Prognostic comparison of cTPA with coronary calcium for cardiovascular risk stratification

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Abstract

Background

Evidence suggests carotid ultrasound has comparable prognostic information regarding cardiovascular events or death when compared to coronary calcium scoring.

Methods and Results

We used standard imaging procedures for carotid total plaque area (cTPA) and coronary calcium Agatston scores (CAC) imaged between 2003 and 2024, performed a follow-up in 472 cardiology patients (69% male, age 60 ± 9 years, 12% in secondary prevention) over 10 ± 7 years and observed 63 events (15 PTCA, 4 CABG, 11 AMI, 5 STROKE/TIA, 28 deaths). Using COX multivariate forward regression with 7 clinical and 3 laboratory variables, the hazard ratio of cTPA>62 mm^2 was 1.42 (95%CI 1.03 - 1.95, p=0.03) and for CAC>100 was 1.74 (95%CI 1.39 - 2.19, p<0.0001). Using 3 categories of risk markers (low-intermediate, high, very high) in Cox regression, posttest risk of cTPA showed a hazard ratio of 1.56 (95%CI 1.14 - 2.13, p=0.0053) and of CAC showed a hazard ratio of 2.26 (95%CI 1.61 - 3.16, p<0.0001), while SCORE2/-OP was excluded from the model. Net reclassification improvement was statistically not significant for cTPA (NRI 3% ± 12% p=0.76), but was significant with CAC (NRI 29% ± 11%, p=0.01). Area under the curve was statistically comparable for SCORE2/-OP, SCOTPA and SCOCAC (0.64, 0.63, 0.69 respectively, p=NS for the difference).

Conclusion

In cardiology patients with initial assessment of cardiovascular risk factors, cTPA and CAC (both imaging markers of cardiovascular risk) added significant and statistically comparable risk information. Given the lower cost and environmentally more friendly manner, cTPA could be the first imaging test to enhance risk prediction beyond cardiovascular risk factors.

Keywords:

Cardiovascular prevention, atherosclerosis, risk factors, carotid plaque, cardiovascular outcome

Abbreviations

AGLA	Working group on lipids and atherosclerosis of the Swiss Society of Cardiology
ARCO	Atherosclerosis Risk on cardiovascular Outcomes Cohort study [1]
CAC	coronary artery calcifications, quantified by Agatston Scores (does not require contrast media injection)
Code	risk coding (1= low or intermediate,, 2= high, 3=very high risk) according to the cutoffs defined by SCORE2/-OP
cTPA	carotid total plaque area
MEDI	MEDI is coded with 0 for no medication; 1= therapy with statins, 2=therapy with antihypertensive drugs, 3=therapy with statins and antihypertensive drugs
NRI	net reclassification improvement
PTP	posttest probability
ROC	receiver operating curves
SCORE2/-OP	risk prediction algorithm: new models to estimate 10-year risk of cardiovascular disease in Europe
SCO2TPA	posttest risk of SCORE2/-OP and cTPA
SCO2CAC	posttest risk of SCORE2/-OP and CAC

Introduction

Cardiovascular risk stratification assists in the prevention of cardiovascular events in primary care. International professional organizations have provided tools to meet this need using cardiovascular risk calculators such as SCORE2/-OP. In Switzerland, the AGLA guidelines apply, which are essentially based on the SCORE2/-OP risk calculator [2]. However, it has been shown that numerically most cardiovascular events occur in the low or intermediate risk groups of patients, which limits the efficiency of correct resource allocation. For further risk stratification, the accuracy of imaging of atherosclerosis is a valuable option [3]. European guidelines recommend additional tests such as calcium score or, if not available, carotid ultrasound [4]. In view of the draw backs of calcium scoring (radiation burden, cost, increase of coronary calcium with statins [5], [6], [7], [8], environmental damage [9]), carotid ultrasound is a preferred method for cardiovascular risk adjustments and atherosclerosis management over time, if the prognostic information from this test is comparable to calcium scoring.

In this study we compare the long-term prognostic information of calcium score and ultrasound-based carotid plaque quantification in a routine cardiological practice.

Methods

Patient selection

We reviewed 21,224 patient records of a total of 9,747 individuals who visited the Kardiolab, an independent cardiology practice with additional affiliation to the Rodiag Diagnostic Center, both located in Olten, between 2003 and 2024. Individuals with a cTPA and CAC measured within 3 months and with follow-up date of at least 1 year were identified (N=473).

Carotid plaque measurements

As described elsewhere [3], the presence of carotid plaque is defined as IMT thickening of at least 1 mm, the carotid arteries were imaged longitudinally, the plaque surface was traced on the screen and the sum of all plaque (cTPA) was calculated from all plaques in both carotid arteries imaged from the clavicle to the jaw (common, internal, external, and bulb). The reproducibility of cTPA has been published elsewhere[10].

Coronary Calcium Measurements

We used the Agatston method to quantify coronary calcifications based on plaque area and plaque density. Between 2003-2006, coronary calcifications were made visible for further processing by using a single-breath hold, Multislice (Aquilion, Toshiba, Japan) ECG-gated, non-contrast enhanced, low-radiation scan sequence and image data were processed by using the NetraMD Software (ScImage Palo Alto, California, USA), which provides reproducible data on total Agatston calcium scores, percentile of Agatston scores, and plaque volumes for all coronary arteries and total plaque volume. The cut-off point to define that a plaque is calcified was set at 130 Hounsfield units. From 2018 to 2024 we used a vendor specific quantification tool provided by General Electric.

SCORE2/-OP risk and posttest risk calculation (subgroup analysis)

In all 473 patients, our database allowed for the calculation of SCORE2/-OP [11]. We used the BAYES formula to calculate posterior probabilities [12]. For accurate comparisons between cTPA and CAC posterior risk prediction, three prerequisites must be met: 1. Test sensitivity and specificity at predefined result cutoffs from cohort studies must be available; 2. Result cutoffs for different tests must be associated with comparable risk; 3. the outcome endpoints should be the same. We used cTPA outcome for values <22 mm^2, 22-62 mm^2, and >62 mm^2 from our ARCO outcome study for the occurrence of MACE (fatal or non-fatal myocardial infarction or stroke). Based upon our literature research, CAC is frequently reported for the outcome of coronary heart disease (CHD) or death, but not MACE. One important exception was presented by the MESA investigators [13]. In this study,

event rates for CAC and CHD or MACE were reported separately and for CAC values of 0, 1-99 and >99 (Supplementary Table 1a, clinical example Supplementary Table 1b). Comparing cTPA cutoffs with CAC cutoffs, we found similar event rates and were able to extract the sensitivities, specificities, and ROC results from these data.

Clinical Intervention and patient management

Patients were referred by their general practitioners, with a median follow-up per patient of 1.3 years (interquartile range 0.9-1.8 years). Whenever possible, cardiovascular risk factors were collected from patient history and laboratory values. Blood pressure was measured in the office with a sphygmomanometer in the sitting position. Medication use was recorded and verified when information appeared unreliable. During the cardiological visit, cTPA was measured in each patient. After the evaluation, patients and their physicians received a detailed report on the appropriate recommendations for the achievement of risk factor goals. During the follow-up visits, the achievement of the goals was checked and corrected if necessary. This quality-control study does not require a formal approval by an ethics committee, as all medical interventions were performed as part of routine medical management, which was the same for all patients. However, since the beginning of data collection, we disposed of a positive ethical committee vote [14] (https://www.docfind.ch/CordicareIIEthikkomissionsBeschluss122005S.pdf) regarding the acceptability of performing cTPA and CAC measurements and collecting follow-up data for scientific purposes within the Vascular Risk Foundation cohort study, which we published in 2021[1].

Statistical analysis

Statistical analysis was performed with MedCalc (MedCalc® Statistical Software version 23.0.2 MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2024), and data were entered into an Excel spreadsheet. The Mann-Whitney test for independent samples or CHI^2 analysis, was used as appropriate. The effect of explanatory independent variables was assessed with regression analysis (logistic regression, multiple regression). Outcome was calculated using Cox hazard regression, ROC and NRI.

The Bayes theorem [12] calculates the posttest risk probability (PTP) using pretest probability = SCORE2-/OP (equal to prevalence PV) in case the imaging test is positive (PTP pos: e.g. Agatston Score >0, carotid Total Plaque Area > 21 mm2), otherwise PTP neg formula is used and from the four-field table, sensitivity (SE) and specificity (SP) of a test can be derived as follows: PTP pos: (PV x SE)/[PV x SE + (1 – PV) x (1 – SP)] and PTP neg: [PV x (1 – SE)]/[PV x (1 – SE) + SP x (1 – PV)].

Statistical significance was set at <0.05.

Results

Baseline clinical data are described in Table 1. There were 473 patients, 69% male, average age 60 ± 9 years, and average follow-up time of 10 ± 7 years. We observed 63 patients with an event (15 PTCA, 4 CABG, 11 AMI, 5 STROKE/TIA, 28 deaths). SCORE2/-OP was significantly higher in patients with events (8.3% ± 4.9%) than without an event (6.2% ± 3.8%, p=0.0002). Posttest risk using cTPA was 15.8% ± 11.6% versus 10.8% ± 9.8% (p=0.0007) and with CAC was 15.8% ± 10.0% versus 9.7% ± 9.2% (p=<0.0001). Systolic blood pressure, total and HDL cholesterol were comparable between patients with and without an event.

Univariate predictors of events are listed in Table 2 and were age, smoking, diabetes mellitus, use of medication for blood pressure and/or lipid lowering, previous cardiovascular events, total cholesterol, SCORE2/-OP, cTPA, and CAC.

Multivariate predictors including cTPA were age, smoking, diabetes mellitus, previous events and cTPA (Table 3a), but not sex, family history, medication, systolic blood pressure, HDL and total cholesterol. The Hazard Ratio of cTPACode was 1.42 (95%CI: 1.03 to 1.95) using multivariate Cox proportional hazard regression (Table 3b).

Multivariate predictors including CAC instead of cTPA were age, smoking, diabetes mellitus, previous events, and CAC (Table 3c), but not sex, family history, medication, systolic blood pressure, HDL and total cholesterol. The Hazard Ratio of CACCode was 1.74 (95%CI: 1.39 to 2.12) using multivariate Cox proportional hazard regression (Table 3d).

Using SCORE2/-OP and posttest risk of cTPA and CAC in a multivariate Cox proportional-hazards regression with 3 categories (Code 1-3) of risk markers (low-intermediate, high, very high), cTPA showed a hazard ratio of 1.38 (95%CI 1.01 – 1.89, p=0.04) and CAC showed a hazard ratio of 2.26 (95%CI 1.61 - 3.16, p<0.0001), while SCORE2/-OP was excluded from the model. Net reclassification improvement was statistically not significantly different for cTPA (NRI 3% ± 12% p=0.76), but was significant with CAC (NRI 29% ± 11%, p=0.01). Area under the curve was statistically comparable for SCORE2/-OP, SCO2TPA and SCO2CAC (0.64, 0.63, 0.69 respectively, p=NS for the difference).

Using Kaplan-Meier Survival Analysis (Table 5) of SCORE2/-OP cTPACode, very high risk (Code=3) showed a Hazard Ratio of 2.09 (95%CI: 1.19 to 3.67, p=0.0019) and SCORE2/-OP CACCode showed significant Hazard Ratios for high risk (Code=2) with 2.26 (95%CI: 1.19 to 4.30) and for very high risk (Code=3) of 5.06 (95%CI: 2.88 to 8.91).

Discussion

We assessed the long-term clinical outcomes (ASCVD events and death) of 473 patients who underwent routine atherosclerosis management in a cardiology practice. These patients were assessed for their 10-year cardiovascular risk at baseline using SCORE/-OP, as well as the posttest risks of cTPA and CAC. We found that cTPA and CAC were superior prognosticators to SCORE/-OP, and that the prognostic information from post-test risk calculations using SCORE/-OP as the prior probability was statistically comparable to the prognostic information from cTPA or CAC but better than SCORE2/-OP alone. This finding highlights the importance of measuring atherosclerosis burden at the start of cardiological treatment to gain a clearer understanding of a patient's future cardiovascular risk.

Similar prognostic information from carotid plaque and coronary calcium

CAC has been studied extensively for its prognostic information regarding major adverse cardiac events[15], [16], but direct comparison for prognostication of incident myocardial infarction, stroke, or both, has rarely been studied. In the MESA cohort [17], CAC was compared with carotid plaque (in the carotid bulb and the internal carotid artery) and carotid intima-media thickness (cIMT) in 6'779 patients with follow-up time of 9.5 years on average. Using Cox proportional hazards regression, the Hazard ratio of CAC was 3.12 (95%CI: 2.44–3.99) and for carotid plaque was 1.61 (95%CI:1.17–2.21), while results for cIMT were statistically not significant (1.20 [95%CI:0.94–1.52]), but plaque within the common carotid artery were not assessed, which reduces the prognostic power of carotid plaque. In the BIOIMAGE cohort [18], CAC was compared to the global carotid plaque burden using total carotid plaque volume (cTPV), a measure of plaque burden with high correlation to cTPA [3] in 5808 patients and a follow-up time of 2.7 years. Using Cox proportional hazards regression, the Hazard ratio of CAC was 2.87 (95%CI: 1.73–4.74) and for cTPA was 2.97 (95%CI: 1.92–4.60).

In the REFINE cohort [19], CAC was compared with cTPA in 948 (509 women) patients with follow-up time of 6.5 years on average. Both cTPA and CAC had similar prognostic information using various pretest models: cTPA AUC was 0.77 (95%CI: 0.71 – 0.83, p=0.019) and CAC AUC was 0.80 (95%CI: 0.74 – 0.86, p<0.0001). Our study extends the knowledge of the prognostic ability of cTPA and CAC in the long-term.

Healthcare integration of cTPA

The cTPA test has several compelling advantages: (1) No radiation exposure, making it safe for repeated assessments and younger populations; (2) Lower cost and greater accessibility, enabling implementation in primary care settings; (3) Environmental sustainability with minimal carbon footprint

compared to CT-based calcium scoring; (4) Comprehensive atherosclerosis assessment that captures both calcified and non-calcified plaque burden; (5) Superior performance in populations with zero CAC scores, where traditional calcium scoring provides limited prognostic information; and (6) a high reproducibility and low inter-observer reproducibility [20], [21].

Since cTPA is easy to learn and does not require any software for quantification, the accessibility of cTPA in the management of atherosclerosis in healthcare is easy and could be implemented in general medicine.

Some limitations have to be acknowledged: 1) Because of the preventive interventions, which took place every 1.3 years on average, the prognostic information of the baseline imaging modalities (cTPA and CAC) is reduced, what explains a lower prognostic information from atherosclerosis imaging than expected [3]; 2) this is a single-center single-observer study and should be validated externally; 3) Future research should help to integrate artificial intelligence and automated plaque quantification tools in order to enhance the clinical applicability of carotid ultrasound based atherosclerosis management.

Conclusion

In cardiology patients with initial assessment of cardiovascular risk factors, cTPA and CAC (both imaging markers of cardiovascular risk) added significant and statistically comparable risk information in the long-term. Given the lower cost and environmentally more friendly manner, cTPA could be the first imaging test to enhance risk prediction beyond cardiovascular risk factors in cardiological practice.

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Tables

Table 1: Baseline clinical and imaging data of patients with and without an event during follow-up

	ALL	EVENT	NO EVENT	p=
Patients	473	63	410	
Male	328	49	279	<0.0001
Male %	69	78	68	
Smoker	122	24	98	0.0166
Smoker %	26	38	24	
Diabetes Mellitus	50	11	39	0.0499
Diabetes Mellitus %	11	17	10	
Fam Hx ASCVD	90	12	78	0.9965
Fam Hx ASCVD %	19	19	19	
Statins and/or BP medication	202	32	170	0.1638
Statins and/or BP medication %	43	51	41	
Secondary Prevention	59	15	44	0.0035
Secondary Prevention %	12	24	11	
cTPA>62 mm2	174	34	140	0.0024
cTPA>62 mm2 %	37	54	34	
CAC> 100	135	46	89	0.0004
CAC> 100 %	29	73	22	
Age ± SD	60 ± 9	62 ± 9	60 ± 9	0.0602
BPs ± SD	131 ± 20	134 ± 20	131 ± 19	0.171
Cholesterol mmol/ll ± SD	5.4 ± 1.0	5.4 ± 0.9	5.4 ± 1.1	0.7769
HDL mmol/l ± SD	1.4 ± 10.4	1.3 ± 0.2	1.4 ± 0.4	0.3388
SCORE2/-OP	6.4 ± 4.1	8.3 ± 4.9	6.2 ± 3.8	0.0002
SCOTPA	11.5 ± 10.2	15.8 ± 11.6	10.8 ± 9.8	0.0007
SCOCAC	10.5 ± 9.6	15.8 ± 10.0	9.7 ± 9.2	<0.0001
cTPA ± SD	62 ± 56	77 ± 59	58 ± 55	0.0082
CAC ± SD	158 ± 513	328 ± 679	155 ± 479	<0.0001
TIME years	10 ± 7	10 ± 6	10 ± 7	0.3847

Table 2: Cox proportional-hazards regression, univariate predictors of outcome

Covariate	b	SE	Wald	P	Exp(b)	95% CI of Exp(b)
Age	0.05	0.0147	9.95	0.**0016**	1.05	1.0177 to 1.0780
Sex	0.21	0.3036	0.47	0.4910	1.23	0.6798 to 2.2350
Smoking	0.51	0.2600	3.88	0.**0488**	1.67	1.0027 to 2.7785
Family history	-0.20	0.3213	0.39	0.5329	0.82	0.4360 to 1.5363
Diabetes mellitus	0.98	0.3329	8.75	**0.0031**	2.68	1.3939 to 5.1411
Medication use	0.27	0.1066	6.49	**0.0109**	1.31	1.0646 to 1.6167
Secondary prevention	1.04	0.2965	12.40	**0.0004**	2.84	1.5891 to 5.0813
Systolic blood pressure	0.00	0.0060	0.66	0.4181	1.00	0.9931 to 1.0169
Cholesterol	-0.26	0.1325	3.85	**0.0496**	0.77	0.5947 to 0.9996
HDL cholesterol	-0.73	0.3959	3.43	0.0639	0.48	0.2210 to 1.0433
SCORE2/-OP	0.12	0.0251	22.04	**<0.0001**	1.13	1.0710 to 1.1817
SCO2code	0.47	0.1873	6.26	**0.0123**	1.60	1.1069 to 2.3065
cTPA	0.01	0.0018	9.73	**0.0018**	1.01	1.0021 to 1.0094
cTPACODE	0.48	0.1570	9.25	**0.0023**	1.61	1.1851 to 2.1927
SCO2TPAcode	0.44	0.1593	7.76	**0.0053**	1.56	1.1407 to 2.1299
CAC	0.00	0.0001	13.40	**0.0003**	1.00	1.0003 to 1.0008
CACCODE	0.55	0.1163	22.07	**<0.0001**	1.73	1.3750 to 2.1691
SCO2CACcode	0.81	0.1725	22.27	**<0.0001**	2.26	1.6093 to 3.1641

Table 3a: Cox proportional-hazards regression, multivariate clinical and cTPA

Covariate	b	SE	Wald	P	Exp(b)	95% CI of Exp(b)
Age	0.044	0.016	7.53	0.0061	1.045	1.0127 to 1.0783
Smoking	0.608	0.279	4.74	0.0295	1.837	1.0626 to 3.1768
Diabetes Mellitus	0.791	0.340	5.41	0.0201	2.206	1.1324 to 4.2991
Secondary prevention	1.037	0.304	11.62	0.0007	2.822	1.5542 to 5.1236
cTPA	0.003	0.002	2.41	0.1207	1.003	0.9992 to 1.0073

Excluded from the model (foreward method): SEX, FAM, MEDI, BPS, CHOL, HDL

Table 3b: Cox proportional-hazards regression, multivariate clinical and cTPACODE

Covariate	b	SE	Wald	P	Exp(b)	95% CI of Exp(b)
Age	0.043	0.016	7.46	0.0063	1.044	1.0121 to 1.0759
Smoking	0.630	0.275	5.26	0.0218	1.877	1.0959 to 3.2162
Diabetes Mellitus	0.843	0.337	6.26	0.0123	2.322	1.2005 to 4.4924
Secondary prevention	1.025	0.301	11.56	0.0007	2.786	1.5433 to 5.0291
cTPACode	0.349	0.164	4.53	0.0332	1.417	1.0281 to 1.9538

Table 3c: Cox proportional-hazards regression, multivariate clinical and CAC

Covariate	b	SE	Wald	P	Exp(b)	95% CI of Exp(b)
Age	0.0462	0.0156	8.7403	0.0031	1.05	1.0157 to 1.0798
Smoking	0.7153	0.2705	6.9901	0.0082	2.04	1.2032 to 3.4748
Diabetes Mellitus	0.7894	0.3363	5.5086	0.0189	2.20	1.1390 to 4.2574
Secondary prevention	0.9251	0.3012	9.4312	0.0021	2.52	1.3975 to 4.5520
CAC	0.0004	0.0002	3.8073	0.0510	1.00	1.0000 to 1.0007

Excluded (foreward method) SEX, FAM, MEDI, BPS, CHOL, HDL

Table 3d: Cox proportional-hazards regression, multivariate clinical and CACCODE

Covariate	b	SE	Wald	P	Exp(b)	95% CI of Exp(b)
Smoking	0.70	0.26	7.05	0.0079	2.01	1.1999 to 3.3559
Secondary prevention	0.98	0.30	10.70	0.0011	2.66	1.4796 to 4.7738
CACCode	0.56	0.12	22.88	<0.0001	1.74	1.3883 to 2.1891

Excluded (foreward method): AGE, SEX, FAM, DIAB, MEDI, BPS, CHOL, HDL

Table 4: multivariate hazard ratios, univariate C-statistics and net reclassification improvement (NRI) of SCORE2/-OP, SCORE2/-OP plus CACCode and SCORE2/-OP plus cTPACode

N=473	HR (95% 95%-CI)	P value	C-Statistic	P value	NRI ± SE
CVD or DEATH (N=63)					
SCORE2/-OP alone	---	---	0.64	0.0003	---
+ CACCode	2.26 (1.61-3.16)	<0.0001	0.66	<0.0001	29% ± 11%
+ cTPACode	1.38 (1.01-1.89)	0.0427	0.60	0.0082	3% ± 11%

Table 5: Kaplan-Meier Survival Analysis for SCORE2TPAcode and SCORE2CAC

cTPA	**Chi-squared**	**12.56**	**Hazard ratio**	**95%CI**
Code=2	DF	2	0.64	0.32 to 1.27
Code=3	Significance	P = 0.0019	2.09	1.19 to 3.67
CAC	**Chi-squared**	**26.85**	**Hazard ratio**	**95%CI**
Code=2	DF	2	2.26	1.19 to 4.30
Code=3	Significance	P<0.0001	5.06	2.88 to 8.91

Figures

Figure 1: Kaplan-Meier Survival Analysis for SCO2TPAcode

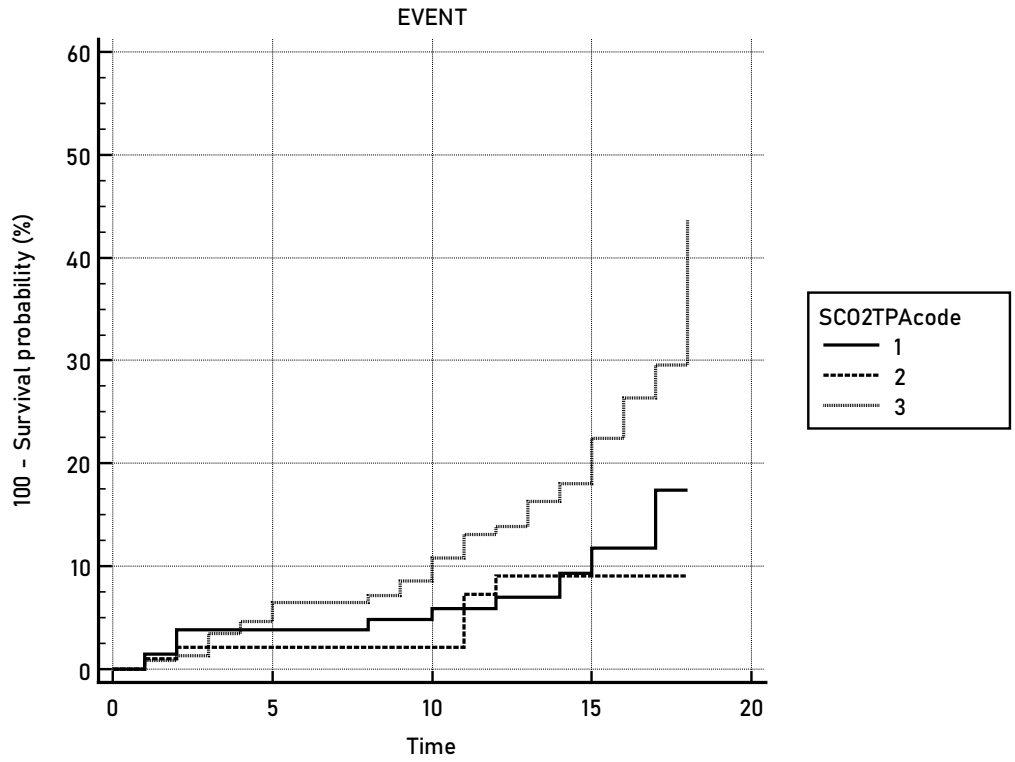
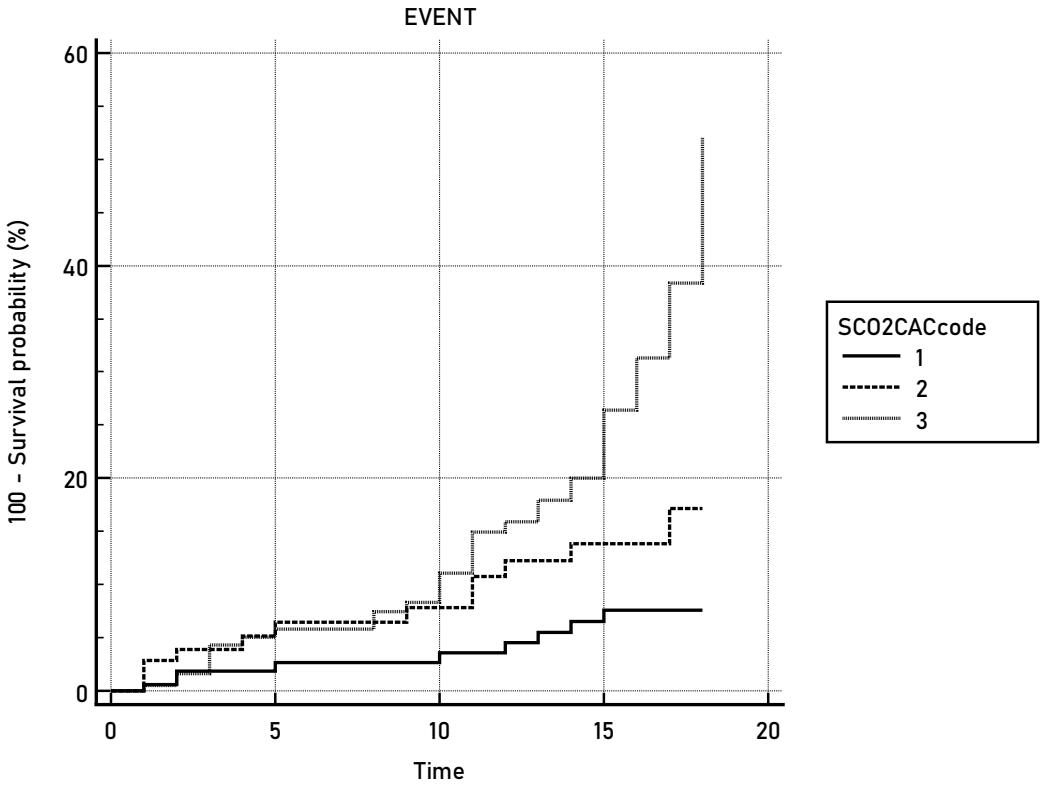


Figure 2: Kaplan-Meier Survival Analysis for SCO2CACcode



Supplementary material

Suppl. Table 1a: comparison of different cTPA and CAC cutpoints for diagnostic values (Area under curve) and associated 5 year outcomes from the ARCO [1] and the MESA study [22].

DIAGNOSTIC ACCURACY OF IMAGING (MESA CAC, ARCO cTPA)								
MESA Coronary Heart Disease								
	CHD	No CHD	ALL	Sens	Spec	AUC1	STANDARD ERROR	5 YEAR RISK
CAC 0	31	2330	2361	0.8072	0.5733	0.738	0.0189	0.7
CAC 1-99	44	1049	1093	0.8072	0.5733			2.1
CAC 100+	90	685	775	0.5422	0.8314			5.8
ALL	165	4064	4229					
MESA MACE						AUC2	STANDARD ERROR	5 YEAR RISK
CAC 0	54	2307	2361	0.7787	0.5788	0.715	0.0161	1.2
CAC 1-99	73	1020	1093	0.7787	0.5788			3.3
CAC 100+	116	659	775	0.54	0.86			7.5
ALL	243	3986	4229					
ARCO MACE						AUC3	STANDARD ERROR	5 YEAR RISK
TPA<22	3	1413	1416	0.9474	0.5074	0.798	0.0214	0.3
TPA 22-61	12	707	719	0.9474	0.5074			1.2
TPA 62+	42	665	707	0.7368	0.7612			6.4
ALL	57	2785	2842					

Suppl. Table 1b: Example of posttest risk for a SCORE2/-OP risk of 0.05 (=5%).

POST TEST RESULTS FOR POSITIVE AND NEGATIVE TESTS (BAYES THEOREM)					
IMAGING TEST NEGATIVE					
	Risk	Sens	Spec	Bayes neg	Risk change
MESA CHD	0.05	0.807	0.5733	0.017	0.033
MESA MACE	0.05	0.779	0.5788	0.020	0.030
ARCO MACE	0.05	0.9474	0.5074	0.005	0.045
IMAGING TEST POSITIVE LOW RISK					
	Risk	Sens	Spec	Bayes pos	
MESA CHD	0.05	0.807	0.5733	0.091	0.041
MESA MACE	0.05	0.779	0.579	0.089	0.039
ARCO MACE	0.05	0.947	0.507	0.092	0.042
IMAGING TEST POSITIVE RELEVANT RISK					
	Risk	Sens	Spec	Bayes pos	
MESA CHD	0.05	0.542	0.8314	0.145	0.095
MESA MACE	0.05	0.540	0.86	0.169	0.119
ARCO MACE	0.05	0.737	0.761	0.140	0.090

Legend: RISK=SCORE2/-OP chosen at 0.05 (=5%). For each cutoff (Table 1a) posttest risk is calculated using the Bayes theorem. Example: with the imaging test being negative (Bayes neg), post test risk decreases from 5% to 2% (Risk change 3%) with MESA MACE sensitivities and specificities; with ARCO MACE, risk decreases to 0.5% (Risk change 4.5%), which is due to the higher sensitivity of cTPA when compared to MESA MACE, where 54 (2.3%) of MACE occurred with CAC0, while only 3 (0.2%) MACE occurred with ARCO.