasive strategy is associated with an increased risk of bleeding and prolonged hospital stay and may not provide long-term benefits to all patients with NSTEACS (7).

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Coronary computed tomography angiography (CTA) has evolved as a logistically simple, accurate and low-risk noninvasive test primarily to rule out CAD (8). We recently reported data from the observational component of the VERDICT (Very Early Versus Deferred Invasive Evaluation Using Computerized Tomography in Patients With Acute Coronary Syndromes) trial, demonstrating that coronary CTA has a high diagnostic accuracy to rule out obstructive CAD in patients with NSTEACS (9). However, whether obstructive CAD and/or the extent of CAD as defined by coronary CTA in NSTEACS patients holds prognostic information similar to findings of ICA remains unknown. Therefore, in this work, we tested the hypothesis that coronary CTA is equivalent to ICA for risk assessment in patients with NSTEACS.

METHODS

STUDY DESIGN. The design of the VERDICT trial and the clinical characteristics of the included patient cohort has previously been reported (9,10). In brief, patients with NSTEACS were included from 9 hospitals in the Capital Region of Copenhagen, Denmark, and randomized to either an acute invasive strategy within 12 h or to a deferred invasive strategy within 48 to 72 h. Treatment strategy was defined as either optimal medical therapy or optimal medical therapy plus coronary revascularization based on ICA findings. In the observational component of the trial, prior to ICA, patients underwent a clinically blinded coronary CTA. Coronary CTA findings remained blinded throughout the entire study period. The trial was conducted as a pragmatic clinical study embedded in routine clinical practice and was approved by the Danish National Committee on Health Research Ethics (journal number H-4-2010-039) and the Danish Data Protection Agency and registered at ClinicalTrials.gov (NCT02061891).

PARTICIPANTS. Patients in whom ICA was deemed clinically indicated and logistically possible within 12 h from time of diagnosis were offered participation in the study. Inclusion criteria were age ≥18 years, clinical suspicion of NSTEACS, and ≥1 of the following high-risk criteria: 1) electrocardiographic (ECG) changes indicating new ischemia (new ST-segment depression, horizontal or downsloping ≥0.05 mV in 2 consecutive leads, and/or T-wave inversion >0.01 mV in 2 leads with prominent R-wave or R/S ratio >1); and 2) an increase in circulating troponin levels. Exclusion criteria were pregnancy; patient inability to understand the trial information; an indication for acute ICA; expected survival <1 year; or known intolerance to platelet inhibitors, heparin, or x-ray contrast, which could not be remedied medically. For coronary CTA, patients with previous coronary artery bypass graft, plasma creatinine >140 μmol/l, known atrial fibrillation, or

ABBREVIATIONS AND ACRONYMS

CAD = coronary artery disease

CI = confidence interval

CTA = computed tomography angiography

ECG = electrocardiography

HR = hazard ratio

ICA = invasive coronary angiography

NSTEACS = non-ST-segment elevation acute coronary syndrome

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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women <45 years of age were not considered eligible. All included patients provided written informed consent.

PROCEDURES. Coronary CTA. Image acquisition was performed using a 320 detector (Aquilion One, Vision Edition, Canon, Otawara, Japan) or a 64 detector (Brilliance, Phillips, Amsterdam, the Netherlands) CT scanner, as previously described (9).

Following completion of the trial, coronary CTA were visually assessed in a core lab by consensus reading between 2 expert coronary CTA readers (J.J.L. and K.F.K.) blinded to clinical data, ICA data, and randomization allocation, using an external work station (Vitrea 2, version 6.9, Vital Images Inc., Minnetonka, Minnesota) as previously described (9). Patients with a nondiagnostic scan were considered as coronary CTA-positive (obstructive and/or high-risk CAD).

Invasive coronary angiography. ICA was performed according to guidelines and clinical practice at the individual invasive center and assessment of coronary pathology was performed visually by the interventional cardiologist. Indication for coronary revascularization was decided based on ICA findings by the interventional cardiologist including a heart team conference when applicable.

Coronary angiography findings. Patients were categorized according to coronary CTA and ICA findings with regard to severity and extent of obstructive CAD. Severity of CAD in each patient was defined as either obstructive (≥1 coronary stenosis ≥50%) or nonobstructive (coronary stenosis <50%) as previously described (6). In this fashion, the patients were categorized both by coronary CTA (coronary $CTA_{obstructive}$ vs. coronary $CTA_{nonobstructive}$) and by ICA ($ICA_{obstructive}$ vs. $ICA_{nonobstructive}$). Extent of obstructive CAD (coronary stenosis ≥50%) was defined as being either high risk (left main stenosis, proximal left anterior descending artery stenosis, or multivessel disease) or non-high risk (all other patients) (11). Multivessel disease was defined as ≥1 obstructive coronary lesion in ≥2 main vascular territories (left anterior descending artery, circumflex artery, or right coronary artery). All patients were thus categorized both by coronary CTA (coronary $CTA_{high\ risk}$ vs. coronary $CTA_{non\text{-}high\ risk}$) and by ICA ($ICA_{high\ risk}$ vs. $ICA_{non\text{-}high\ risk}$).

STUDY OUTCOMES. Clinical outcomes were recorded from time of ICA and until all patients had been followed for ≥18 months after randomization. The primary endpoint was a composite of death from any cause, nonfatal recurrent myocardial infarction, hospital admission for refractory myocardial ischemia, or clinical heart failure, as previously described (10). Primary endpoints and its individual components were recorded by review of patients' electronic and hard copy medical files. Adjudication of events was performed by an event committee blinded to coronary CTA and ICA findings and index management strategy, respectively. In this work, patients with clinical events occurring before or between coronary CTA and ICA were excluded.

STATISTICAL ANALYSES. Continuous variables with normal distribution are presented as mean ± SD and compared using Student's *t*-test. Variables with non-normal distribution are presented as median (interquartile range) and compared using Mann-Whitney *U* test. Discrete variables are presented as n (%) and compared using Fisher exact test. For the outcome analysis, the intention-to-diagnose principle was used according to severity and extent of CAD as defined by coronary CTA or ICA. In the randomized component of the VERDICT trial, no significant difference in coronary CTA diagnostic accuracy or in clinical outcome was noted between patients undergoing very early versus standard treatment strategy. Therefore, clinical outcome data were analyzed for the entire study cohort. Time to first event outcomes are presented as cumulative incidence curves and compared with the log-rank test. Events associated with outcome were estimated using univariable Cox regression, and hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated. Proportional hazards assumptions were verified with Schoenfeld residuals. Statistical analyses were performed with R, version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Among patients included in the VERDICT trial, coronary CTA was performed in 1,023 patients, all of whom underwent ICA. Prior to, or between, coronary CTA and ICA, 45 patients experienced a primary endpoint and were excluded from further analysis. Clinical characteristics of included patients (n = 978) are given in **Table 1**. The median time interval between coronary CTA and ICA was 2 h.

With regard to CAD severity, coronary CTA identified 73.4% of the patients (718 of 978) as having obstructive CAD (coronary $CTA_{obstructive}$) as compared to 66.9% (654 of 978) by ICA ($ICA_{obstructive}$). Coronary CTA and ICA findings were concordant in 88.5% of all patients (Supplemental Table 1). Clinical characteristics as defined by severity of CAD are given in **Table 2**. Assessed by either coronary CTA or ICA, the

TABLE 1 Clinical Characteristics (N = 978)

Male	651 (66.6)
Age, yrs	61.6 ± 11.7
BMI, kg/m^2	26.9 ± 4.4
Diabetes	125 (12.8)
Previous smoking	349 (35.7)
Current smoking	331 (33.8)
Hypertension	458 (46.8)
Pulmonary disease	119 (12.2)
Previous stroke	73 (7.5)
History of CVD	223 (22.8)
History of valve disease	29 (3.0)
Previous AMI	136 (13.9)
Previous PCI	124 (12.7)
Ischemia in ECG	390 (40.0)
GRACE score ≥140	408 (42.4)
Increased troponins	756 (77.3)
Revascularization at index	501 (51.2)

Values are n (%) or mean ± SD.

AMI = acute myocardial infarction; BMI = body mass index; CVD = cardiovascular disease; ECG = electrocardiogram; GRACE = Global Registry of Acute Coronary Events; PCI = percutaneous coronary intervention.

obstructive CAD patient groups were more frequently men, slightly older, more frequently smokers, and more frequently with a history of previous percutaneous coronary intervention than were the corresponding nonobstructive CAD patient groups. Similarly, positive troponin and ischemic ECG changes at clinical presentation were more frequent in the obstructive CAD groups than in the corresponding nonobstructive CAD patient groups. Coronary revascularization at index were more frequently performed in patients with obstructive CAD.

With regard to extent of obstructive CAD, 51% of the patients (499 of 978) were by coronary CTA categorized to be in the $CTA_{high\ risk}$ group compared with 36.8% (360 of 978) by ICA in the $ICA_{high\ risk}$ group. Coronary CTA and ICA findings were concordant in 76.8% of all patients (Supplemental Table 2). Patient groups and clinical characteristics as defined by extent of obstructive CAD are given in **Table 3**. Assessed by either coronary CTA or ICA, the high-risk CAD patient groups, compared with the corresponding non-high-risk CAD patient groups, were more frequently men, slightly older, more frequently smokers, more frequently diabetics, with previous cardiovascular disease, and more frequently with a history of previous percutaneous coronary intervention. Similarly, positive troponins, ischemic ECG changes, and GRACE (Global Registry of Acute Coronary Events) score >140 at clinical presentation were more frequent in the high-risk CAD groups than in the corresponding non-high-risk CAD groups. Coronary revascularizations at index were more frequently performed in patients with high-risk CAD.

During a median follow-up time of 4.2 years (interquartile range: 2.8 to 5.5 years), 255 primary events occurred in 208 patients (21%). The primary endpoint and subcomponents in each of the groups as categorized by either coronary CTA or ICA are given in **Tables 2 and 3** (bottom). In patients who were concordant and nonconcordant by CTA and ICA, the primary endpoint is given in Supplemental Tables 3 and 4. Among patients nonconcordant with regard to severity of coronary CAD, frequency of the primary endpoint was not significantly different in either coronary CTA- or ICA-positive patients (Supplemental Table 3). Similar findings were noted regarding extent of coronary CAD (Supplemental Table 4).

The rate of the primary endpoints was 1.7-fold higher in patients with obstructive CAD than in those with non-obstructive CAD (HR: 1.74; 95% CI: 1.22 to 2.49; p = 0.002), when patients were grouped according to the coronary CTA extent of CAD. Similar findings were noted when patients were grouped according to ICA (HR: 1.54; 95% CI: 1.13 to 2.11; p = 0.007). In the subgroup of patients without increase in troponin, similar trends were noted (Supplemental Table 5). Cumulative incidence curves according to coronary CTA or ICA are given in the **Central Illustration** (top panels). HRs for individual components of the primary endpoint according to severity of CAD by coronary CTA and ICA are given in Supplemental Table 6. The increased risk of obstructive CAD was primarily related to development of refractory ischemia. Among patients with nonobstructive CAD by coronary CTA (n = 310), subsequent ICA did not identify patients at increased risk (HR: 1.66; 95% CI: 0.88 to 3.13; p = 0.117). Similarly, among patients with nonobstructive CAD by ICA (n = 324), coronary CTA did not identify patients at increased risk (HR: 1.66; 95% CI: 0.10 to 2.99; p = 0.09).

When patients were grouped according to the coronary CTA extent of obstructive CAD, the rate of the primary endpoint was almost 1.6-fold higher in patients with high-risk CAD than in those with non-high risk CAD (HR: 1.56; 95% CI: 1.18 to 2.07; p = 0.002). A similar trend was noted when patients were grouped according to ICA, but this did not reach statistical significance (HR: 1.28; 95% CI: 0.98 to 1.69; p = 0.07). In the subgroup of patients without increase in troponin, similar findings were noted (Supplemental Table 5). Cumulative incidence curves according to coronary CTA or ICA are given in the **Central Illustration**. HRs for individual components of the primary endpoint according to extent of

TABLE 2 Clinical Characteristics and Outcomes According to CAD Severity

	Coronary CTA			ICA		
	Nonobstructive (n = 260)	Obstructive (n = 718)	p Value	Nonobstructive (n = 324)	Obstructive (n = 654)	p Value
Clinical characteristics						
Male	113 (43.5)	538 (74.9)	<0.001	149 (46.0)	502 (76.8)	<0.001
Age, yrs	58.9 ± 12.1	62.6 ± 11.4	<0.001	60.1 ± 12.2	62.3 ± 11.3	0.006
BMI, kg/m^2	26.3 ± 4.4	27.0 ± 4.4	0.022	26.4 ± 4.7	27.1 ± 4.3	0.037
Diabetes	25 (9.6)	100 (13.9)	0.094	28 (8.6)	97 (14.8)	0.009
Previous smoking	98 (37.7)	251 (35.0)	0.476	123 (38.0)	226 (34.6)	0.329
Current smoking	60 (23.1)	271 (37.7)	<0.001	82 (25.3)	249 (38.1)	<0.001
Hypertension	105 (40.4)	353 (49.2)	0.018	137 (42.3)	321 (49.1)	0.053
Pulmonary disease	28 (10.8)	91 (12.7)	0.487	35 (10.8)	84 (12.8)	0.415
Previous stroke	24 (9.2)	49 (6.8)	0.260	29 (9.0)	44 (6.7)	0.265
History of CVD	44 (16.9)	179 (24.9)	0.011	65 (20.1)	158 (24.2)	0.175
History of valve disease	10 (3.8)	19 (2.6)	0.445	12 (3.7)	17 (2.6)	0.448
Previous AMI	20 (7.7)	116 (16.2)	0.001	37 (11.4)	99 (15.1)	0.138
Previous PCI	12 (4.6)	112 (15.6)	<0.001	28 (8.6)	96 (14.7)	0.010
Ischemia in ECG	93 (35.9)	297 (41.5)	0.684	120 (37.2)	270 (41.5)	0.220
GRACE score ≥140	78 (30.4)	330 (46.8)	0.131	110 (34.5)	298 (46.3)	0.001
Increased troponins	145 (56.0)	611 (85.1)	<0.001	194 (60.1)	562 (85.9)	<0.001
Revascularization at index	11 (4.2)	475 (66.2)	<0.001	4 (1.2)	482 (73.7)	<0.001
Clinical outcomes						
Primary endpoint	37 (14.2)	171 (23.8)	0.002	52 (16.0)	156 (23.9)	0.006
Death	20 (7.7)	71 (9.9)	0.358	30 (9.3)	61 (9.3)	1.000
Nonfatal AMI	13 (5.0)	58 (8.1)	0.134	20 (6.2)	51 (7.8)	0.429
Refractory ischemia	2 (0.8)	56 (7.8)	<0.001	4 (1.2)	54 (8.3)	<0.001
Heart failure admission	11 (4.2)	24 (3.3)	0.641	20 (3.2)	15 (4.2)	0.564

Values are n (%) or mean ± SD. Primary endpoint is a composite of death from any cause, nonfatal recurrent myocardial infarction, hospital admission for refractory myocardial ischemia, or clinical heart failure.

CAD = coronary artery disease; CTA = computed tomography angiography; ICA = invasive coronary angiography; other abbreviations as in Table 1.

obstructive CAD by coronary CTA and ICA are given in Supplemental Table 7. The increased risk of high-risk CAD according to CTA was primarily related to development of de novo myocardial infarction or refractory ischemia.

Among patients with non-high risk CAD by coronary CTA (n = 479), subsequent ICA did not identify patients at increased risk (HR: 1.60; 95% CI: 0.63 to 3.10; p = 0.167). In contrast, among patients with non-high risk CAD by ICA (n = 618), coronary CTA identified patients at increased risk (HR: 1.76; 95% CI: 1.23 to 2.53; p = 0.002).

DISCUSSION

In this work we found coronary CTA to be equivalent, but not identical, to ICA for the assessment of long-term risk in patients with NSTEACS. Overall, more patients with obstructive CAD were recorded when using coronary CTA than when using ICA. Nevertheless, we found that patients with ≥1 coronary artery stenosis ≥50% as defined by either coronary CTA or by ICA had an up to 1.7-fold higher risk of experiencing a major cardiovascular event than did patients with nonobstructive CAD, within a median time of 4.2 years after the index hospitalization. Importantly, subsequent ICA in patients with nonobstructive CAD by coronary CTA or vice versa did not provide further risk stratification.

Our findings are consistent with and further extend results from a recent meta-analysis including more than 120,000 patients with acute coronary syndrome (6). Obstructive CAD defined as coronary artery stenosis ≥50% assessed by ICA was found to be associated with significantly higher cardiovascular risk than was nonobstructive CAD. To our knowledge, our study is the first to compare the prognostic value of coronary CTA versus ICA in patients with NSTEACS undergoing both tests. Our findings suggest that coronary CTA has similar prognostic accuracy as ICA to identify patients with obstructive CAD associated with worsened clinical outcome. The prognostic value of coronary CTA has previously been assessed in patients with stable chest pain suspected of CAD,

TABLE 3 Clinical Characteristics and Outcomes According to Extent of Obstructive CAD

	Coronary CTA			ICA		
	Non-High Risk (n = 479)	High Risk (n = 499)	p Value	Non-High Risk (n = 618)	High Risk (n = 360)	p Value
Clinical characteristics						
Male	270 (56.4)	381 (76.4)	<0.001	367 (59.4)	284 (78.9)	<0.001
Age, yrs	59.9 ± 11.9	63.2 ± 11.3	<0.001	60.0 ± 11.8	64.2 ± 11.0	<0.001
BMI, kg/m^2	26.4 ± 4.3	27.3 ± 4.5	0.003	26.8 ± 4.6	27.0 ± 4.1	0.611
Diabetes	47 (9.8)	78 (15.6)	0.009	66 (10.7)	59 (16.4)	0.013
Previous smoking	173 (36.1)	176 (35.3)	0.834	227 (36.7)	122 (33.9)	0.409
Current smoking	144 (30.1)	187 (37.5)	0.017	196 (31.7)	135 (37.5)	0.076
Hypertension	209 (43.6)	249 (49.9)	0.058	275 (44.5)	183 (50.8)	0.065
Pulmonary disease	58 (12.1)	61 (12.2)	1.000	70 (11.3)	49 (13.6)	0.341
Previous stroke	37 (7.7)	36 (7.2)	0.856	40 (6.5)	33 (9.2)	0.156
History of CVD	89 (18.6)	134 (26.9)	0.003	128 (20.7)	95 (26.4)	0.050
History of valve disease	14 (2.9)	15 (3.0)	1.000	20 (3.2)	9 (2.5)	0.646
Previous AMI	46 (9.6)	90 (18.0)	<0.001	73 (11.8)	63 (17.5)	0.017
Previous PCI	36 (7.5)	88 (17.6)	<0.001	67 (10.8)	57 (15.8)	0.031
Ischemia in ECG	168 (35.2)	222 (44.7)	0.003	227 (36.9)	163 (45.4)	0.011
GRACE score ≥140	167 (35.2)	241 (49.5)	<0.001	224 (36.7)	184 (52.3)	<0.001
Increased troponins	329 (68.8)	427 (85.6)	<0.001	444 (72.0)	312 (86.7)	<0.001
Revascularization at index	177 (37.0)	309 (61.9)	<0.001	260 (42.1)	226 (62.8)	<0.001
Clinical outcomes						
Primary endpoint	81 (16.9)	127 (25.5)	0.001	121 (19.6)	87 (24.2)	0.107
Death	36 (7.5)	55 (11.0)	0.076	50 (8.1)	41 (11.4)	0.110
Nonfatal AMI	27 (5.6)	44 (8.8)	0.073	46 (7.4)	25 (6.9)	0.871
Refractory ischemia	21 (4.4)	37 (7.4)	0.061	31 (5.0)	27 (7.5)	0.148
Heart failure admission	13 (2.7)	22 (4.4)	0.210	20 (3.2)	15 (4.2)	0.564

Values are n (%) or mean ± SD. Primary endpoint is a composite of death from any cause, nonfatal recurrent myocardial infarction, hospital admission for refractory myocardial ischemia, or clinical heart failure.

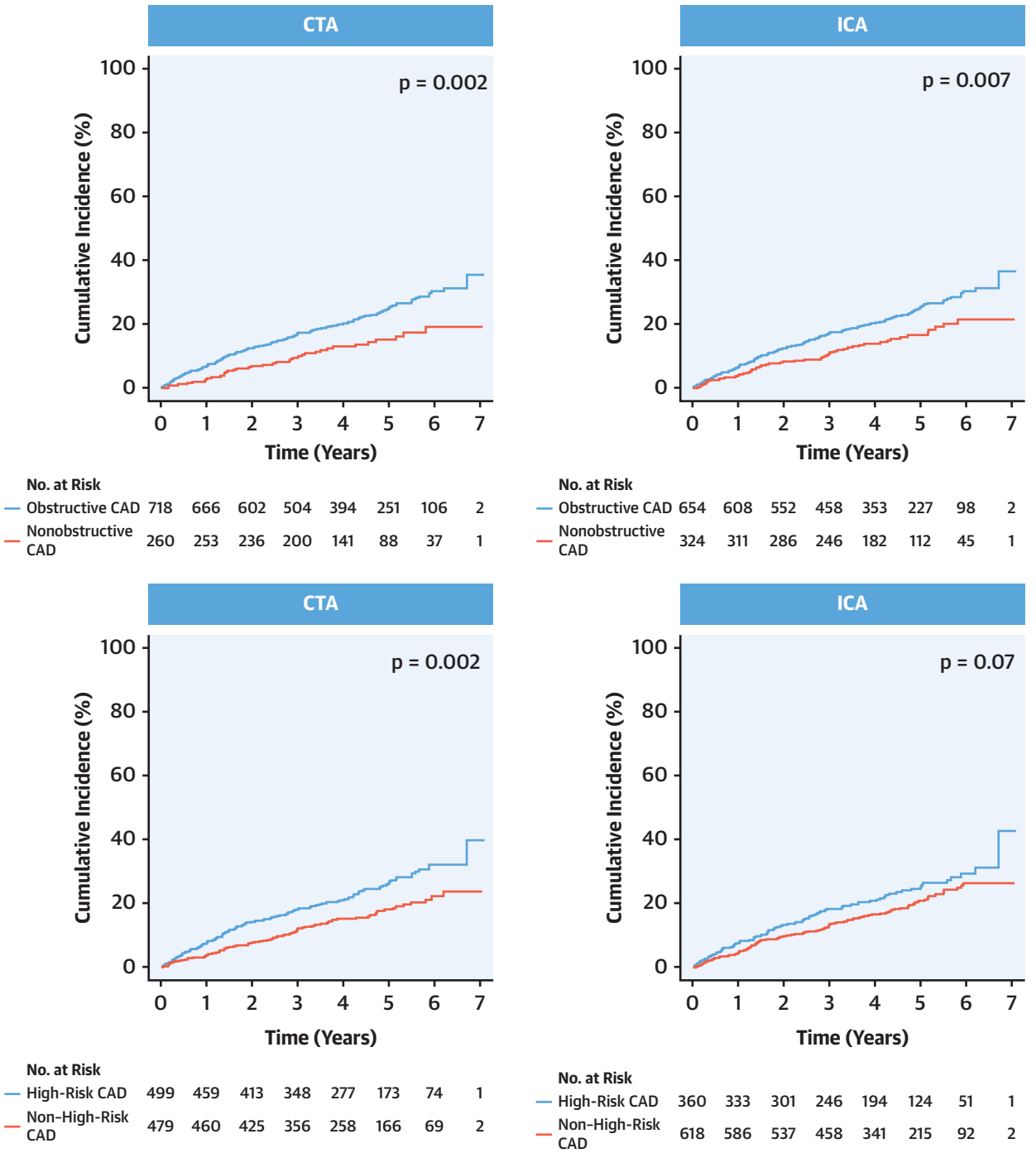
Abbreviations as in Tables 1 and 2.

yet not in patients also undergoing ICA (12–14). These studies demonstrated that patients with obstructive CAD as determined by coronary CTA had poorer prognosis than did patients with nonobstructive disease.

The presence of left main, proximal left anterior descending artery stenosis, and/or multivessel disease as defined by coronary CTA was associated with an elevated risk of cardiovascular events than was less extensive CAD. A nominally increased risk in patients with extensive, high-risk angiographic findings according to ICA was also observed, but this finding only reached borderline significance. The explanation for this apparent difference between coronary CTA and ICA is unknown. Coronary CTA identified more patients as having high-risk CAD than ICA, which is consistent with our previous finding of a decreased specificity of coronary CTA when ICA was the reference method (9). Possibly more atherosclerotic burden may be detected by coronary CTA than ICA. Furthermore, whereas the extent of CAD by ICA was determined during the invasive procedure to decide on treatment strategy, coronary CTA was evaluated while clinically blinded without the connotation of subsequent treatment implications. It could be speculated that this difference in analytic setting might have influenced the assessment of CAD extent, thus contributing to the potentially discordant findings. Interestingly, data from the ACSIS (Acute Coronary Syndrome Israeli Survey) also found that extensive high-risk CAD in patients with NSTEACS as defined by ICA was associated with an elevated cardiovascular risk (11). Overall, our findings support the notion that in patients with NSTEACS coronary CTA is as least as good as ICA for the prediction of clinical outcome based on either the severity and/or the extent of CAD.

In patients suspected of having NSTEACS, the clinical relevance of coronary angiography is to confirm the diagnosis of NSTEACS related to obstructive epicardial CAD, establish whether coronary revascularization is indicated, and assess the contribution of CAD to short- and long-term risk of the patient (1,2). We previously demonstrated in the VERDICT trial that coronary CTA has a high diagnostic accuracy to rule out obstructive CAD in

CENTRAL ILLUSTRATION **Time-to-Event Curves for the Combined Primary Endpoint**



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The time-to-event curves show the severity of coronary artery disease (CAD) **(top)** and the extent of obstructive CAD **(bottom)**. The combined primary endpoint is all-cause death, nonfatal recurrent myocardial infarction, hospital admission for refractory myocardial ischemia, or hospital admission for heart failure. Obstructive CAD is defined as having ≥1 coronary stenosis ≥50% and nonobstructive CAD as having coronary stenosis <50%. High-risk CAD group includes patients with left main stenosis, proximal left anterior descending artery stenosis, or multivessel disease; whereas non-high-risk CAD encompasses all other patients. CTA = coronary computed tomography angiography; ICA = invasive coronary angiography.

patients with NSTEACS (9). We found that compared with patients with obstructive CAD, patients with nonobstructive disease identified by coronary CTA had substantially lower rates of subsequent cardiovascular events. These findings appear to support that coronary CTA could be used to identify patients with NSTEACS in whom it would be safe to treat medically alone, without performing ICA. Interestingly, during the ongoing coronavirus disease 2019 pandemic such coronary CTA-guided management is recommended by the European Society of Cardiology in hemodynamically stable patients with NSTEACS without ongoing dynamic ECG changes and/or recurrent symptoms (15).

In accordance with previous studies, we found that the cardiovascular risk in patients with nonobstructive CAD as defined by coronary CTA was not negligible (6). As demonstrated in the PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) trial, major adverse cardiovascular events after acute coronary syndrome may frequently be attributable to lesions that were nonobstructive at the index ICA (16). These and our present findings highlight the importance of treatment beyond coronary revascularization in patients with NSTEACS to reduce long-term risk, such as cardiovascular rehabilitation and optimized medical treatment. Extensive high-risk CAD as defined by coronary CTA was associated with an almost 10% higher absolute event rate compared with the event rate for less extensive obstructive CAD. In this context, it should be noted that all VERDICT patients underwent ICA-guided coronary revascularization including heart team–defined referral to coronary artery bypass graft according to contemporary guidelines. The landmark FRISC-II (FRagmin and Fast Revascularisation During Instability in Coronary Artery Disease II) trial published 20 years ago documented that a routine invasive treatment strategy conveyed a reduced mortality, which most likely was mediated by revascularization of patients with left main stem and/or multivessel disease (17,18). In high-risk NSTEACS patients, further improvements of treatment algorithms are urgently needed, and our results suggest that strategies that could include first-line coronary CTA warrant further study.

STUDY LIMITATIONS. The limitations of the VERDICT trial related to coronary CTA have previously been described (9). In brief, patients with impaired renal function, known atrial fibrillation, previous coronary artery bypass graft, and women <45 years of age were not included in the study; not all patients of the VERDICT cohort underwent coronary CTA; and functional assessment of coronary artery stenosis hemodynamic significance using invasive or noninvasive fractional flow reserve was not systematically conducted. Our results should therefore be interpreted accordingly. Stenosis severity was graded visually in clinically relevant intervals. Grading of stenoses using quantitative coronary angiography and a continuous scale could potentially have increased the associations between outcome and ICA or CTA. Furthermore, coronary plaque morphology analysis by invasive intracoronary techniques such as intravascular ultrasound, optical coherence tomography, and near-infrared spectroscopy or quantitative coronary CTA analysis including vascular calcification, plaque volume, or high-risk plaque features, which may have prognostic implications, was not performed (19,20). However, at the current time, the clinical relevance of coronary plaque morphology remains unclear and such investigations were outside the scope of the present work. Lastly, the primary endpoint was a composite of both severe and less severe clinical events and sample size precluded analysis of individual components.

CONCLUSIONS

Severity and extent of CAD as defined by coronary CTA are equivalent to corresponding measures defined by ICA for the assessment of long-term risk in patients with NSTEACS.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: Coronary CTA is an alternative to invasive, catheter-based coronary angiography for risk assessment in patients with NSTEACS and identifies those with nonobstructive coronary disease who can forego invasive angiography.

TRANSLATIONAL OUTLOOK: Randomized trials are needed to define patterns of CAD identified by CTA in patients with NSTEACS for which revascularization improves clinical outcomes.

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KEY WORDS acute coronary syndrome, angiography, cardiac computed tomography, risk stratification, prognosis

APPENDIX For supplemental tables, please see the online version of this paper.