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Prognostic Value of Coronary CTA in Coronary Bypass Patients

A Long-Term Follow-Up Study

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OBJECTIVES The goal of this study was to determine the long-term prognostic value of coronary computed tomography angiography (CTA) in a large coronary artery bypass graft (CABG) population.

BACKGROUND Coronary CTA has shown prognostic utility in patients without previous revascularization. However, prognostication with coronary CTA in CABG patients has not been fully assessed.

METHODS Between March 2005 and April 2009, 887 consecutive CABG patients (mean age 66.8 ± 8.4 years) were considered for the inclusion in the study. Patients were classified by the number of unprotected coronary territories (UCTs) and a summary of native vessel disease and graft patency: the coronary artery protection score (CAPS). A primary endpoint (cardiovascular [CV] death, nonfatal myocardial infarction [MI]) and a secondary combined adverse events endpoint (CV death, MI, unstable angina, and late revascularizations) were recorded.

RESULTS Among the 887 evaluated, 166 did not meet the inclusion criteria. The final study population consisted of 721 subjects. Ten patients were excluded for unevaluable coronary CTA images. Of the remaining 711 patients, follow-up (mean 73.5 ± 14 months) was obtained in 698. Three hundred forty-seven events were recorded. By univariable analysis, the strongest coronary CTA predictors of events were UCT 2 and 3 (hazard ratio [HR] for CV death/MI: 7.5 and 10.19, $p < 0.0001$ and $p < 0.0003$, respectively) and CAPS 4 (HR for CV death/MI: 24.1, $p < 0.0001$). A high number of UCTs was also a strong multivariable independent predictor of CV death/MI (HR: 7.78 and 10.18 for UCT 2 and 3, $p < 0.0001$ and $p < 0.0007$, respectively). Cumulative survival rates for CV death/MI and composite adverse CV events were 86% and 73% with UCT 0, 84% and 49% with UCT 1, 53% and 3% with UCT 2, and 29% and 0% with UCT 3, respectively.

CONCLUSIONS Coronary CTA appears to be a promising tool for long-term risk stratification of CABG patients. The UCT score has significant prognostic value to predict CV deaths/MI. (J Am Coll Cardiol Img 2014;7:580–9) © 2014 by the American College of Cardiology Foundation

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Coronary computed tomography angiography (CTA) is a noninvasive diagnostic tool useful for the detection of obstructive coronary artery disease (CAD) and assessment of coronary artery bypass grafts (CABG) (1–3). The method demonstrated significant prognostic value in patients with suspected CAD, predicting all-cause mortality and major adverse cardiac events (4–6). However, the prognostic utility of coronary CTA in CABG patients has been investigated by

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2 studies only, both with a follow-up no longer than 20 months, and in 1 case, enrolling a relatively small (250 patients) population. Nevertheless, they suggested that anatomic data provided by coronary CTA may help in determining the prognosis of patients after CABG (7,8). Indeed, previous studies using invasive coronary angiography (ICA) demonstrated that the completeness of revascularization is an important predictor of outcome and that the number of diseased arterial territories lacking a patent graft is a key determinant of mortality (9). Therefore, the objective of the present study was to evaluate the incremental prognostic value of coronary CTA in a large population of CABG patients undergoing long-term follow-up.

METHODS

Patient population. Between March 2005 and April 2009, 887 consecutive patients with a history of previous CABG undergoing coronary CTA were prospectively enrolled in our study. Indications for coronary CTA were chest pain, dyspnea, and equivocal or abnormal stress test. One-hundred forty-five patients were excluded because of abnormal (<55%) left ventricular ejection fraction (n = 30), prior PCI/stent procedure (n = 95), or significant valve disease (n = 20). Moreover, a total of 21 patients were excluded because of contraindications to contrast agents (n = 5), impaired renal function (creatinine clearance <60 ml/min) (n = 8), inability to sustain a 15-s breath hold (n = 3), and arrhythmias (n = 5). Thus, the study population consisted of 721 subjects. The mean time between previous CABG and coronary CTA investigation was 72 ± 41 months (range 21 to 139 months, median 61.9 months). The study was approved by our institution's scientific and ethical committees, and all patients gave written informed consent. A structured interview and a detailed medical history were acquired at the time of coronary CTA.

Coronary CTA scan protocol, image reconstruction, and patient preparation. Metoprolol was administered intravenously before coronary CTA with a titration dose up to 25 mg in patients with heart rate >65 beats/min. In all patients, coronary CTA was performed using a 64-slice scanner (LightSpeed VCT Medical System, GE Healthcare, Milwaukee, Wisconsin) (64 × 0.625-mm collimation, 330-ms gantry rotation time). Dose modulation was attained with electrocardiographic (ECG) gating for a maximum gantry delivery between 40% and 80% during the R-R interval. A bolus of 80 to 110 ml of high-concentration contrast (Iomeron 400 mg/ml, Bracco, Milan, Italy) was administered intravenously at 5 ml/s, followed by 50 ml of saline injected at the same infusion rate. The scan was initiated according to the bolus-tracking technique. Image datasets were analyzed using multiplanar reconstruction on post-processing workstations (CardioQ3 package, Advantage Workstation version 4.2, GE Healthcare).

Coronary CTA data analysis. All coronary CTA examinations were evaluated by 2 expert readers unaware of patient clinical data. In case of disagreement, a joint reading was performed, and a consensus decision was reached. Revascularizations were classified in terms of the coronary territories supplied by grafts (left anterior descending coronary artery [LAD], left circumflex coronary artery [LCx], or right coronary artery). Two models of CAD severity were used to assess coronary CTA prognostic value: unprotected coronary territories (UCTs) and coronary artery protection score (CAPS). The UCTs categorized patients according to the number of vascular territories that were not protected by grafts (0, 1, 2, or 3) (9). In each patient, 3 coronary territories, corresponding to the 3 major epicardial coronary arteries (LAD, LCx, right coronary artery), and their corresponding branches (diagonal and marginal arteries) were evaluated. Patients with obstructive CAD in the diagonal or obtuse marginal branches were included in the LAD and LCx obstructive CAD groups, respectively. A coronary territory was deemed unprotected if: 1) an ungrafted native coronary artery had a significant stenosis; 2) a significant stenosis in the native artery was distal to the graft insertion; or 3) significant

ABBREVIATIONS AND ACRONYMS

AUC = area under the curve
CABG = coronary artery bypass grafts
CAD = coronary artery disease
CAPS = coronary artery protection score
CTA = computed tomography angiography
CV = cardiovascular
ECG = electrocardiography
HR = hazard ratio
ICA = invasive coronary angiography
LAD = left anterior descending coronary artery
LCx = left circumflex coronary artery
MI = myocardial infarction
NRI = net reclassification improvement
UCT = unprotected coronary territory

stenoses were present in both the native artery and its graft (9). The left main coronary artery was assigned 2 or 3 coronary territories in a right-dominant or left-dominant coronary system, respectively. Similarly, the LCx was assigned 2 coronary territories when the native coronary system was left dominant. The CAPS combined the severity of both native coronary and graft disease (CAPS 1: single-vessel disease ± 1 protected territory; CAPS 2: 2-vessel disease + 2 protected territories; CAPS 3: 2-vessel disease + 1 protected territory; CAPS 4: 2-vessel disease + 0 protected territories; CAPS 5: 3-vessel disease + 3 protected territories; CAPS 6: 3-vessel disease + 2 protected territories; CAPS 7: 3-vessel disease + 1 protected territory; and CAPS 8: 3-vessel disease + 0 protected territories) (9). We have grouped CAPS into 4 categories because it seemed some groups had too few events: CAPS 1, which includes CAPS 1 and 2; CAPS 2, which includes CAPS 3 and 4; CAPS 3, which includes CAPS 5 and 6; and CAPS 4, which includes CAPS 7 and 8.

Follow-up. The follow-up was performed either by clinical visit or telephone interview by researchers blinded to coronary CTA and clinical data. Hospital records were screened for clinical events to confirm the obtained information. Outcome measures were a primary endpoint including cardiovascular (CV) death and nonfatal myocardial infarction (MI), and a secondary combined adverse events endpoint (CV death, nonfatal MI, unstable angina requiring hospitalization, and revascularization). The diagnosis of nonfatal MI was based on the simultaneous presence of all these criteria: typical chest pain, elevated cardiac enzymes, and typical ECG changes (10). Unstable angina was defined as acute chest pain with or without the presence of ECG abnormalities and no cardiac enzyme elevation (11). All deaths were reviewed and classified as cardiac (death caused by acute MI, ventricular arrhythmias, or refractory heart failure) or noncardiac. All revascularizations were classified as early (elective revascularization within 6 months after coronary CTA) or late. Only late revascularizations were considered as cardiac events, whereas patients with elective early revascularization were excluded from analysis.

Statistical analysis. Statistical analysis was performed using SAS (version 9.1.3, SAS Institute, Cary, North Carolina) and SPSS version 13.0 software (SPSS, Chicago, Illinois). Statistical significance was defined as $p < 0.05$. Continuous variables are presented as mean ± SD, and discrete variables as absolute numbers and percentages. To compare patient characteristics and coronary CTA data, chi-square or Fisher exact tests were used for categorical variables, and Student *t* test for continuous variables. All continuous variables were normally distributed and compared using nonparametric Mann-Whitney test. To identify the association between coronary CTA variables and outcomes, Cox regression analysis was used. First, univariable analysis of clinical characteristics and coronary CTA variables was performed to identify potential predictors. Hazard ratios (HR) were calculated with 95% confidence intervals as an estimate of the risk associated with a particular variable. To determine independent predictors of the composite endpoints, multivariable analysis of coronary CTA variables with $p \leq 0.05$ in univariable analysis was performed, which was corrected for baseline characteristics (male sex, age, CV risk factors). We developed 2 different multivariable models for CV death/MI and combined adverse CV events to reduce bias introduced by events such as angina or revascularization. The first model was adjusted for UCTs and clinical baseline characteristics. The second model was adjusted for CAPS and clinical baseline characteristics. Cumulative event-free survival rates as a function over time were obtained by Kaplan-Meier method. Event-free survival curves for CV death/MI and composite adverse CV events were compared using the log-rank test. Area under the receiver-operating characteristic curve (AUC), net reclassification improvement (NRI), and integrated discrimination improvement were used to assess the incremental prognostic value of coronary CTA among post-CABG patients. Moreover, we analyzed the improvement of the model related to UCT or CAPS, respectively.

RESULTS

Of the 887 patients prospectively enrolled, 166 were excluded because they did not meet the inclusion criteria. Others (10 patients) were excluded because coronary CTA images were not assessable. Of the remaining 711 patients, 13 were lost to follow-up, whereas 698 (98%) had a complete follow-up (mean 73.5 ± 14 months, up to 87 months). In them, indications for coronary CTA were chest pain (24%), dyspnea (29%), and equivocal or abnormal stress test (47%). In all patients, left ventricular ejection fraction was ≥55%. There was no significant difference in clinical characteristics and coronary CTA results between patients who underwent long-term follow-up and those lost to follow-up. Three hundred forty-seven cardiac events were recorded. Of them, 49 were CV deaths, 67 nonfatal

Table 1. Clinical Characteristics of the Study Population, Coronary CTA Results, and Patient Clinical Outcome

	All Patients (N = 698)	Patients With Combined Adverse CV Events (n = 316)	Patients Without Combined Adverse CV Events (n = 382)	Patients With CV Death/MI (n = 72)	Patients Without CV Death/MI (n = 626)
Clinical characteristics					
Age	67 ± 8	67 ± 8	66 ± 8	67 ± 9	67 ± 8
Male	577 (83)	262 (83)	315 (83)	63 (87)	514 (82)
BMI, kg/m^2	27.2 ± 5.2	28.1 ± 5.6	26.7 ± 5	27.7 ± 5.5	27.1 ± 4.8
Hypercholesterolemia	445 (65)	220 (71)	225 (60)*	45 (62)	400 (64)
Hypertension	518 (75)	239 (77)	279 (75)	147 (77)	371 (75)
Family history of CAD	155 (23)	61 (20)	94 (25)	10 (14)	145 (23)†
Diabetes	174 (25)	90 (29)	84 (22)*	21 (29)	153 (24)
Smoking	211 (31)	88 (29)	123 (33)	16 (22)	195 (31)†
Positive stress test	329 (47)	173 (25)	156 (22)	64 (89)	265 (42)
Medical therapy					
Nitrates	318 (47)	178 (59)	140 (38)*	45 (62)	273 (44)†
Beta-blockers	484 (71)	216 (71)	268 (72)	54 (75)	430 (69)
Aspirin	627 (93)	286 (94)	341 (91)	64 (89)	563 (90)†
Calcium channel blockers	187 (28)	83 (27)	104 (28)	11 (15)	176 (28)†
ACE-inhibitors	299 (44)	137 (45)	162 (43)	36 (50)	263 (42)
AT1 blockers	100 (15)	49 (16)	51 (14)	15 (21)	85 (13)
Diuretics	180 (27)	99 (33)	81 (22)*	32 (44)	148 (24)†
Amiodarone	56 (8)	27 (9)	29 (8)	8 (11)	48 (8)
Statins	448 (66)	203 (67)	245 (66)	40 (55)	408 (66)†
UCT					
0	299 (43)	68 (21)	231 (60)*	13 (18)	286 (45)†
1	294 (42)	150 (47)	144 (38)	26 (36)	268 (43)
2	93 (13)	86 (27)	7 (2)	26 (36)	67 (11)
3	12 (2)	12 (4)	0 (0)	11 (15)	1 (1)
CAPS					
1	169 (24)	25 (8)	144 (38)*	2 (3)	167 (27)†
2	92 (13)	62 (20)	30 (8)*	8 (11)	84 (13)
3	338 (48)	138 (43)	200 (53)*	30 (41)	308 (49)
4	99 (15)	91 (29)	8 (2)*	32 (44)	67 (11)

Values are mean ± SD or n (%). *$p < 0.05$ versus patients with events. †$p < 0.05$ versus patients with hard events.
ACE = angiotensin-converting enzyme; AT1 = angiotensin 1 receptor; BMI = body mass index; CAD = coronary artery disease; CAPS = coronary artery protection score; CTA = computed tomography angiography; CV = cardiovascular; MI = myocardial infarction; UCT = unprotected coronary territory.

Table 2. Coronary CTA Evaluation of CABG Patency

Type of Graft	Patent	Stenosis ≤50%	Stenosis >50%	Occlusion	Total
Right-IMA	62 (74.0)	2 (2.0)	0 (0.0)	20 (24.0)	84
Left-IMA	594 (91.0)	1 (0.2)	5 (0.8)	54 (8.0)	654
Radial artery	28 (62.0)	3 (7.0)	2 (4.0)	12 (27.0)	45
Vein graft	565 (63.0)	41 (5.0)	72 (8.0)	218 (24.0)	896
Total	1,249 (74.0)	47 (3.0)	79 (5.0)	304 (18.0)	1,679

Values are n (%) or n.
CABG = coronary artery bypass graft; IMA = internal mammary artery.

Table 3. Clinical and Coronary CTA Univariable Predictors of Events

	Combined Adverse CV Events HR (95% CI)	p Value	CV Death/MI HR (95% CI)	p Value
Clinical characteristics				
Age	1.00 (0.99–1.02)	0.33	1.06 (1.03–1.10)	<0.0001†
Male	1.01 (0.75–1.36)	0.91	1.44 (0.71–2.89)	0.30
BMI	1.02 (1.01–1.03)	0.23	1.05 (1.01–1.08)	0.12
Hypercholesterolemia	1.47 (1.15–1.88)	0.0018*	1.13 (0.68–1.88)	0.63
Hypertension	1.19 (0.92–1.55)	0.18	1.34 (0.74–2.42)	0.32
Family history of CAD	0.78 (0.59–1.03)	0.08	0.55 (0.28–1.08)	0.08
Diabetes	1.29 (1.01–1.65)	0.03	1.35 (0.80–2.26)	0.25
Smoking	0.79 (0.61–1.01)	0.06	0.59 (0.33–1.04)	0.06
Positive stress test	1.74 (1.04–2.91)	0.03	2.43 (0.97–6.11)	0.05
Medical therapy				
Nitrates	1.86 (1.48–2.34)	<0.0001*	2.61 (1.57–4.36)	0.0002†
Beta-blockers	0.99 (0.77–1.26)	0.92	1.63 (0.89–2.98)	0.11
Aspirin	1.47 (0.90–2.40)	0.11	2.08 (0.65–6.65)	0.21
Calcium channel blockers	0.97 (0.75–1.25)	0.82	0.46 (0.24–0.88)	0.01
ACE-inhibitors	1.05 (0.84–1.32)	0.64	1.28 (0.96–1.71)	0.08
AT1 blockers	1.20 (0.89–1.64)	0.22	1.57 (0.97–2.54)	0.06
Diuretics	1.50 (1.18–1.91)	0.0009*	2.75 (1.70–4.45)	<0.0001†
Amiodarone	1.19 (0.80–1.76)	0.38	1.48 (0.70–3.10)	0.29
Statins	1.03 (0.81–1.31)	0.76	0.71 (0.43–1.16)	0.17
UCT				
0	1.00		1.00	
1	2.75 (2.06–3.66)	<0.0001*	1.24 (0.65–2.35)	0.51
2	8.39 (6.07–11.61)	<0.0001*	7.58 (4.02–14.30)	<0.0001†
3	8.47 (4.57–15.70)	<0.0001*	10.19 (2.9–35.43)	0.0003†
CAPS				
1	1.00		1.00	
2	6.77 (4.7–10.8)	<0.0001*	3.71 (1.11–12.36)	0.03
3	3.09 (2.01–4.73)	<0.0001*	3.76 (1.31–10.76)	0.01
4	12.6 (8.1–19.8)	<0.0001*	24.12 (8.35–69.65)	<0.0001†

*p < 0.05 versus patients with combined adverse CV events. †p < 0.05 versus patients with CV death/MI.
CI = confidence interval; HR = hazard ratio; other abbreviations as in Table 1.

MI, 124 unstable angina, and 76 were late revascularizations. Thirty-one patients with early elective revascularizations were excluded from event-free survival analysis.

Clinical and coronary CTA data. Table 1 shows clinical characteristics, coronary CTA results, and patient outcomes. Prevalence of dyslipidemia and diabetes was significantly higher in patients with events than in those without events. The rate of events progressively increased with increasing UCT score. Particularly, 100% of patients with UCT 3 had events (with a 99% rate of CV death/MI). Table 2 shows the coronary CTA evaluation of CABG patency. Notably, 595 of 654 (91%) left internal mammary arteries were free from significant stenosis, whereas 8% and 24% of saphenous vein grafts showed >50% stenosis or occlusion, respectively.

Univariable predictors of events. Clinical and coronary CTA univariable predictors of events are reported in Table 3. Significant clinical predictors of events were dyslipidemia and diabetes for combined adverse CV events, and age, family history of CAD, and smoking for CV deaths and MI. A positive stress test had a HR for CV death/MI of 2.43. Regarding coronary CTA predictors using the UCT

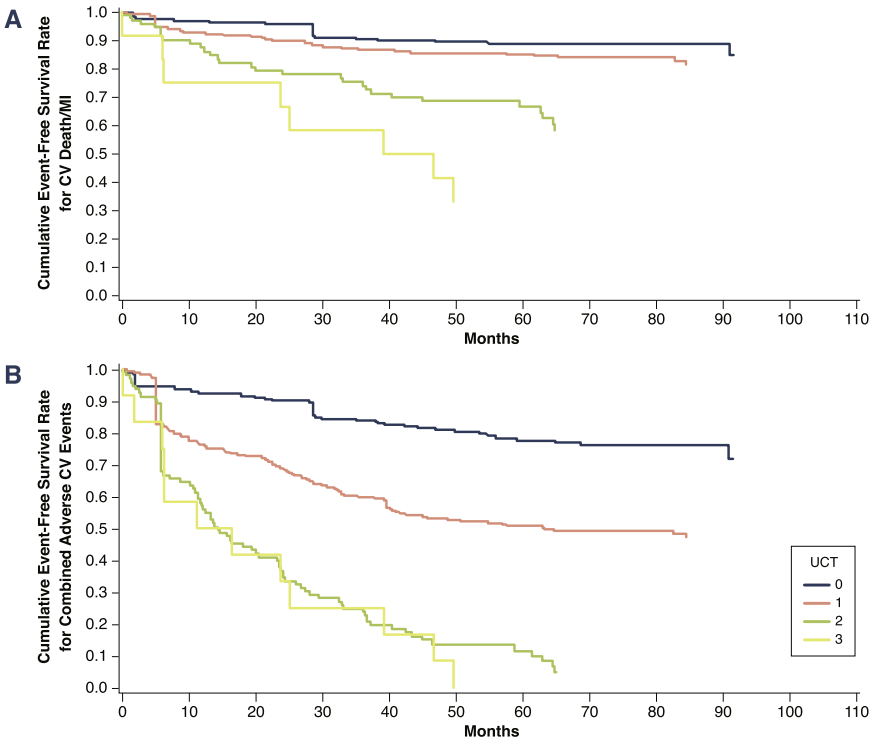

Figure 1. UCT Survival Analysis

Kaplan-Meier curves for cardiovascular (CV) death/myocardial infarction (MI) **(A)** and for composite adverse CV events **(B)** in patients with unprotected coronary territory (UCT) 0, 1, 2, or 3.

model, HRs were particularly increased in patients with UCT 2 (7.58 for CV death/MI and 8.39 for combined adverse CV events) and UCT 3 (10.19 for CV deaths/MI and 8.47 for combined adverse CV events). Regarding CAPS, patients with CAPS 4 showed the highest HRs (24.12 and 12.6 for CV deaths/MI and combined adverse CV events, respectively).

Survival analysis. Kaplan-Meier survival curves based on UCT 0 to 3 and CAPS 1 to 4 are shown in Figures 1 and 2, respectively. Regarding CV death/MI, the 73-month cumulative event-free survival rates in patients with UCT 0, 1, 2, and 3 were 86%, 84%, 53%, and 29%, respectively. Including revascularizations and unstable angina, the event-free survival rates with UCT 0, 1, 2, and 3 were 73%, 49%, 3%, and 0%, respectively (log-rank $p = 0.0001$). Regarding CAPS, cumulative event-free survival rates were 97% for CV death/MI and 82% for composite adverse CV events, respectively, in patients with CAPS 2, and 47% and 4% for CV death/MI and composite adverse CV events, respectively, with CAPS 4.

Multivariable predictors of events. In multivariable analysis, coronary CTA characteristics that were significant by univariable analysis were corrected for baseline characteristics. Multivariable predictors of events, calculated with the 2 models (UCT and CAPS), are reported in Table 4. Significant independent coronary CTA predictors of events were UCT 1, 2, and 3 and CAPS 2 and 4. The HRs were particularly high for UCT 2 and 3 (7.78 and 10.14, respectively, for CV death/MI, and 5.42 and 12.13, respectively, for combined adverse CV events) and for CAPS 2 and 4 (2.98 and 15.28, respectively, for CV death/MI, and 6.76 and 7.92, respectively, for combined adverse CV events).

Incremental prognostic value of coronary CTA. The incremental prognostic value of coronary CTA among post-CABG patients is assessed with the AUC and the NRI for the model with and without the variable of interest (UCT or CAPS), adjusted for age, sex, smoking, hypercholesterolemia, hypertension, diabetes, and family history of CAD. For the primary endpoint (CV death/MI), there is a statistically significant difference between the

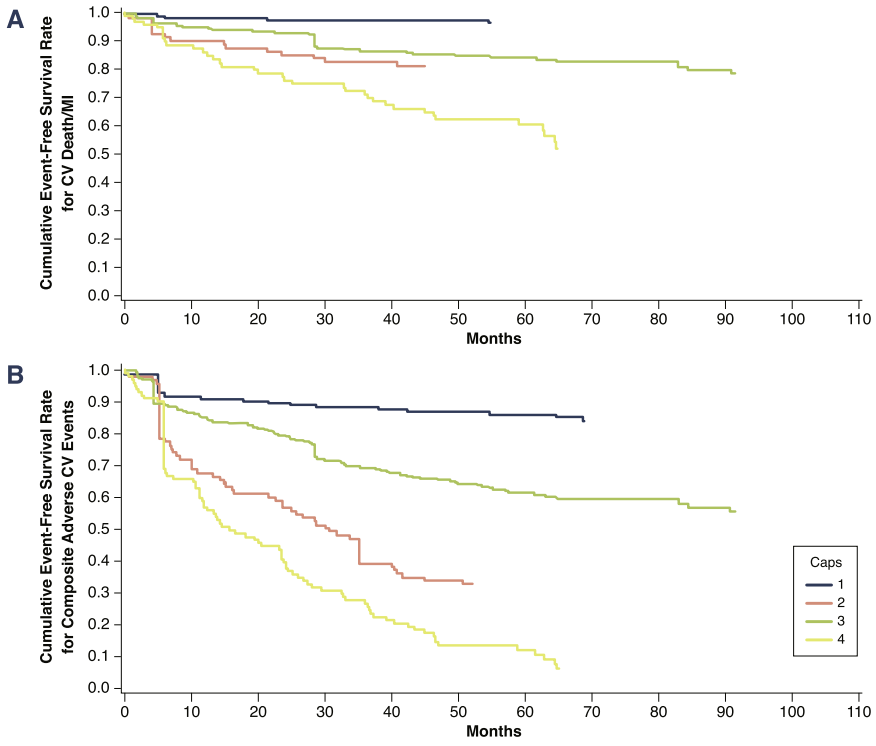

Figure 2. CAPS Survival Analysis

Kaplan-Meier curves for CV death/MI **(A)** and for composite adverse CV events **(B)** in patients with coronary artery protection score (CAPS) 1 to 4. Abbreviations as in Figure 1.

AUC for both UCT and CAPS ($p < 0.01$). NRI was computed to evaluate the improvement of the new models. Moreover, we compared UCT and CAPS, showing that the UCT index adds more prognostic value in the model in comparison to the CAPS index for the composite adverse CV events (NRI = −0.7976 [95% confidence interval: −0.938 to −0.657] $p < 0.0001$).

DISCUSSION

The prognostic value of coronary CTA as a noninvasive tool has been demonstrated in patients with suspected CAD and in those without a history of revascularization (4,6,12–14). On the other hand, the usefulness of risk stratification of CABG patients on the basis of graft anatomy has been shown with ICA. Liao et al. (9) developed an ICA prognostic model for patients with previous CABG showing that the graft index and number of unprotected coronary territories predicted all-cause mortality. However, the possibility of translating this model to coronary CTA is less certain. Indeed, CABG patients typically have severe native CAD and diffuse coronary calcifications that may hamper the diagnostic accuracy of coronary CTA (15,16). This may negatively affect the ability to determine prognosis and may limit coronary CTA clinical utility in the CABG population. In fact, when assessing the prognosis of patients after CABG surgery, it is essential to complete the anatomic data on bypass grafts with those on native coronary arteries (9). For this reason, in the present study, we used 2 scores to capture anatomic information regarding both bypass grafts and native coronary arteries, as suggested by the literature (7,8).

There are only 2 previous studies assessing the prognostic utility of coronary CTA in CABG patients. One by Small et al. (8) classified 657 patients using UCT and CAPS with a mean follow-up of 20 months and another by Chow et al. (7) that enrolled 250 patients who were classified with the UCT score and were followed for 20 months. In comparison to them, our study had a longer follow-up in a larger group of CABG patients. The main findings of the present study are that coronary CTA is able to provide long-term prognostic information in CABG patients and may predict CV death/MI.

Table 4. Multivariable Significant Predictors of Events

	Combined Adverse CV Events HR (95% CI)	p Value	CV Death/MI HR (95% CI)	p Value
Model 1: UCT				
Age	0.99 (0.97–1.01)	0.59	1.00 (0.97–1.04)	0.63
Male	0.79 (0.51–1.22)	0.29	0.97 (0.44–2.14)	0.95
Smoking	0.74 (0.51–1.07)	0.11	0.44 (0.23–0.84)	0.012
Dyslipidemia	1.37 (0.94–1.99)	0.03	1.46 (0.79–2.70)	0.21
Diabetes	1.64 (1.15–2.34)	0.005	1.48 (0.84–2.58)	0.16
Hypertension	1.49 (1.02–2.19)	0.03	1.32 (0.69–2.53)	0.38
Family history of CAD	0.68 (0.44–1.06)	0.09	0.57 (0.25–1.27)	0.17
Statins	0.64 (0.45–0.89)	0.008	0.51 (0.29–0.90)	0.02
Nitrates	1.76 (1.38–2.25)	<0.0001	2.56 (1.67–3.9)	<0.0001
Positive stress test	2.38 (1.23–4.58)	0.009	2.17 (0.73–6.40)	0.15
UCT 1	2.42 (1.65–3.55)	<0.0001	1.42 (0.71–2.83)	0.31
UCT 2	5.42 (3.57–8.24)	<0.0001	7.78 (3.90–15.51)	<0.0001
UCT 3	12.13 (4.57–32.22)	<0.0001	10.14 (2.66–38.52)	<0.0007
Model 2: CAPS				
Age	0.99 (0.97–1.01)	0.61	1.00 (0.97–1.04)	0.63
Male	0.86 (0.56–1.32)	0.49	0.94 (0.42–2.06)	0.88
Smoking	0.74 (0.52–1.06)	0.11	0.44 (0.24–0.82)	0.009
Dyslipidemia	1.34 (0.93–1.94)	0.11	1.44 (0.78–2.65)	0.24
Diabetes	1.36 (0.95–1.94)	0.08	1.41 (0.81–2.46)	0.22
Hypertension	1.47 (1.00–2.17)	0.04	1.30 (0.68–2.48)	0.42
Family history of CAD	0.77 (0.50–1.19)	0.24	0.56 (0.25–1.25)	0.15
Statins	0.70 (0.50–0.98)	0.04	0.57 (0.33–0.99)	0.04
Nitrates	2.12 (1.55–2.9)	<0.0001	2.37 (1.55–3.64)	<0.0001
Positive stress test	2.26 (1.19–4.30)	0.01	2.22 (0.75–6.60)	0.14
CAPS 2	6.76 (3.56–12.80)	<0.0001	2.98 (0.84–10.56)	0.08
CAPS 3	2.29 (1.32–3.94)	0.002	2.71 (0.92–7.93)	0.06
CAPS 4	7.92 (4.46–14.05)	<0.0001	15.28 (5.19–44.97)	<0.0001

Abbreviations as in Tables 1 and 3.

Specifically, we found that the best parameter to predict cardiac events is the number of unprotected territories. This finding was confirmed by both UCT and CAPS assessment. Indeed, evaluating the UCT score, we found that the risk of both CV death/MI and combined adverse CV events progressively increases from UCT 1 to UCT 3 at univariable analysis (HR for UCT 1: 1.24 and 2.75 for CV death/MI and combined adverse CV events, respectively, and HR for UCT 3: 10.1 and 8.47 for CV death/MI and combined adverse CV events, respectively). Moreover, high-grade UCTs were also demonstrated to be strong multivariable independent predictors of CV death/MI, exhibiting a HR of 7.7 and 10.1 for UCT 2 and 3, respectively. The Kaplan-Meier survival curves confirmed the important prognostic value of UCT 2 and 3, with event-free survival rates for CV death/MI of 53% for UCT 2 and 29% for UCT 3 at 73-month follow-up. Thus, the number of UCTs allowed the identification of patient subgroups with progressively worse outcomes. These findings are in agreement with the study by Chow et al. (7) demonstrating that UCTs were predictors of major adverse cardiac events at 20-month follow-up. Using CAPS, we were able to confirm the UCT findings. Indeed, the CAPS value associated with higher risk for CABG patients was CAPS 4, which included 2 scores corresponding to at least 2 UCTs. Notably, patients with CAPS 4 showed the highest

HRs for CV death/MI at both univariable (24.1) and multivariable (15.2) analysis. Moreover, patients with CAPS 2, which includes also people with 2 unprotected territories (patients with 2-vessel disease and 1 protected territory, and 2-vessel disease and 0 protected territories) had higher HR for both CV death/MI and combined adverse CV events in comparison with patients with CAPS 3, which includes people with not more than 1 unprotected territory (patients with 3-vessel disease and 3 protected territories, and 3-vessel disease and 2 protected territories). The 73-month event-free survival rates by Kaplan-Meier curves with respect to CV death/MI were 97% for CAPS 1 and 48% for CAPS 4. Therefore, CAPS analysis showed that the number of unprotected territories seems to be the best predictor of cardiac events in CABG patients, as compared with the number of native coronary arteries exhibiting significant CAD alone. So, coronary CTA–derived UCTs seems to be a feasible and simple score to adopt in clinical practice and therefore may be used as a reliable method with prognostic value for risk stratification of CABG patients. Moreover, although the analysis of AUC, NRI, and integrated discrimination improvement to assess the incremental prognostic value of coronary CTA showed that both UCT and CAPS add a statistically significant improvement in the model adjusted for age, sex, smoking, hypercholesterolemia, hypertension, diabetes, and family history of CAD, the comparison between UCT and CAPS demonstrated that the UCT index adds a greater improvement in the model. Finally, concerning the potential hazard of radiation exposure, it should be noted that recent studies demonstrated high accuracy in the evaluation of CABG, native postanastomotic coronary arteries, and nongrafted coronaries, even when low-radiation-exposure techniques were used (2).

Study limitations. First, this is a relatively small, single-center study evaluating mainly Caucasian patients. Thus, its results may not necessarily reflect the patient population of other centers or countries. Second, despite the percentage of patients with complete follow-up being remarkably high (98%), we recognize that incomplete follow-up may result in underreporting of cardiac events. Third, although an independent prognostic role of coronary CTA anatomic evaluation was demonstrated by our study, additional information about the amount and distribution of regional ischemia by means of imaging stress testing would have been important to assess the potential complementary prognostic value of these diagnostic approaches.

CONCLUSIONS

The identification by means of coronary CTA of CABG patients with 2 or more UCTs, who as demonstrated by our long-term follow-up study are at high risk for cardiac events, is of clinical relevance, suggesting that a subgroup of them may require closer clinical surveillance eventually associated with timely treatment.

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Key Words: coronary artery bypass grafts ■ coronary artery disease ■ coronary computed tomography angiography.