Research papers

Impact on mortality of coronary and non-coronary cardiovascular findings in non-gated thoracic CT by malignancy status

Gastón A. Rodriguez-Granillo[a,*], Exequiel Reynoso[a], Carlos Capunay[a], Héctor M. Garcia-Garcia[b], Patricia Carrascosa[a]

[a] Department of Cardiovascular Imaging, Diagnóstico Maipú, Buenos Aires, Argentina
[b] MedStar Washington Hospital Center, Washington, DC, United States

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ABSTRACT

Purpose: The prognostic value of coronary artery calcification (CAC) assessed on non-gated thoracic CT scans has only been explored in population-based studies. We explored the impact of the presence and extension of CAC, as well as of non-coronary atherosclerosis cardiovascular findings (NCACVF) in survival of patients with and without malignancies undergoing clinically indicated non-gated thoracic computed tomography (CT) scans.

Materials and methods: Between August and December 2012, a total of 1.901 patients aged between 35 and 74 years underwent clinically indicated non-gated, non-enhanced thoracic CT scans and followed for mortality through September 2016.

Results: Three hundred and thirty two (17.5%), 250 (13.2%), and 329 (17.3%) patients showed CAC in 1, 2, and 3 vessels, respectively, and the remaining had no CAC. Two hundred and fifty five (13.4%) patients had evidence of extensive calcification (CACSIS > 5). Only 62 (3.3%) had major NCACVF whereas 1635 (86%) had none or minimal NCACVF. After a median follow-up of 3.7 (3.5–3.9) years, 217 (11.4%) deaths occurred. Age [HR 1.03 (95% CI 1.01–1.05), p = 0.001], a history of malignancy [HR 8.04 (95% CI 5.95-10.9), p < 0.0001], and the NCACVF class [HR 1.79 (95% CI 1.45-2.19), p < 0.0001] were identified as independent predictors of death. CACSIS was found an independent predictor of death only among patients without malignancy (HR 1.10 (95% CI 1.02–1.20), p = 0.019).

Conclusions: In this study including clinically indicated non-gated standard thoracic CT scans, survival rates were associated to the CAC extension among patients without malignancy, and to the NCACVF class independent from the malignancy status.

1. Introduction

The presence and extension of coronary artery calcium (CAC) assessed by ECG-gated computed tomography (CT) has been consistently identified as an independent predictor of major cardiovascular events and death [1–4]. Indeed, CAC outperformed net reclassification indexes compared to traditional risk score algorithms, family history of premature coronary artery disease, C-reactive protein, and other non-invasive techniques [5,6].

Aside from conventional gated acquisitions, CAC can be identified and quantified on non-gated thoracic CT scans. This can be accomplished using Agatston CAC scoring, as well as by means of visual semi-quantitative analysis, and has shown a good correlation with gated scans as well as prognostic value in population-based studies [7–14].

Reporting CAC derived from non-gated thoracic CT scans performed for diverse clinical indications, if consistently proven to bestow incremental prognostic value, might potentially influence screening strategies. Recently, data from large prospective invasive and non-invasive studies have underscored the role of non-obstructive coronary atherosclerosis, with non-obstructive but extensive disease (particularly assessed using the segment-involvement score) conferring a similar risk of hard events than the presence of obstructive but non-extensive disease [15,16].

CAC assessment during routine non-gated thoracic CT scans is largely underreported, either due to an educational deficit, lack of awareness, or uncertainty regarding its clinical implications [17]. In parallel, other potentially relevant non-coronary atherosclerosis cardiovascular findings (NCACVF) can be identified during non-gated

Table 1

Non-coronary atherosclerosis cardiovascular findings classification (NCACVF).

I)	No cardiovascular findings; or mild thoracic aorta or valve calcification; mild right ventricular adipose tissue; or minimum recess or posterior pericardial fluid
II)	Minor findings: Calcification of the thoracic aorta and cardiac valves; o diffuse aortic or cardiac valve calcification; or aortic dilatation (< 40 mm in ascending aorta and < 35 mm in descending aorta); pericardial cyst, mild pericardial effusion; isolated right aortic arch, aberrant right subclavian artery; significant adipose tissue in the right ventricle; left atrium dilatation; lipomatous interatrial septum; coronary artery anomalies; pulmonary artery dilatation; mild endocardial calcification or mild isolated left ventricular adipose tissue.
III)	Major findings: Chronic myocardial infarction (lipomatous metaplasia or calcification); intracavitary mass/calcification; cardiomegaly; significant adipose tissue in both right and left ventricles; pericardial calcification, moderate to severe pericardial effusion; aortic aneurysm.

thoracic CT scans, and their clinical relevance remains poorly understood.

Accordingly, we sought to explore the association of the presence and extent of CAC, as well as of NCACVF and survival of patients with and without malignancies undergoing clinically indicated non-gated thoracic CT scans.

2. Methods

2.1. Study population

The study cohort consisted of all consecutive patients aged between 35–74 years who underwent non-gated, non-enhanced thoracic CT scans in an imaging clinic between August and December 2012, which was the initial date when picture archiving and communication system (PACS) was fully incorporated and therefore all patients' images became available. The dataset of this study consists of a combination of data from 3 centers of the same institution. Patients were referred for thoracic CT scans for numerous clinical indications, including known malignancy history (cancer staging or follow-up), suspected malignancy (based on clinical history or previous studies), lung disease (non-malignant), respiratory symptoms of unknown etiology, non-respiratory pathology (non-malignant), and non-respiratory symptoms of unknown etiology. Patients with evidence of implants (valve prosthesis, aortic endografts, cardiac pacemaker, implantable cardiac defibrillator, o resynchronizer), revascularization (coronary stents or bypass), or multiple trauma were excluded. In patients with repeated scans during the inclusion period, only the first scan was included. Patients were followed for mortality through September 2016, and those lost to follow-up were further excluded.

Images were acquired on 16-, 64-, 128-, and 256-slice CT scanners (Brilliance CT family; Philips Healthcare, Cleveland, USA) and in a 16-slice CT scanner (Discovery STE, GE Healthcare, Milwaukee, USA) with a single breath-hold from the thoracic inlet to the lung bases. Acquisition parameters were: 16×1.25 mm, 16×1.5 mm, 64×0.625 mm, 128×0.625 mm, and 256×0.625 mm according to the CT scanner; 120 kV; 150–300 mAs (z-axis modulation was used on 64- and 256-slices CT scanners); variable pitch; 0.5–0.75 rotation time; DFOV adjusted for each patient size; reconstructions using 1-1.5 mm slice thickness and 0.5 mm interval. Evaluated images were unenhanced and non-gated.

2.2. Data analysis

Clinical records and scan reports were reviewed by a radiologist (ER). In our institution, clinical questionnaire of patients referred for thoracic CT scans are particularly pointed to the history of cancer. Accordingly, data regarding coronary risk factors is incomplete in this population. Patients were further classified into two groups according to the presence of a history of malignancy, defined as current malignancy or a history of malignancy with complete remission. Patients with confirmed malignancy in the CT scan, or with identification of nodules or masses with high suspicion of malignancy were also classified in the former (malignancy) group. Patients without a history of malignancy, or with a history of benign tumors or basal cell carcinoma were classified as without malignancy.

All scans were reviewed by a cardiologist (GRG) blinded to the clinical data and the scan report, with experience (> 10 years) in cardiovascular imaging, using PACS software (Carestream Vue PACS version 11.4, New York, USA). Axial, coronal, and sagittal planes were used to assess coronary findings and non-coronary atherosclerotic cardiovascular findings (NCACVF). Coronary findings were assessed using axial planes and, if necessary, curved multiplanar reconstructions. The CAC burden was classified according to the segment involvement score (CACSIS), using the 16-segment modified American Heart Association classification [18]. The CACSIS reflected the total number of segments involved, ranging from 0 to 16. Using the CACSIS, patients were classified according the absence (CACSIS 0), or presence of mild (CACSIS 1–5) or extensive (CACSIS > 5) coronary calcification. Additionally, patients were further classified according to the number of vessels with any calcification. Patients with CAC at the left main coronary artery were considered as two-vessel CAC. Patients were further classified according to the presence of NCACVF using a visual qualitative analysis (Table 1 and Figs. 1–3) [19]. In order to assess the interobserver variability, 50 cases were randomly selected and assigned to be evaluated by a third independent observer (CC), who was a radiologist with experience (> 10 years) in cardiovascular imaging.

The primary endpoint of the study was time to death from all causes. Death status was ascertained by a combined query of the Social Security death index, and Civil Registry database.
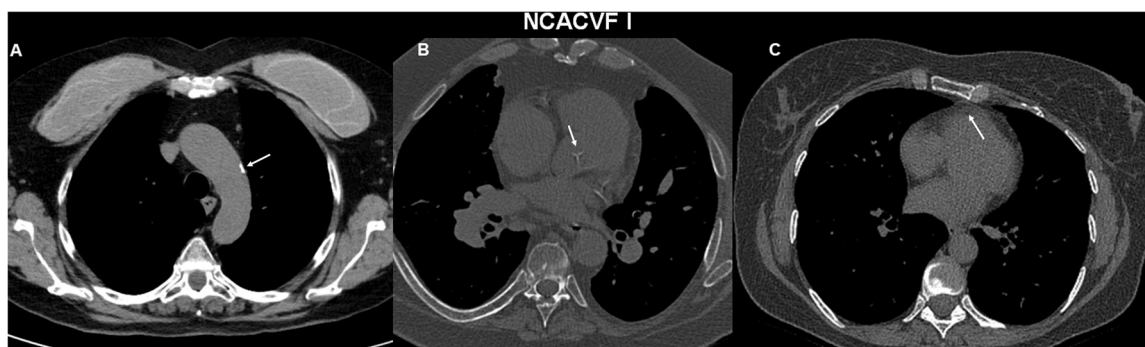

Fig. 1. Non-coronary atherosclerosis cardiovascular findings (NCACVF) classification. Examples of NCACVF I: none or minimal findings [A, minimal aortic calcification (arrow); B, minimal aortic valve calcification (arrow); C, mild adipose tissue at the right ventricle (arrow)].
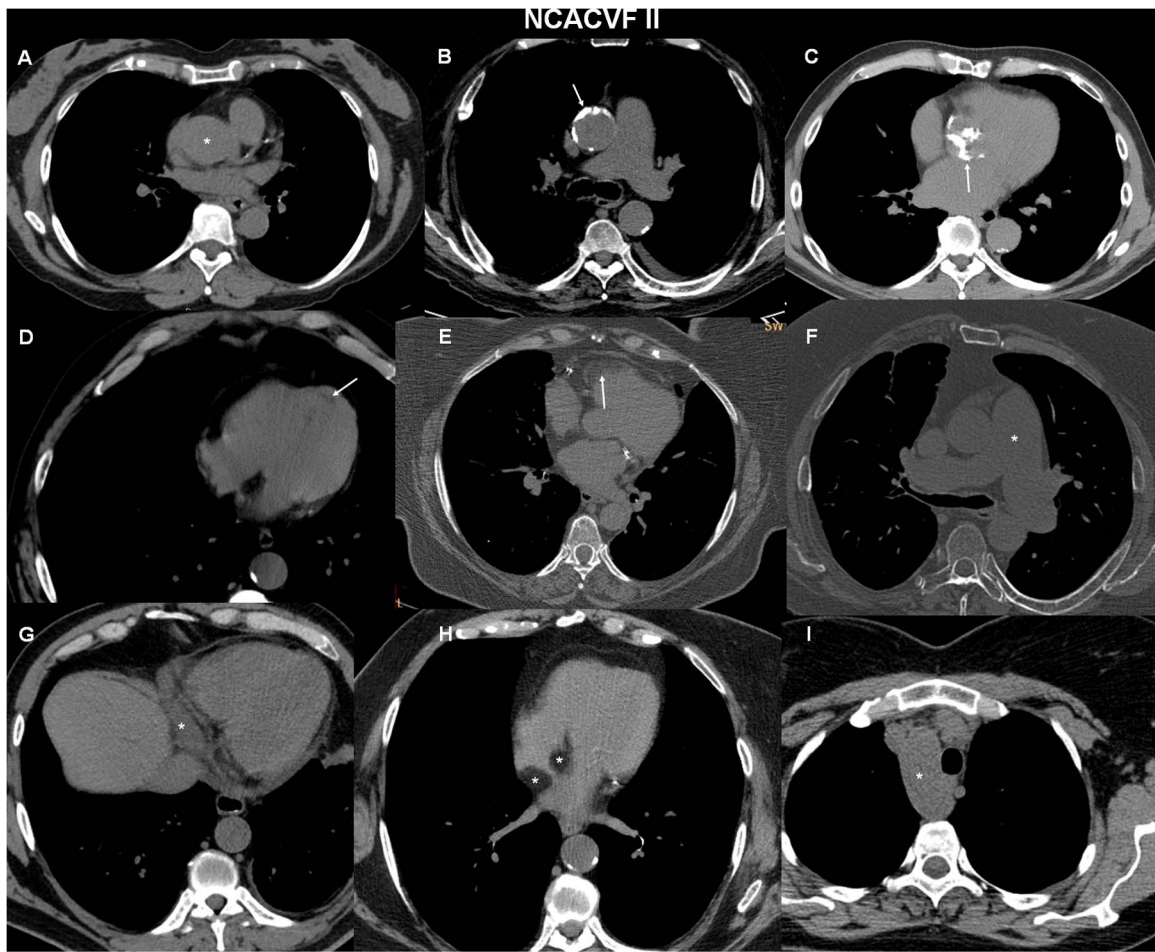
Fig. 2. Examples of NCACVF II: minor findings [A, mild aortic dilatation (*); B, diffuse aortic calcification (arrow); C, diffuse aortic valve calcification (arrow); D, unspecific adipose tissue infiltration of the left ventricle (arrow); E, diffuse adipose tissue in the right ventricular wall (arrow); F, pulmonary artery dilatation (*); G, mild pericardial effusion (*); H, lipomatous *hypertrophy* of the interatrial septum (*); I, right aortic arch (*)].

All procedures performed were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments. Informed consent to undergo thoracic CT scan was obtained from all individual participants included in the study. A separate Committee approval was obtained for habeas data waive and for corroboration of the occurrence of death.

2.3. Statistical analysis

Results are expressed as means ± standard deviation for
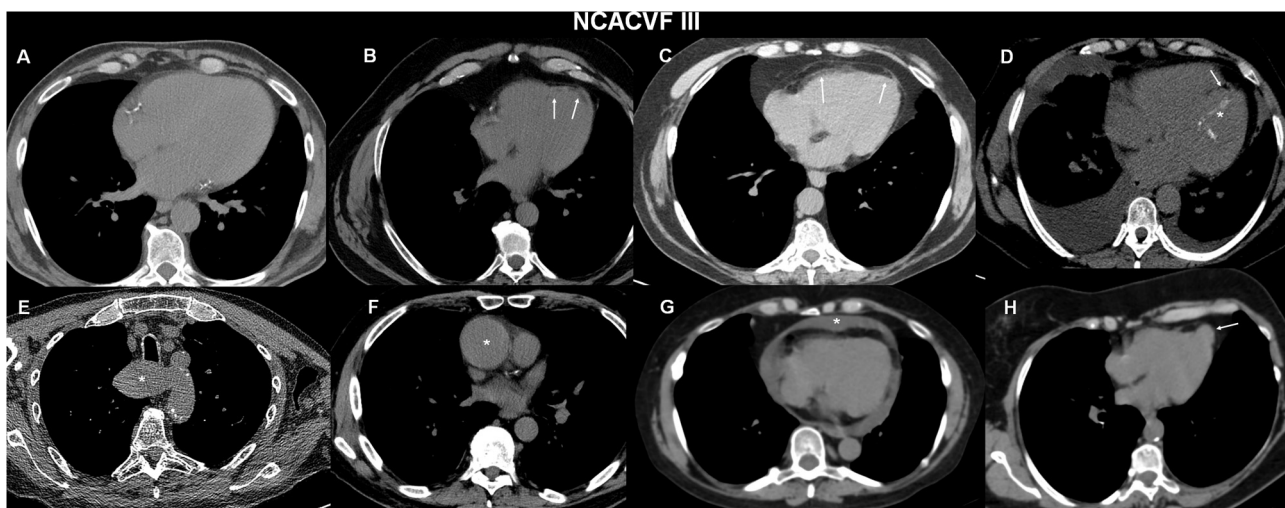
Fig. 3. Examples of NCACVF III: major findings [A, cardiomegaly; B, lipomatous metaplasia of the left ventricular anterior wall (chronic infarct, arrows); C diffuse adipose tissue in the right ventricular wall and regions of the left ventricular apex (arrows); D, intraventricular partially calcified mass (*) in a patient with apical lipomatous metaplasia (chronic myocardial infarction, arrow); E, aneurysm of an aberrant right subclavian artery (*); F aortic aneurysm (*); G moderate to severe pericardial effusion (*); H, left ventricular apical aneurysm (arrow)].

continuous variables with normal distribution, or median (interquartile range) for non-Gaussian distribution. Categorical variables are reported as frequencies and percentages. Differences between groups were assessed using the chi-square test for categorical variables, and independent-samples T-test and one-way analysis of variance for continuous variables, with Kruskal-Wallis tests performed for non-parametric analyses. Survival analysis was performed by the Kaplan-Meier method, and differences in survival parameters were evaluated using the log-rank test. Cox proportional hazards regression analysis was used to evaluate the relationship between CACSIS, NCACVF, and all-cause death, summarized by hazard ratios (HR) and associated 95% confidence intervals. Different models were used, adjusting for sex, age, history of malignancy, CACSIS, and NCACVF class. One of the models included the presence of emphysema as a potential confounder. The interobserver variability was explored using Cohen's Kappa coefficient for the assessment of categorical variables (CAC), and intraclass correlation coefficients (using a two-way random effect model, absolute agreement, and average measurement) with 95% confidence intervals for the assessment of the number of vessels with CAC, CACSIS, and NCACVF. Statistical analyses were performed using SPSS software, version 22.0 (IBM SPSS Statistics for Windows, Armonk, NY) and MedCalc Software (Ostend, Belgium). A two-sided p value of less than 0.05 indicated statistical significance.

3. Results

Between August and December 2012, a total of 2.076 non-gated thoracic CT scans were performed in our institution. One hundred and seventy five scans were excluded (102 due to repeated scans, 21 due to the presence of cardiovascular implants, 39 due to revascularization procedures, 6 due to scans in multiple trauma, and 7 were lost to follow-up), leading to a final inclusion of 1.901 patients. The mean age was 57.2 ± 9.9 years and 1042 (54.8%) patients were female (Table 2). Five hundred (26.3%) patients had a history of malignancy, 57 (11.4%) under complete (> 5 year) remission, and 134 (28.8%) with metastasis. The clinical indication for the CT scan and the malignancy history are depicted in Table 3.

Nine hundred and eleven (47.9%) patients showed evidence of at least one segment with CAC. Regarding the number of vessels with CAC, 332 (17.5%), 250 (13.2%), and 329 (17.3%) patients showed CAC in 1, 2, and 3 vessels respectively. The mean CACSIS overall was 1.94 ± 2.86 and 255 (13.4%) patients had evidence of extensive calcification (CACSIS > 5). Regarding the presence of NCACVF, only 62 (3.3%) had major findings, whereas 1635 (86%) had none or minimal findings (Figs. 1–3).

Table 3
Clinical presentation and malignancy history.

	N(%)
Clinical presentation (n = 1901)	
Suspected malignancy (%)	288 (15.1%)
Known malignancy (%)	426 (22.4%)
Lung disease (non-malignant) (%)	504 (26.5%)
Respiratory symptoms of unknown etiology (%)	449 (23.6%)
Non-respiratory pathology (non-malignant) (%)	125 (6.6%)
Non-respiratory symptoms of unknown etiology (%)	109 (5.7%)
Malignancy history (n = 500)	
Lung (%)	137 (27.4%)
Breast (%)	100 (20.0%)
Colorectal (%)	53 (10.6%)
Kidney (%)	55 (11.0%)
Other (%)	155 (31.0%)
Complete Remission (%)	57 (11.4%)
Metastasic (%)	134 (28.8%)

In order to address the degree of intricacy of CAC assessment, a radiologist (CC) re-assessed thirty randomly selected examinations and calculated the time spent for each measurement. In this regard, CAC assessment was significantly faster than the evaluation of the number of vessels with CAC and CACSIS, respectively (5.2 ± 2.1 s vs. 7.0 ± 1.3 s vs. 8.7 ± 3.2 s, p < 0.0001). Furthermore, we did not identify differences between scanners regarding median CACSIS (p = 0.78).

The mean CACSIS was significantly higher in older patients [35–49 years, CACSIS 0.4 ± 1.2; 50–64 years, CACSIS 1.8 ± 2.6; 65–75 years, CACSIS 3.3 ± 3.3 (p < 0.0001)]. Among the group under 50 years old, 70 (15.7%) patients had evidence of CAC and 8 (1.8%) patients showed a CACSIS > 5.

After a median follow-up of 3.7 (3.5–3.9) years, 217 (11.4%) deaths occurred, 158/500 (31.6%) in patients with a history of malignancy and 59/1401 (4.2%) in patients without history of malignancy (p < 0.0001). In the overall population, survival rates were significantly lower in patients with malignancy history (p < 0.0001, log rank). The presence of any CAC, number of vessels with CAC, CACSIS extension, and NCACVF class were also related to worse survival (Fig. 4). After stratification according to the malignancy history (Fig. 5), the presence of CAC and the CACSIS were related to worse survival only among patients without a history of malignancy CAC (p < 0.0001, log rank). An increasing NCACVF class was related to worse survival independent of the malignancy history. Among patients without malignancy history, death rates were significantly related to

Table 2
Baseline characteristics.

Variable	All (n = 1.901)	Malignancy (n = 500)	Non-malignancy	p value
Male (%)	859 (45.2%)	229 (45.8%)	630 (45.0%)	0.75
Age (years ± SD)	57.2 ± 9.9	58.8 ± 9.4	56.6 ± 10.1	< 0.0001
Death (%)	217 (11.4%)	158 (31.6%)	59 (4.2)	< 0.0001
CAC	911 (47.9%)	264 (52.8%)	647 (46.2%)	0.011
CAC n vessels				0.033
1-vessel (%)	332 (17.5%)	87 (17.4%)	245 (17.5%)	
2-vessel (%)	250 (13.2%)	74 (14.8%)	176 (12.6%)	
3-vessel (%)	329 (17.3)	103 (20.6%)	226 (16.1%)	
CACSIS (mean ± SD)	1.94 ± 2.9	2.30 ± 3.1	1.81 ± 2.7	0.001
CACSIS 0	990 (52.1%)	236 (47.2%)	754 (53.8%)	0.012
CACSIS 1–5	656 (34.5%)	181 (36.2%)	475 (33.9%)	
CACSIS > 5	255 (13.4%)	83 (16.6%)	172 (12.3%)	
NCACVF				0.013
I (none of minimal)	1635 (86.0%)	411 (82.2%)	1224 (87.4%)	
II (minor)	204 (10.7%)	66 (13.2%)	138 (9.9%)	
III (major)	62 (3.3%)	23 (4.6%)	39 (2.8%)	
Emphysema	693 (36.5%)	150 (30.0%)	543 (38.8%)	< 0.0001

CAC refers to coronary artery calcification; SIS refers to segment involvement score; NCACVF refers to non-coronary atherosclerosis cardiovascular findings
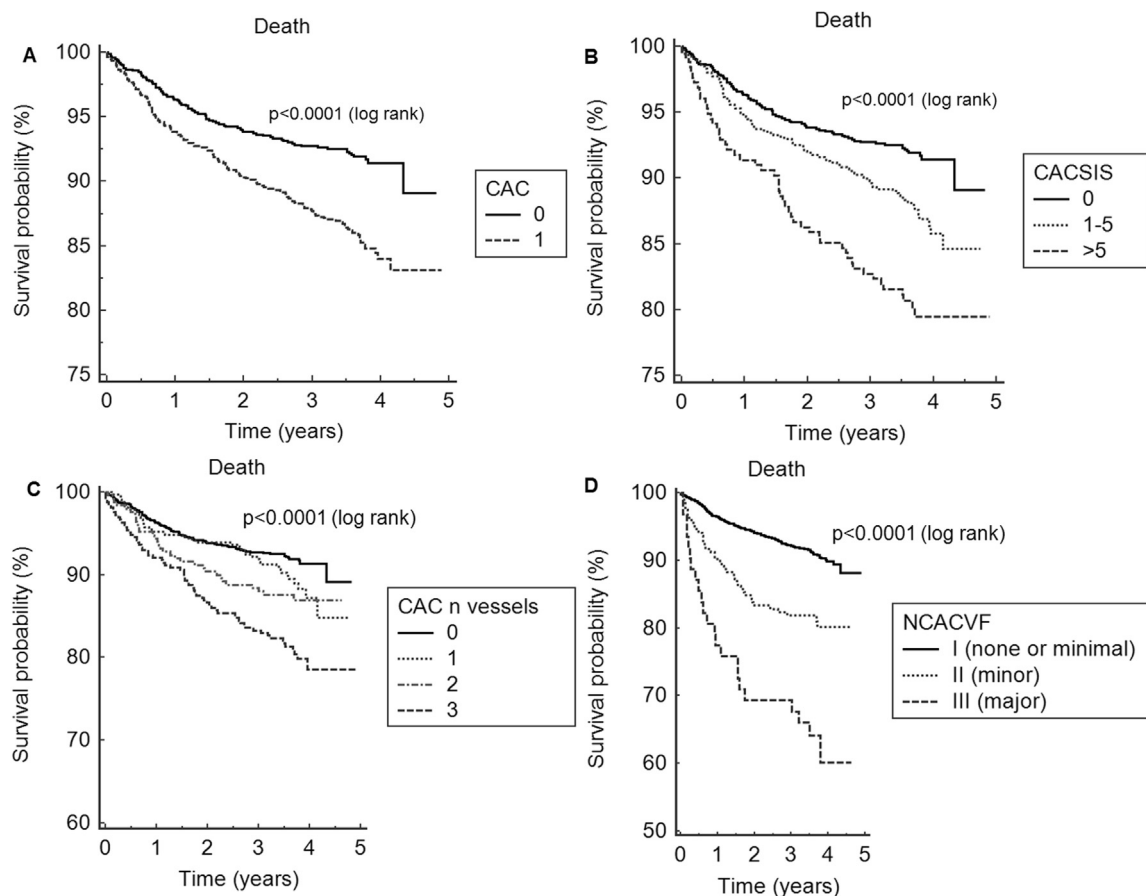
Fig. 4. Unadjusted all-cause Kaplan-Meier survival according to the presence of any coronary artery calcification (CAC), to the CAC segment involvement score (CACSIS), number of vessels with CAC, and to the non-coronary atherosclerosis cardiovascular findings (NCACVF) classification.

the CACSIS and to the NCACVF class (Fig. 6).

3.1. Cox regression analysis

Three different models were built to identify predictors of all-cause mortality. In the overall population (model 1), age [HR 1.03 (95% CI 1.01-1.05), p = 0.001], a history of malignancy [HR 8.04 (95% CI 5.95-10.9), p < 0.0001], and the NCACVF class [HR 1.79 (95% CI 1.45-2.19), p < 0.0001] were identified as independent predictors of death. CACSIS was found an independent predictor of death only among patients without malignancy [no malignancy HR 1.10 (95% CI 1.02-1.20), p = 0.019; with malignancy HR 1.02 (95% CI 0.96-1.08), p = 0.58]. Stratified models according to the history of malignancy and presence of emphysema are depicted in Table 4.

Finally, the age and sex adjusted HR for all-cause mortality of CACSIS > 5 was HR 1.58 (95% CI 1.02-2.45) in the overall population, HR 2.36 (95% CI 1.06-5.23) among patients without malignancy, and HR 1.16 (95% CI 0.67-2.02) among patients with malignancy history. The age and sex adjusted HR of major NCACVF was HR 3.77 (95% CI 2.40-5.91) overall, HR 6.30 (95% CI 2.96-13.43) among patients without malignancy, and HR 2.70 (95% CI 1.53-4.76) among patients with malignancy history (Table 5).

There was an excellent agreement between observers regarding CAC [Kappa 0.95 (95% CI 0.85-1.0), p < 0.0001], number of vessels with CAC [ICC 0.98 (95% CI 0.96-0.99), p < 0.0001]; and CACSIS [ICC 0.98 (95% CI 0.97-0.99), p < 0.0001]. The agreement between observers regarding the NCACVF was good [ICC 0.78 (95% CI 0.57-0.89), p < 0.0001].

4. Discussion

The importance of the assessment of coronary and non-coronary cardiac findings among patients undergoing thoracic CT scans is underscored by the results of the National Lung Screening Trial, where the leading cause of death was cardiovascular illness [20]. Furthermore, CAC outperformed both forced expiratory volume and the extent of pulmonary emphysema for the prediction of all-cause mortality in a cohort of heavy smokers within the Multicentric Italian Lung Detection trial [21].

To the best of our knowledge, this is the first study to address a number of issues related to CAC evaluated during non-gated thoracic CT scans. Our findings can be summarized as follows. Firstly, the presence and extension of CAC was identified as a predictor of all-cause mortality in clinically indicated thoracic CT scans. Secondly, the CAC segment involvement score (CACSIS), evaluated for the first time using non-gated, unenhanced CT scans, was identified as an independent predictor of death. Third, this is the first study of this kind to perform a discriminated analysis according to the history of malignancy. Finally, we demonstrated the presence of major NCACVF as an independent predictor of death irrespective of the history of malignancy.

4.1. Prognostic value of coronary artery calcification measures

CAC is a surrogate of atherosclerosis, being significantly related both to plaque area and to increasing age [22,23]. Numerous studies have consistently identified CAC assessed by gated CT as an independent predictor of death, providing a significant incremental prognostic value over established risk stratification algorithms [1–3]. Particularly, patients without coronary calcifications have a very low
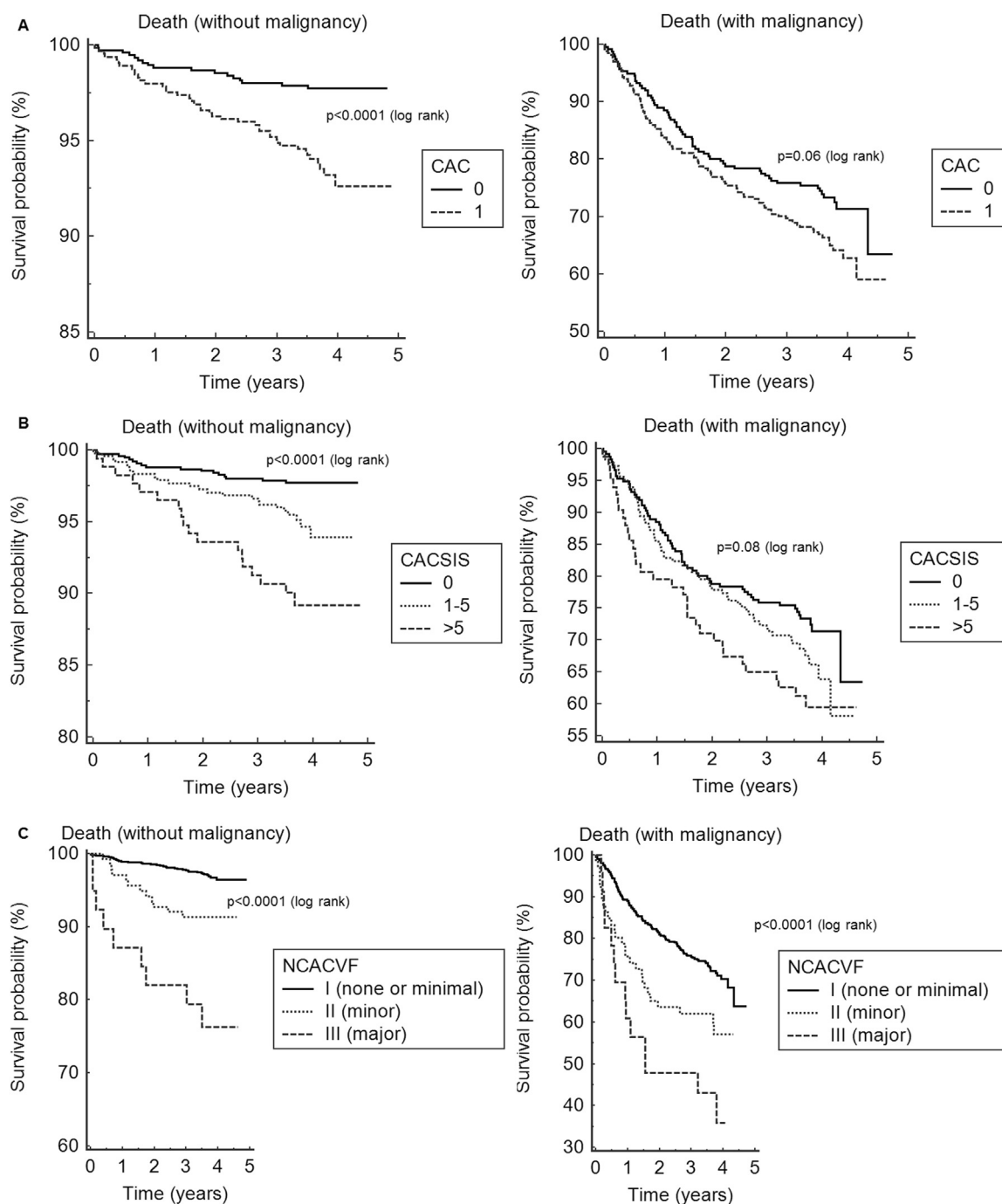
Fig. 5. Unadjusted all-cause Kaplan-Meier survival according to the presence of any coronary artery calcification (CAC), to the CAC segment involvement score (CACSIS), and to the non-coronary atherosclerosis cardiovascular findings (NCACVF) classification. Results are discriminated between patients without malignancy (left) and with a history of malignancy (right).

incidence of events at long-term follow-up, providing a safety window of at least 5 years among asymptomatic low to intermediate risk patients, with a 0.10% annual risk of events [4,24].

A number of studies have demonstrated that the assessment of CAC by means of non-gated thoracic CT scans is not only feasible and correlates well to gated examinations, but also has shown to provide a significant prognostic value [9–13,21,25]. Nonetheless, most of these studies consisted of population-based lung cancer screening trials performed using low-dose CT scans, while only one has reported the prognostic value using standard thoracic CT scans. Of note, the study of Hughes-Austin et al. evaluated standard CT scans using 6 mm reconstructions and comprised a completely different population compared to the present study, including predominantly asymptomatic and

self-referred individuals for whole-body CT scans [10]. On the contrary, ours is the first study to evaluate the prevalence and prognostic value of CAC using standard CT scans at 1 mm slice thickness reconstructions, which is the standard reconstruction protocol of thoracic CT scans in our institution. Importantly, our study comprised all-comers to a standard thoracic CT scan in a tertiary imaging clinic, thus representing a population more comparable to the "real world" clinical practice. Furthermore, we did not identify differences in the extension of CACSIS between scanner generations (from 16-slice to 256-slice). In this setting, survival rates were significantly lower in patients with any CAC, and were also associated to the number of vessels with CAC, and to the CACSIS extension.

To date, there is not a consensus on whether to report CAC and non-

Fig. 6. Death rates of patients with or without a history of malignancy according to the CACSIS (A) and the NCACVF class (B).
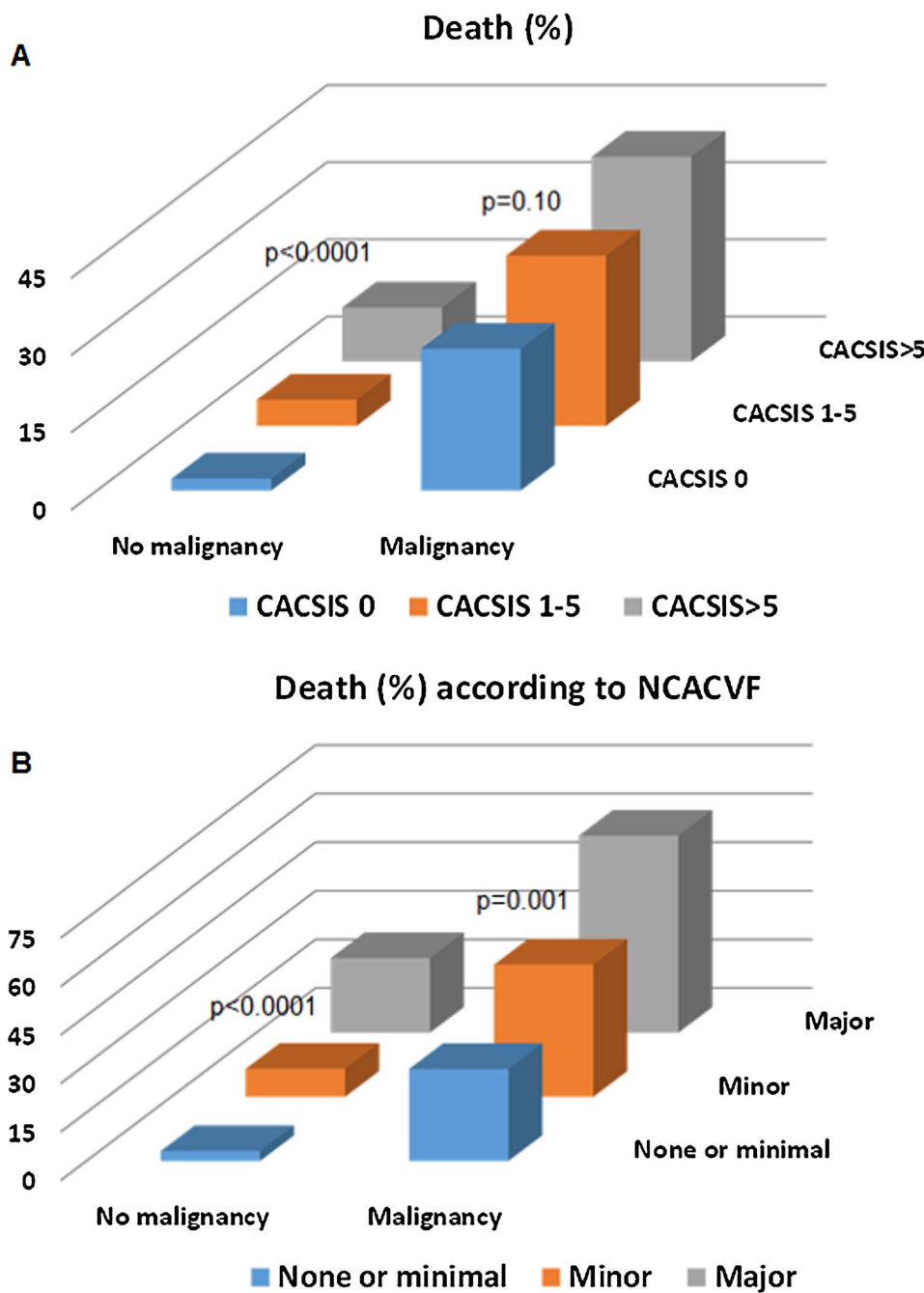
coronary cardiovascular findings on low-dose or standard thoracic CT scans. The Agatston score has been extensively validated on gated CT scans, and appears to be also adequate for non-gated CT scans [7,8,10,11]. Assessment of CAC during non-gated standard thoracic CT might potentially lead to a significant decrease in the number of gated CT scans specifically performed for CAC imaging. Nonetheless, Agatston CAC scoring for non-gated scans requires specific software and might seem impractical in general practice [11].

Shemesh et al. have previously shown that the visual assessment of CAC acquired by low-dose CT screening scans provides an incremental prognostic value over sex, age, and smoking status [12].

More recently, Chiles et al. reported data from the National Lung Screening Trial, where they compared three CAC scoring methods (overall visual assessment, segmented vessel-specific scoring, and Agatston scoring), and demonstrated that the simplest visual analysis is comparable to Agatston scoring. Such reporting might be universally applied and more enthusiastically embraced by general radiologists [11].

4.2. Prognostic value of non-coronary atherosclerosis measures

A number of studies have explored the prognostic value of non-coronary findings measured during gated CAC scans, yielding rather conflicting findings [26–28]. In the most recent study, non-coronary measures assessed during gated CAC including left atrium size and thoracic aortic calcification have shown to provide incremental prognostic value over CAC and established risk factors [28]. It is noteworthy that these studies have focused in quantitative measures such as thoracic aortic calcification, epicardial adipose tissue volume, and left ventricular and atrial area index. While important, acquaintance of these measures is time consuming and requires specific training. Accordingly, as abovementioned, such reporting will probably fail to be

Table 4
Predictors of all-cause death (Cox regression).

	Model 1	p	Model 2			
	(Overall)		No Malignancy	p	Malignancy	p
Sex	0.99 (0.74–1.32)	0.92	0.72 (0.41–1.25)	0.24	1.13 (0.81–1.59)	0.47
Age	1.03 (1.01–1.05)	0.001	1.08 (1.04–1.12)	< 0.0001	1.01 (0.99–1.03)	0.23
Malignancy	8.04 (5.95–10.9)	< 0.0001				
CACSIS	1.04 (0.99–1.09)	0.103	1.10 (1.02–1.20)	0.019	1.02 (0.96–1.08)	0.58
NCACVF	1.79 (1.45–2.19)	< 0.0001	2.29 (1.57–3.33)	< 0.0001	1.62 (1.26–2.09)	< 0.0001

	Model 3 (with emphysema)			
	No malignancy	p	Malignancy	p
Sex	0.73 (0.42–1.27)	0.27	1.13 (0.80–1.59)	0.50
Age	1.08 (1.04–1.13)	< 0.0001	1.01 (0.99–1.03)	0.23
Emphysema	0.85 (0.50–1.44)	0.54	1.07 (0.76–1.50)	0.70
CACSIS	1.10 (1.02–1.20)	0.017	1.02 (0.96–1.08)	0.61
NCACVF	2.29 (1.57–3.34)	< 0.0001	1.62 (1.26–2.09)	< 0.0001

CAC refers to coronary artery calcification; SIS refers to segment involvement score; NCACVF refers to non-coronary atherosclerosis cardiovascular findings

Table 5
Age and sex adjusted hazard ratio, with 95% confidence intervals, for all-cause mortality.

	Model 1 (Overall)		Model 2			
		p	No malignancy	p	Malignancy	p
CAC	1.25 (0.92–1.71)	0.16	1.46 (0.79–2.70)	0.23	1.13 (0.78–1.65)	0.50
CAC 3 vessels	1.55 (1.12–2.15)	0.008	2.47 (1.39–4.39)	0.002	1.19 (0.80–1.77)	0.40
CACSIS 1–5	1.18 (0.84–1.65)	0.35	1.30 (0.66–2.54)	0.45	1.10 (0.74–1.64)	0.63
CACSIS > 5	1.58 (1.02–2.45)	0.039	2.36 (1.06–5.23)	0.035	1.16 (0.67–2.02)	0.60
NCACVF						
Minor	1.84 (1.29–2.63)	0.001	1.86 (0.96–3.62)	0.067	1.65 (1.09–2.51)	0.019
Major	3.77 (2.40–5.91)	< 0.0001	6.30 (2.96–13.43)	< 0.0001	2.70 (1.53–4.76)	0.001

CAC refers to coronary artery calcification; SIS refers to segment involvement score; NCACVF refers to non-coronary atherosclerosis cardiovascular findings

adopted by radiologists in their routine clinical practice.

We therefore explored the prognostic value of relatively simple, and validated in the case of the segment involvement score, scoring systems for the evaluation of both coronary atherosclerosis and non-coronary atherosclerosis measures. In this regard, a CACSIS > 5 and the presence of CAC in the 3 vessels are straightforward measures that can potentially be easily and readily reported during standard CT scans, and have shown to provide a significant age and sex adjusted prognostic value in our study.

Indeed, for the sake of providing the least complex means to identify patients with extensive coronary atherosclerosis, using the number of vessels with CAC instead of CACSIS might be advocated as a both precise and straightforward surrogate.

Moreover, a NCACVF class III also might appear an unsophisticated means to identify high risk patients regardless of the malignancy history. Though merely hypothesis generating, recognition of these findings among patients with a history of malignancy might potentially aid chemotherapy scheme strategies.

We recognize that despite comparable results have been published between qualitative and quantitative findings, the former analysis might not be as accurate as the quantitative analysis. Notwithstanding, we purposely performed this sort of analysis since we believe that the previous will not likely be encouraged to be incorporated into clinical practice in the context of non-gated standard thoracic CT scans. Our institution has a strong background in cardiovascular CT and local radiologists are trained accordingly, therefore extrapolation of our results to less experienced institutions might be troublesome and deserves further investigation. Given the retrospective nature of the study, and due to the fact that clinical questionnaires of patients undergoing thoracic CT scans in our institution are targeted to the malignancy antecedents, we did not have complete data regarding traditional coronary risk factors. Despite we recognize this as a limitation of the study, it should also be acknowledged that most previous studies exploring the role of CAC for the prediction of all-cause mortality have not reported the history of malignancy, a major drawback considering that this is the strongest predictor of mortality. Furthermore, as aforementioned, CAC has consistently been identified as a predictor of adverse events independent of cardiovascular risk factors. Finally, Social Security death index and Civil Registry databases do not include the cause of death. Therefore, although we provided data regarding malignancy antecedents our models might include mortality not related to cardiovascular disease. Nevertheless, it is worth mentioning that the bias related to death misclassification is not present in all-cause mortality models.

5. Conclusions

In this study including clinically indicated non-gated standard thoracic CT scans, survival rates were associated to the CAC extension among patients without malignancy, and to the NCACVF class independent from the malignancy status. Further studies are required to explore whether the reporting of CAC presence and extension, and potentially of NCACVF, should be incorporated into standard thoracic CT examination reports.

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