Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Clinical Imaging 89 (2022) 49–54

Contents lists available at ScienceDirect

Clinical Imaging

journal homepage: www.elsevier.com/locate/clinimag

Cardiothoracic Imaging

Role of the coronary and non-coronary cardiovascular findings on non-cardiac gated thoracic CT in predicting mortality in SARS-CoV-2 infection

Aziz Inan Celik [a,*], Tahir Bezgin [a], Nart Zafer Baytugan [a], Resit Coskun [b], Muhammet Bugra Karaaslan [c], Metin Cagdas [a]

[a] Department of Cardiology, Gebze Fatih State Hospital, Heart Center, Kocaeli, Turkey
[b] Department of Cardiology, Faculty of Medicine, Hitit University, Corum, Turkey
[c] Department of Cardiology, Faculty of Medicine, Erzincan Binali Yildirim University, Erzincan, Turkey

ARTICLE INFO

Keywords:
SARS-CoV-2 infection
Coronary artery calcification
Non-coronary atherosclerosis cardiovascular findings
Mortality

ABSTRACT

Background: The potential effects of cardiovascular comorbidities on the clinical outcomes in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection remain unclear. Identification of the coronary and non-coronary cardiovascular findings may help to stratify the patients' prognosis. Therefore, we aimed to evaluate the prognostic impact of the coronary and the non-coronary cardiovascular findings in SARS-CoV-2 patients.

Methods: We studied a total of 594 SARS-CoV-2 patients who were hospitalized and performed a non-cardiac gated thoracic computed tomography. Two blinded radiologists assessed the coronary artery calcification segment involvement score (CACSIS) and non-coronary atherosclerosis cardiovascular findings (NCACVF). The baseline characteristics of the patients and CT findings were evaluated according to survival status. Logistic regression analyses were performed to identify the independent predictors of mortality.

Results: At a mean follow-up of 8 (4–12.5) days, 44 deaths occurred (7.4%). Compared to survivors, non-survivors had increased CACSIS [27.3% (CACSIS = 0) vs 25% (CACSIS 1–5) vs 47.7% (CACSIS >5), $p < 0.001$]. Similarly, on NCACVF, non-survivors had much more major findings compared to survivors (29.5% vs. 2.7%, respectively, $p < 0.001$). At multivariable analysis, age ($p = 0.009$), creatinine ($p < 0.001$), hs-cTnI ($p = 0.004$) and NCACVF (HR 1.789; 95% CI 1.053–3.037; $p = 0.031$) maintained a significant independent association with in-hospital mortality.

Conclusion: Our study shows that coronary and non-coronary cardiovascular findings on non-cardiac gated thoracic CT may help to predict mortality in patients with SARS-CoV-2 infection.

1. Introduction

A new enveloped non-segmented RNA coronavirus called severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) leads to a frightening pandemic outbreak [1]. Although most SARS-CoV-2 infection manifests as mild or self-limiting respiratory illness, up to 30% of patients may experience acute respiratory distress syndrome, multiple organ failure, and death [2]. Severe complications more frequently occur in advanced age, male gender, smoking, and patients with any comorbidity, including cerebrovascular disease, chronic obstructive pulmonary disease, chronic kidney disease, cardiovascular disease, cardiac arrhythmia, hypertension, diabetes mellitus, dementia, cancer, and dyslipidemia [3–5]. Thoracic computed tomography (CT) has cornerstone importance in diagnosing SARS-CoV-2 infection and determining the lung involvement that causes morbidity and mortality. Multifocal ground-glass opacities, consolidations, and reticulations close to the visceral pleural surface with a posterior predominant are the typical thoracic CT findings for SARS-CoV-2 pneumonia [6–8].

Coronary artery calcification (CAC) is a marker of coronary atherosclerosis and a crucial cardiac risk predictor [9]. The presence and extension of CAC assessed by cardiac gated computed tomography (CT) and has been widely used as a predictor of major cardiovascular events [10,11]. Except for cardiac gated thoracic CT scans, CAC can be identified and quantified with non-cardiac gated thoracic CT scans. Different

* Corresponding author at: Department of Cardiology, Gebze Fatih State Hospital, Osman Yilmaz Neighborhood, Istanbul Street, 127, Kocaeli, Turkey.
E-mail address: azizinanmd@hotmail.com (A.I. Celik).

https://doi.org/10.1016/j.clinimag.2022.06.002
Received 7 May 2022; Received in revised form 24 May 2022; Accepted 4 June 2022
Available online 9 June 2022

scoring systems are defined to investigate the burden of coronary artery calcification and coronary artery disease risk. Moreover, thoracic CT scans give us much more information beyond the CAC. Non-coronary atherosclerosis cardiovascular findings (NCACVF) such as; aortic, valvular, and myocardial calcifications, myocardial tissue disturbances, pericardial effusion, dilatations, and cardiac anomalies can be identified during non-gated thoracic CT scans. However, their clinical relevance has remained unearthed yet.

This study aimed to investigate the association of CAC, NCACVF, and in-hospital mortality of SARS-CoV-2 patients. To the best of our knowledge, this is the first study to evaluate CAC and NCACVF in predicting mortality in SARS-CoV-2 patients using non-cardiac gated thoracic CT scans.

2. Methods

2.1. Study population

We conducted a single-center, retrospective, observational study between December 2020 and February 2021. All consecutive patients who were diagnosed with SARS-CoV-2 infection and underwent non-cardiac gated thoracic CT scans on admission were incorporated into the study. In this study, we included solely hospitalized patients (both service and intensive care unit), and the study's primary endpoint was in-hospital mortality. Patients who had a percutaneous coronary intervention, coronary artery bypass graft surgery, heart valve surgery, aortic endograft, cardiac pacemaker, implantable cardiac defibrillator implantation, or multiple trauma were excluded.

The baseline demographic and clinical characteristics and laboratory findings on admission were obtained from the hospital's electronic database system. Complete blood counts and biochemical parameters, including blood glucose, creatinine, aspartate aminotransferase (AST) and alanine aminotransferase (ALT), c-reactive protein (CRP), ferritin, and high-sensitive cardiac troponin I (hs-cTnI), were procured upon admission. In addition to laboratory data, hemodynamic parameters such as; heart rate, systolic blood pressure, oxygen saturation, and fever were also recorded. According to the Declaration of Helsinki, the present study was reviewed and approved by the Republic of Turkey Ministry of Health and Local Ethics Committee (Ethics Committee of the Kocaeli Derince Training and Research Hospital).

2.2. Thoracic CT imaging and data analysis

Thoracic CT imaging was performed using a 64-slice CT scanner (Aquilion 64, Toshiba Medical Systems, Japan) with 3-mm reconstructed slice thickness. All patients were examined in the supine position, end of inspiration, and hands raised by the side. Tube current and tube voltages were 300 mA, 120 kV, respectively, and gantry rotation time 0.4 s. All images were unenhanced and non-gated.

Thoracic CT scans were reviewed by two independent radiologists blinded to the study with experience in cardiovascular imaging. PACS software (Carestream Vue PACS version 11.4, New York, USA) was used to analyze the data. Axial, coronal, and sagittal planes were used to assess CAC and NCACVF. The CAC was classified by the 16-segment modified American Heart Association classification [12], called coronary artery calcification segment involvement score (CACSIS). The CACSIS represented the total numbers of involved segments and classified according to the points 0 to 16. CACSIS 0: Absence of the coronary calcification, CACSIS 1–5: Mild coronary calcification, CACSIS >5 Extensive coronary calcifications (Fig. 1). Patients were classified according to the number of vessels with any calcification, and the left main coronary artery was considered as two-vessel CAC. Thoracic CT of the patients was analyzed pursuant to NCACVF and stratified as; none or minimal; minor or major findings (the criterias of the NCACVF were given in Table 1, and image examples were given in Fig. 2).

2.3. Statistical analysis

Data were analyzed using SPSS 22.0 version (SPSS Inc., Chicago, Illinois). Descriptive statistics were given as mean ± standard deviation and median with minimum-maximum values for continuous variables depending on their distribution. Numbers and percentages were used for

Table 1
Non-coronary atherosclerosis cardiovascular findings classification (NCACVF) [27]

None or minimal	No cardiovascular findings or mild thoracic aorta calcification or aortic valve calcification or mild right ventricular adipose tissue or minimum recess or posterior pericardial fluid.
Minor	Calcification of the thoracic aorta and cardiac valves; or diffuse aortic or cardiac valve calcification; or aortic dilatation; 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.
Major	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.

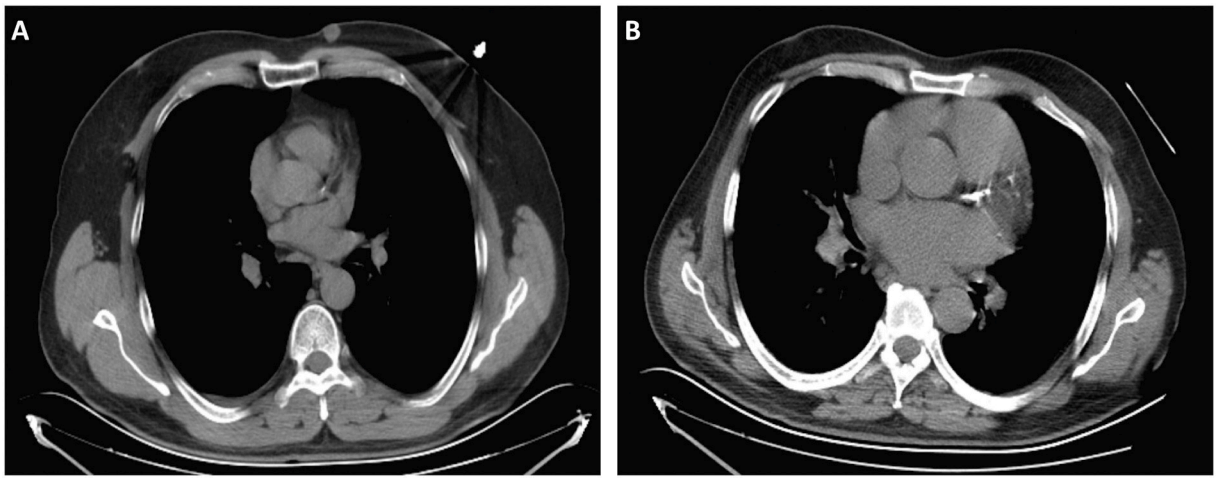

Fig. 1. Examples of coronary calcifications. A: Mild coronary calcification. B: Extensive coronary calcification.

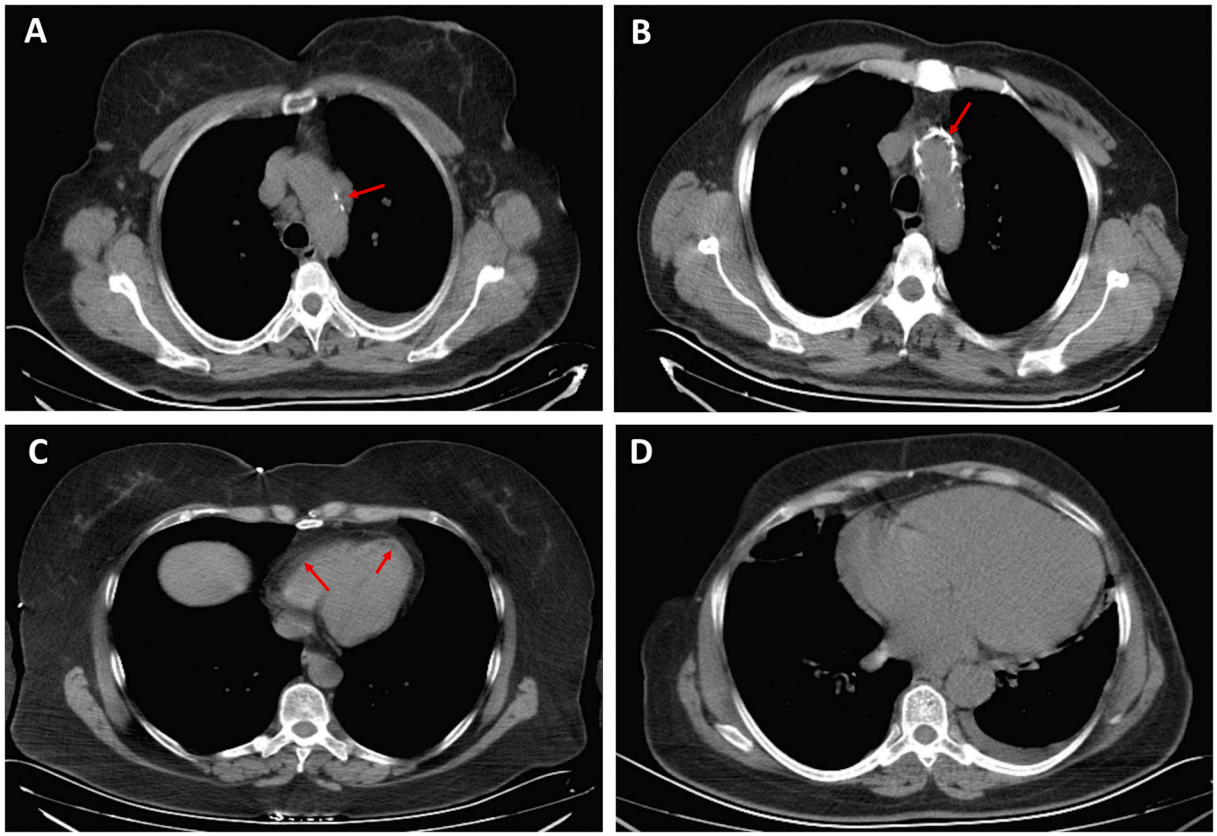

Fig. 2. Examples of the non-coronary atherosclerosis cardiovascular findings. A: Mild thoracic aorta calcification (arrow). B: Diffuse aortic calcification (arrow). C: Lipomatous metaplasia of the left ventricular anterior wall and diffuse adipose tissue in the right ventricular wall and regions of the left ventricular apex (arrows). D: Cardiomegaly.

categorical variables. The normal distribution of the numerical variables was analyzed by the Shapiro-Wilk, Kolmogorov-Smirnov, and Anderson-Darling tests. The Independent Samples *t*-test was used in comparing two independent groups where numerical variables had a normal distribution. The One-Way ANOVA test compared more than two independent groups where numerical variables had a normal distribution. For variables without normal distribution, the Kruskal Wallis test was applied. Pearson Chi-Square and Fisher's Exact tests were used to compare the differences between categorical variables. For the analyses in which parametric tests were used, the differences between the groups were evaluated with the Tukey or LSD tests when data was homogeneous based on its distribution. Cox regression analysis was performed to assess the relationship between CACSIS, NCACVF, and death as the outcome, summarized by hazard ratios (HR) and associated 95% confidence intervals. Survival analysis was performed by the Kaplan-Meier method, and differences in survival parameters were evaluated using the log-rank test. The significance level (*p*-value) was set at 0.05 in all statistical analyses.

3. Results

3.1. Baseline characteristics

A total of 594 SARS-CoV-2 patients hospitalized and had a non-cardiac gated thoracic CT performed were enrolled in the study. Five hundred fifty patients were discharged from the hospital, and 44 patients were deceased (7.4%) in the hospital. Baseline characteristics and clinical and laboratory parameters of the study population are demonstrated in Table 2 according to survival status (survival and non-survival). The median age was 45 (34–58), and 263 patients (44.3%) were female. One hundred eighty-six patients (31.3%) were smokers, 82 patients (13.8%) had diabetes mellitus, 141 patients (23.7%) had hypertension, 14 patients (2.4%) had congestive heart failure and 69 patients (11.6) had chronic obstructive pulmonary disease.

3.2. Comparison of survivors and non-survivors

Non-survivors were older [median age 72 (63–80) vs 44 (33–55), $p < 0.001$] and had a higher prevalence of smoking (43.2% vs 30.4%, $p < 0.001$), hypertension (50% vs 21.6%, $p < 0.001$), cognestive heart failure (CHF) (18.2% vs 1.1%, $p < 0.001$), and chronic obstructive pulmonary disease (COPD) (34.1% vs 9.8%, $p < 0.001$).

According to the hemodynamic parameters and laboratory assays on admission there were significant differences between two groups. Compared to survivors, non-survivors had higher fever [38.0 (37.7–38.6) vs 37.0 (36.6–38) ^{o}C, $p = 0.002$] and lower systolic blood pressure [105 ± 17 mmHg vs 115 ± 9 mmHg, $p = 0.01$]. On laboratory examination, non-survivors had higher fasting blood glucose [134 (106–235) vs 97 (87–115) mg/dL, $p < 0.001$], creatinine [1.2 (0.8–2.2) vs 0.8 (0.7–0.9) mg/dL, $p < 0.001$], aspartate aminotransferase (AST) [31.5 (23–46.5) vs 22 (17–30) U/L, $p < 0.001$], c-reactive protein (CRP) [93.2 (43.8–192) vs 7.4 (2–22.6) mg/L, $p < 0.001$], ferritin [401 (153.5–585) vs 98 (41–220.1) ng/mL, $p < 0.001$], white blood cell count (11.8 ± 6.5 vs 6.6 ± 2.6 × 10 [3]/μl, $p < 0.001$], and high-sensitivity cardiac troponin I (hs-cTnI) [30 (9–132) vs 1 (0.1–3) pg/mL, $p < 0.001$]. However, hemoglobulin levels (11.5 ± 2.6 vs 13.6 ± 1.6 g/dL, $p < 0.001$) were lower in non-survivors, significantly.

3.3. Analysis of the thoracic CT

Patients were evaluated according to CACSIS and NCACVF. Compared to survivors, non-survivors had increased coronary

Table 2
Baseline characteristics of the patients admitted with SARS-CoV-2 infection.

		Survivors ($n = 550$)	Non-survivors ($n = 44$)	Total ($n = 594$)	p value
Age		44 (33–55)	72 (63–80)	45 (34–58)	<0.001
Gender (Female), n (%)		243 (44.2)	20 (45.5)	263 (44.3)	0.870
Smoking, n (%)		167 (30.4)	19 (43.2)	186 (31.3)	<0.001
Diabetes mellitus, n (%)		74 (13.5)	8 (18.2)	82 (13.8)	0.382
Hypertension, n (%)		119 (21.6)	22 (50.0)	141 (23.7)	<0.001
Congestive heart failure, n (%)		6 (1.1)	8 (18.2)	14 (2.4)	<0.001
Chronic obstructive pulmonary disease, n (%)		54 (9.8)	15 (34.1)	69 (11.6)	<0.001
Heart rate on admission, bpm		96 ± 14	109 ± 19	97 ± 14	0.190
Systolic blood pressure on admission, mmHg		115 ± 9	105 ± 17	115 ± 10	0.01
Oxygen saturation on admission, %		96 ± 2	87 ± 8	95 ± 3	<0.001
Fever on admission, °C		37 (36.6–38)	38 (37.7–38.6)	37 (36.6–38)	0.002
Fasting blood glucose, mg/dL		97 (87–115)	134 (106–235)	99 (88–118)	<0.001
Creatinine, mg/dL		0.8 (0.7–0.9)	1.2 (0.8–2.2)	0.8 (0.7–0.9)	<0.001
ALT, U/L		22 (16–35)	22 (15–37.5)	22 (16–35)	0.897
AST, U/L		22 (17–30)	31.5 (23–46.5)	23 (17–31)	<0.001
CRP, mg/L		7.4 (2–22.6)	93.2 (43.8–192)	7.5 (2.2–30.1)	<0.001
Ferritin, ng/mL		98 (41–220.1)	401 (153.5–585)	107.1 (43–262.7)	<0.001
Hemoglobin, g/dL		13.6 ± 1.6	11.5 ± 2.6	13.4 ± 1.8	<0.001
White blood cell count, x10 [3]/μl		6.6 ± 2.6	11.8 ± 6.5	7.0 ± 3.3	<0.001
Platelet count, x10 [3]/μl		220 (178–269)	194 (155–338)	218 (175–272)	0.374
hs-cTnI, pg/mL		1 (0.1–3)	30 (9–132)	1.3 (0.2–4)	<0.001
CACSIS, n (%)	0	464 (84.4)	12 (27.3)	476 (80.1)	<0.001
	1–5	59 (10.7)	11 (25)	70 (11.8)	
	>5	27 (4.9)	21 (47.7)	48 (8.1)	
NCACVF, n (%)	None or minimal	438 (79.6)	12 (27.3)	450 (75.8)	<0.001
	Minor	97 (17.6)	19 (43.2)	116 (19.5)	
	Major	15 (2.7)	13 (29.5)	28 (4.7)	
Follow-up (day)		5 (3–7)	8 (4–12.5)	5 (3–8)	<0.001

Abbreviations: ALT: Alanine aminotransferase, AST: Aspartate transaminase, CRP: C-reactive protein, hs-cTnI: High-sensitivity cardiac troponin I, CACSIS: Coronary artery calcification segment involvement score, NCACVF: Non-coronary atherosclerosis cardiovascular findings classification.

calcification burden and this was reflected to CACSIS [27.3% (CACSIS = 0) vs 25% (CACSIS 1–5) vs 47.7% (CACSIS >5), $p < 0.001$]. Regarding to NCACVF, 13 (29.5%) patients had major findings in non-survivors group, while only 15 (2.7%) patients had major findings in the survivors group ($p < 0.001$). ROC analysis revealed that CACSIS ≥1 predicted in-hospital mortality with a sensitivity of 72.7% and specificity of 84.3% (AUC: 0.805, 95% CI: 0.771–0.836; $p < 0.001$) and NCACVF major findings predicted in-hospital mortality with a sensitivity of 72.7% and specificity of 79.6% (AUC: 0.782, 95% CI: 0.747–0.815; p < 0.001).

3.4. Clinical outcomes

After a mean follow-up of 8 (4–12.5) days, in-hospital mortality ensued in 44 (7.4%) patients. The vast majority of deceased patients were in the intensive care unit [34 patients (77.3%)]. Table 3 and Table 4 demonstrated the univariable and multivariable Cox regression analysis for factors associated with in-hospital mortality. In addition to the Cox regression model, Kaplan-Meier analysis was performed to evaluate the survival according to CACSIS and NCACVF.

Table 3 showed age (HR 1.046; 95% CI 1.016–1.076; $p = 0.002$), creatinine (HR 1.468; 95% CI 1.182–1.822; $p = 0.001$), and hs-cTnI (HR 1.050; 95% CI 1.011–1.091; $p = 0.012$) levels were associated with in-hospital mortality. However, CACSIS (HR 1.050; 95% CI 0.578–1.904; $p = 0.874$) was not independently associated with in-hospital mortality, when these variables added to the model.

Table 4 indicated age (HR 1.034; 95% CI 1.008–1.060; $p = 0.009$), creatinine (HR 1.482; 95% CI 1.217–1.804; $p < 0.001$), and hs-cTnI (HR 1.057; 95% CI 1.018–1.098; $p = 0.004$) levels were associated with in-hospital mortality. When added to these variables, NCACVF (HR 1.789; 95% CI 1.053–3.037; $p = 0.031$) pursued independent association with in-hospital mortality. Kaplan-Meier curves showed significant differences in the probability of in-hospital mortality with CACSIS ($p < 0.001$), and NCACVF (p < 0.001) (Fig. 3).

4. Discussion

This study demonstrated that CAC and NCACVF, which can easily be accessible on admission, were associated with the short-term clinical outcome in SARS-CoV-2 patients. When these thoracic CT findings were evaluated after adjusting for significant clinical and laboratory variables, NCACVF was found as independently associated with in-hospital mortality (HR 1.789, $p = 0.031$). However, CACSIS was not significant when the clinical (especially older age) and laboratory parameters were added to the model (HR 1.050, $p = 0.874$).

Atherosclerosis, which results from chronic inflammation and immune system dysregulation, presents an ideal inflammatory environment for SARS-Cov2 infection. Endothelial cells are one of the best targets for the virus, which explains the multiorgan failure in SARS-Cov2 infection. Atherosclerosis is associated with endothelial dysfunction, which may cause aggressive viral replication, inflammatory response, and clinical manifestations. As a result, direct and indirect viral effects may lead to clinical or subclinical myocardial injury [13–15].

Table 3
Independent predictors of in-hospital mortality at Cox regression analysis and the effect of the coronary artery calcification segment involvement score.

Univariable	p value	HR	95% CI		Multivariable	p value	HR	95% CI	
			Lower	Upper				Lower	Upper
Age	<0.001	1.065	1.044	1.086	Age	0.002	1.046	1.016	1.076
Gender (Female)	0.898	1.041	0.566	1.913	–	–	–	–	–
Hypertension	0.097	1.681	0.911	3.100	–	–	–	–	–
DM	0.904	0.953	0.440	2.064	–	–	–	–	–
Smoking	0.415	1.287	0.702	2.359	–	–	–	–	–
COPD	0.013	2.271	1.191	4.328	–	–	–	–	–
CHF	0.001	3.799	1.667	8.656	–	–	–	–	–
Creatinine, mg/dl	<0.001	1.779	1.504	2.104	Creatinine, mg/dl	0.001	1.468	1.182	1.822
hs-cTnI, pg/ml	<0.001	1.071	1.041	1.102	hs-cTnI, pg/mL	0.012	1.050	1.011	1.091
CACSIS	<0.001	2.795	1.949	4.007	CACSIS	0.874	1.050	0.578	1.904

Abbreviations: DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease, CHF: Congestive heart failure, hs-cTnI: High-sensitivity cardiac troponin I, CACSIS: Coronary artery calcification segment involvement score.

Table 4
Independent predictors of in-hospital mortality at Cox regression analysis and the effect of the noncoronary atherosclerosis cardiovascular findings.

Univariable	*p* value	HR	95% CI		Multivariable	p value	HR	95% CI	
			Lower	Upper				Lower	Upper
Age	<0.001	1.065	1.044	1.086	Age	0.009	1.034	1.008	1.060
Gender (female)	0.898	1.041	0.566	1.913	–	–	–	–	–
Hypertension	0.097	1.681	0.911	3.100	–	–	–	–	–
DM	0.904	0.953	0.440	2.064	–	–	–	–	–
Smoking	0.415	1.287	0.702	2.359	–	–	–	–	–
COPD	0.013	2.271	1.191	4.328	–	–	–	–	–
CHF	0.001	3.799	1.667	8.656	–	–	–	–	–
Creatinine, mg/dl	<0.001	1.779	1.504	2.104	Creatinine, mg/dl	<0.001	1.482	1.217	1.804
hs-cTnI, pg/ml	<0.001	1.071	1.041	1.102	hs-cTnI, pg/mL	0.004	1.057	1.018	1.098
NCACVF	<0.001	3.085	2.077	4.580	NCACVF	0.031	1.789	1.053	3.037

Abbreviations: DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease, CHF: Congestive heart failure, hs-cTnI: High-sensitivity cardiac troponin I, NCACVF: Noncoronary atherosclerosis cardiovascular findings classification.

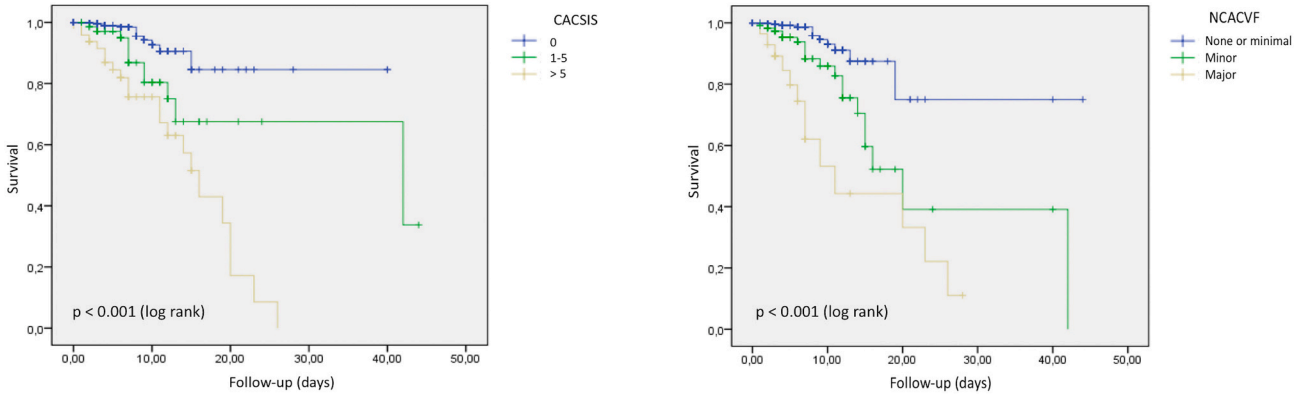

Fig. 3. Kaplan-Meier survival according to the presence of any coronary artery calcification, to the coronary artery calcification segment involvement score, and the non-coronary atherosclerosis cardiovascular findings classification.

The essential coronary artery findings are varying degrees of CAC, which was detected on thoracic CT scans. CAC is a well-known marker to determine individuals for high cardiovascular risk [16,17]. ECG-gated thoracic CT is the best option for CAC examination. However, some studies demonstrated that CAC assessment via non-gated thoracic CT scans is feasible and provided a significant prognostic value [18–20]. In the SARS-CoV-2 pandemic, non-gated thoracic CT is the preferred imaging modality in most emergency departments. Subclinical CAC on the thoracic CT was associated with a worse prognosis in SARS-CoV-2 patients [21,22].

Gupta et al. demonstrated that SARS-CoV-2 patients with CAC were more likely to require intubation and had higher mortality rates than those without CAC. Also, increasing CAC and the number of affected arteries were associated with mortality [21]. Similar results were found by Dillinger et al., in which the presence and extent of CAC were associated with worse outcomes [22]. On the other hand, CAC burden and myocardial injury can be affected by many conditions. In a recent study, Bergström et al. included 25.182 individuals without known coronary artery disease and subclinical coronary artery atherosclerosis evaluated using coronary computed tomography angiography. They found that coronary atherosclerosis is more common in older individuals and male gender [13]. This close relationship between advanced age and CAC may also cause conflicting results in determining the mortality of SARS-CoV-2 patients. A study conducted by Ferrante et al. reported that patients with myocardial injury had a higher prevalence of a CAC. However, the CAC did not emerge as a predictor of myocardial injury and mortality in the multivariable logistic regression analysis. Advanced age and lower estimated glomerular filtration rate were independent predictors for both myocardial injury and death [23]. Our study found that the CAC was significantly higher in the deceased group and had an association with in-hospital mortality by univariable analysis only. However, when we added the variables into the Cox proportional-hazards model, the CAC didn't provide incremental value for in-hospital mortality independently.

Coronary artery calcification alone provides limited information about the cardiovascular system, including myocardium, pericardium, great vessels, and heart valves. Some studies have explored the prognostic value of non-coronary findings measured during CAC scans [24–26]. These studies focused on thoracic aortic calcification, epicardial adipose tissue, left ventricular and left atrial size [26]. Rodriguez-Granillo et al. designed a new scoring system that includes almost whole cardiovascular findings on thoracic CT (Table 1) [27]. These findings were stratified according to cardiovascular involvement and were investigated for the prognostic value on malignancy. They found that major NCACVF findings were significantly associated with mortality in patients with malignancy and without malignancy. However, few studies were performed about the relationship between cardiovascular involvement and SARS-CoV-2 infection mortality, except CAC. The study by Giannini et al. is one of them, and they found that aortic valve and thoracic aorta calcifications on non-gated thoracic CT were significantly related to the SARS-CoV-2 patient mortality. Another study conducted by Slipczuk et al. indicated that epicardial adipose tissue thickness is a robust independent predictor of mortality from SARS-CoV-2 infection [28]. When the current literature was reviewed, it was seen that only a few specific findings in thoracic CT scans, other than CAC, were studied in SARS-CoV-2 patients. Therefore, our study used the NCACVF scoring system, which includes the broadest cardiovascular findings. Major NCACVF score was associated with in-hospital mortality, and this result showed a significant prognostic value.

4.1. Limitations of the study

The present study has several limitations. First, this study was a retrospective single-center study, and the results were retrospectively evaluated and adjudicated. Secondly, we only included the hospitalized patients; therefore, our study sample couldn't represent the SARS-CoV-2 population. Thirdly, CAC couldn't reach a significant statistical value to predict in-hospital mortality in our study, but the main reason may be the small sample size. Fourthly, although experienced radiologists evaluated the thoracic CT images (both CACSIS and NCACVF), scores were not quantitatively analyzed. Finally, we investigated only the in-hospital mortality of the SARS-CoV-2 patients. However, we didn't examine the other adverse events, including stroke, acute myocardial infarction, venous thromboembolism, and acute limb ischemia.

5. Conclusion

Non-cardiac gated thoracic CT scan is a cornerstone diagnostic tool for pulmonary involvement in SARS-CoV-2 infection. Apart from pulmonary parenchyma involvement, it also inholds many findings that can predict the patient's prognosis. In this study, CACSIS and NCACVF, obtained from non-cardiac gated thoracic CT scans, showed that these scores may help predict in-hospital mortality easily and quickly. Further studies are needed to explore more comprehensive and detailed scores in foreseeing SARS-CoV-2 infection damage.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

None.

References

1. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z, Yu T, Xia J, Wei Y, Wu W, Xie X, Yin W, Li H, Liu M, Xiao Y, Gao H, Guo L, Xie J, Wang G, Jiang R, Gao Z, Jin Q, Wang J, Cao B. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497–506.
2. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, Zhao Y, Li Y, Wang X, Peng Z. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA 2020;323:1061–9.
3. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L, Wei Y, Li H, Wu X, Xu J, Tu S, Zhang Y, Chen H, Cao B. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054–62.
4. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. JAMA 2020;323:1239–42.
5. Izcovich A, Ragusa MA, Tortosa F, Lavena Marzio MA, Agnoletti C, Bengolea A, Ceirano A, Espinosa F, Saavedra E, Sanguine V, Tassara A, Cid C, Catalano HN, Agarwal A, Foroutan F, Rada G. Prognostic factors for severity and mortality in patients infected with COVID-19: a systematic review. PLoS One 2020;15(11):e0241955. https://doi.org/10.1371/journal.pone.0241955.
6. Ding X, Xu J, Zhou J, Long Q. Chest CT findings of COVID-19 pneumonia by duration of symptoms. Eur. J. Radiol. 2020:109009. https://doi.org/10.1016/j.ejrad.2020.109009.
7. Zhao W, Zhong Z, Xie X, Yu Q, Liu J. Relation between chest CT findings and clinical conditions of coronavirus disease (COVID-19) pneumonia: a multicenter study. AJR 2020;214:1072–7. https://doi.org/10.2214/ajr.20.22976.
8. Lei J, Li J, Li X, Qi X. CT imaging of the 2019 novel coronavirus (2019-nCoV) pneumonia. Radiology 2020;295(1):18. https://doi.org/10.1148/radiol.2020200236.
9. Budoff MJ, Shaw LJ, Liu ST, Weinstein SR, Mosler TP, Tseng PH, Flores FR, Callister TQ, Raggi P, Berman DS. Long-term prognosis associated with coronary calcification: observations from a registry of 25,253 patients. J Am Coll Cardiol 2007;49:1860–70. https://doi.org/10.1016/j.jacc. 2006.10.079.
10. Detrano R, Guerci AD, Carr JJ, Bild DE, Burke G, Folsom AR, Liu K, Shea S, Szklo M, Bluemke DA, O'Leary DH, Tracy R, Watson K, Wong ND, Kronmal RA. Coronary calcium as a predictor of coronary events in four racial or ethnic groups. New Engl J Med 2008;358(13):1336–45.
11. Sarwar A, Shaw LJ, Shapiro MD, Blankstein R, Hoffmann U, Cury RC, Abbara S, Brady TJ, Budoff MJ, Blumenthal RS, Nasir K. Diagnostic and prognostic value of absence of coronary artery calcification. JACC Cardiovasc Imaging 2009;2(6):675–88.
12. Min JK, Shaw LJ, Devereux RB, Okin PM, Weinsaft JW, Russo DJ, Lippolis NJ, Berman DS, Callister TQ. Prognostic value of multidetector coronary computed tomographic angiography for prediction of all-cause mortality. J Am Coll Cardiol 2007;50(12):1161–70.
13. Bergström G, Persson M, Adiels M. Prevalence of subclinical coronary artery atherosclerosis in the general population. Circulation 2021;144(12):916–29. https://doi.org/10.1161/CIRCULATIONAHA.121.055340.
14. Nishiga M, Wang DW, Han Y, Lewis DB, Wu JC. COVID-19 and cardiovascular disease: from basic mechanisms to clinical perspectives. Nat. Rev. Cardiol. 2020:543–58. https://doi.org/10.1038/s41569-020-0413-9.
15. Evans PC, Rainger GE, Mason JC, Guzik TJ, Osto E, Stamataki Z, Neil D, Hoefer IE, Fragiadaki M, Waltenberger J, Weber C, Bochaton-Piallat ML, Bäck M. Endothelial dysfunction in COVID-19: a position paper of the ESC working group for atherosclerosis and vascular biology, and the ESC council of basic cardiovascular science. Cardiovasc. Res. 2020:2177–84. https://doi.org/10.1093/cvr/cvaa230.
16. Miedema MD, Dardari ZA, Nasir K, Blankstein R, Knickelbine T, Oberembt S, Shaw L, Rumberger J, Michos ED, Rozanski A, Berman DS, Budoff MJ, Blaha MJ. Association of coronary artery calcium with long-term, cause-specific mortality among young adults. JAMA Netw Open 2019;2(7):e197440. https://doi.org/10.1001/jamanetworkopen.2019.7440.
17. Kim J, Budoff MJ, Nasir K, Wong ND, Yeboah J, Al-Mallah MH, Shea S, Dardari ZA, Blumenthal RS, Blaha MJ, Cainzos-Achirica M. Thoracic aortic calcium, cardiovascular disease events, and all-cause mortality in asymptomatic individuals with zero coronary calcium: the multi ethnic study of atherosclerosis (MESA). Atherosclerosis 2017;257:1–8. https://doi.org/10.1016/j.atherosclerosis.2016.12.012.
18. Hughes-Austin JM, Dominguez 3rd A, Allison MA, Wassel CL, Rifkin DE, Morgan CG, Daniels MR, Ikram U, Knox JB, Wright CM, Criqui MH, Ix JH. Relationship of coronary calcium on standard chest CT scans with mortality. JACC Cardiovasc Imaging 2016;9(2):152–9.
19. Chiles C, Duan F, Gladish GW, Ravenel JG, Baginski SG, Snyder BS, Desjardins SS, Munden RF, DeMello S, NLST Study Team. Association of Coronary artery calcification and mortality in the national lung screening trial: a comparison of three scoring methods. Radiology 2015;276(1):82–90.
20. Jacobs PC, Prokop M, van der Graaf Y, Gondrie MJ, Janssen KJ, de Koning HJ, Isgum I, van Klaveren RJ, Oudkerk M, van Ginneken B, Mali WP. Comparing coronary artery calcium and thoracic aorta calcium for prediction of all-cause mortality and cardiovascular events on low-dose non-gated computed tomography in a high risk population of heavy smokers. Atherosclerosis 2010;209(2):455–62.
21. Gupta YS, Finkelstein M, Manna S, Toussie D, Bernheim A, Little BP, Concepcion J, Maron SZ, Jacobi A, Chung M, Kukar N, Voutsinas N, Cedillo MA, Fernandes A, Eber C, Fayad ZA, Hota P. Coronary artery calcification in COVID-19 patients: an imaging biomarker for adverse clinical outcomes. Clin Imaging 2021;77:1–8.
22. Dillinger JG, Benmessaoud FA, Pezel T, Voicu S, Sideris G, Chergui N, Hamzi L, Chauvin A, Leroy P, Gautier JF, Sène D, Henry P. COVID research Group of Lariboisiere Hospital. Coronary artery calcification and complications in patients with COVID-19. JACC Cardiovasc Imaging 2020;13:2468–70.
23. Ferrante G, Fazzari F, Cozzi O, Maurina M, Bragato R, D'Orazio F, Torrisi C, Lanza E, Indolfi E, Donghi V, Mantovani R, Liccardo G, Voza A, Azzolini E, Balzarini L, Reimers B, Stefanini GG, Condorelli G, Monti L. Risk factors for myocardial injury and death in patients with COVID-19: insights from a cohort study with chest computed tomography. Cardiovasc Res 2020;116(14):2239–46. https://doi.org/10.1093/cvr/cvaa193.
24. Wong ND, Gransar H, Shaw L, Polk D, Moon JH, Miranda-Peats R, Hayes SW, Thomson LE, Rozanski A, Friedman JD, Berman DS. Thoracic aortic calcium versus coronary artery calcium for the prediction of coronary heart disease and cardiovascular disease events. JACC Cardiovasc Imaging. 2009:319–26.
25. Yeboah J, Carr JJ, Terry JG, Ding J, Zeb I, Liu S, Nasir K, Post W, Blumenthal RS, Budoff MJ. Computed tomography derived cardiovascular risk markers, incident cardiovascular events, and all-cause mortality in nondiabetics: the multi-ethnic study of atherosclerosis. Eur J Prev Cardiol 2014:1233–41.
26. Mahabadi AA, Lehmann N, Mohlenkamp S, Pundt N, Dykun I, Roggenbuck U, Moebus S, Jöckel KH, Erbel R, Kälsch H. Heinz nixdorf investigative group. Noncoronary measures enhance the predictive value of cardiac CT above traditional risk factors and CAC score in the general population. JACC Cardiovasc Imaging 2016:1177–85.
27. Rodriguez-Granillo GA, Reynoso E, Capunay C, Garcia-Garcia HM, Carrascosa P. Impact on mortality of coronary and non-coronary cardiovascular findings in non-gated thoracic CT by malignancy status. Eur J Radiol 2017;93:169–77. https://doi.org/10.1016/j.ejrad.2017.05.030.
28. Slipczuk L, Castagna F, Schonberger A, Novogrodsky E, Sekerak R, Dey D, Jorde UP, Levsky JM, Garcia MJ. Coronary artery calcification and epicardial adipose tissue as independent predictors of mortality in COVID-19. Int J Cardiovasc Imaging 2021;37(10):3093–100. https://doi.org/10.1007/s10554-021-02276-2.