



CT coronary artery calcification score as a prognostic marker in COVID-19

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Background: Coronary artery calcification (CA) score has been established as a quantitative imaging biomarker to reflect arteriosclerosis and general vessel status. It is established as an important prognostic factor for coronary heart disease but also for other disease entities. Our aim was to use this imaging marker derived from computed tomography (CT) images to elucidate the prognostic relevance in patients with coronavirus disease 2019 (COVID-19).

Methods: The clinical database was retrospectively screened for patients with COVID-19 between 2020 and 2022. A total of 241 patients (85 female patients, 35.3%) were included into the analysis. CA scoring was performed semiquantitatively on thoracic CT images with the established Weston score.

Results: Overall, 61 patients (25.3%) of the investigated patient sample died. In survivors, the mean CA score was 2.3 ± 3.0 and in non-survivors, it was 4.2 ± 4.1 ($P=0.002$). In univariable regression analysis, CA was associated with 30-day mortality [odds ratio (OR) =1.15; 95% confidence interval (CI): 1.06–1.25, $P<0.001$]. These results were confirmed by the multivariable regression analysis adjusted for age and sex, the CA score predicted 30-day mortality (OR =1.28; 95% CI: 1.08–1.4, $P=0.002$).

Conclusions: CA score is an independent risk factor in COVID-19. As CA scoring can easily be performed by the radiologist, it should be further investigated as an imaging marker in patients with COVID-19 and potentially be translated into clinical routine.

Keywords: Coronary artery calcification score (CA score); computed tomography (CT); coronavirus disease 2019 (COVID-19)

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Introduction

The ongoing coronavirus disease 2019 (COVID-19) pandemic is still globally to this date.

The symptomatology of infected patients is highly

variable. Early on in the first wave of the pandemic, it became evident that most patients only have a mild disease course. Yet, a minority of patients can rapidly suffer from severe or critical illness, leading to the admission to intensive care unit

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or even fatal outcome (1-4). Consequently, the frequency of fatal cases was over 10% in most European countries during the first wave of the pandemic (2). It seems plausible that correct and early prediction of an unfavorable course of COVID-19 can be crucial for patient care (2). Previously identified prognostic factors are older age than 60 years and male sex with hazard ratios of 2.6 for age of 60 years and above and 1.4 for male sex, respectively (5,6). Notably, a short time period between onset of the symptoms and admission to the hospital was also a risk factor. Important comorbidities include cardiovascular diseases comprising chronic heart failure and peripheral vascular disease are also clinical predictors of an unfavorable course (6).

Computed tomography (CT) plays an important role in the diagnostic work up for COVID-19, especially in detection of pulmonary consolidations (7-11). It is acquired without contrast media application, preferably in low-dose technique. Very early during the course of the pandemic, typical, yet unspecific imaging findings for COVID-19 were identified and rapidly reported in the literature (4). Typically described finding comprise peripheral ground-glass opacities involving both lungs (2,12). Other reported imaging signs were vascular enlargement, lower lobe and posterior predilection. In more severe cases, there were also consolidations in the affected lung lobes.

Coronary artery calcification (CA) scoring is commonly utilized to quantify the number of calcified regions of the coronary vessels. The involvement of calcified vessels harbors prognostic relevance especially in patients with

coronary heart disease (13-16). Thus, there was a strong association between CA score and major cardiovascular events in asymptomatic individuals, which highlighted this imaging finding in the literature (13-16).

Moreover, CA was also shown to be a good predictor of general vessel status, which could also be of prognostic relevance in patients with COVID-19, as COVID-19 can also induce cardiac injury. Yet, there are only few reliable data in patients with COVID-19 regarding the prognostic relevance of CA scoring. Moreover, the widely used Agatston score is calculated on cardiac-gated CT images but the more recently developed Weston score can be semiquantitatively calculated on non-gated CT images and, therefore, can be obtained by routine chest CT images, which are used to image patients with COVID-19 (16).

Therefore, the rationale of the present analysis was to investigate the possible prognostic role of CA score in patients with COVID-19. We present this article in accordance with the STROBE reporting checklist (available at <https://jtd.amegroups.com/article/view/10.21037/jtd-23-728/rc>).

Methods

Acquisition of the patient sample

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The retrospective analysis was approved by the Ethics Committee of Otto von Guericke University Magdeburg, Magdeburg, Germany (No. 25/21). Individual consent for this retrospective analysis was waived.

All consecutive patients from the University Hospital of Otto von Guericke University Magdeburg with polymerase chain reaction (PCR)-proven COVID-19 were analyzed between March 2020 and December 2022.

As inclusion criteria were defined: sufficient CT images at the time point of the hospital admission; available clinical data regarding clinical signs, serological parameters and follow up.

Exclusion artifacts were: severe image artifacts, especially at the level of the heart.

Overall, 241 patients (85 female patients, 35.3%) were included into the present study. The median age was 64 years, ranging from 18 to 93 years. The primary end point of the study was the impact of CA on 30-day mortality after diagnosis of COVID-19.

Imaging technique

CT was performed at the time point of the hospital admission

Highlight box

Key findings

- Coronary calcifications defined by computed tomography (CT) is associated with prognosis in patients with coronavirus disease 2019 (COVID-19). The coronary calcification score was associated with 30-day mortality [odds ratio =1.15; 95% confidence interval: 1.06–1.25; P<0.001].

What is known and what is new?

- Cardiovascular risk factors are known to be of prognostic relevance in patients with COVID-19.
- The present study provides the prognostic relevance of coronary calcifications quantified in CT images with a semiquantitative method.

What is the implication, and what should change now?

- The radiologist should report the severity of coronary calcifications in patients with COVID-19 in chest CT images to provide a prognostic imaging finding.

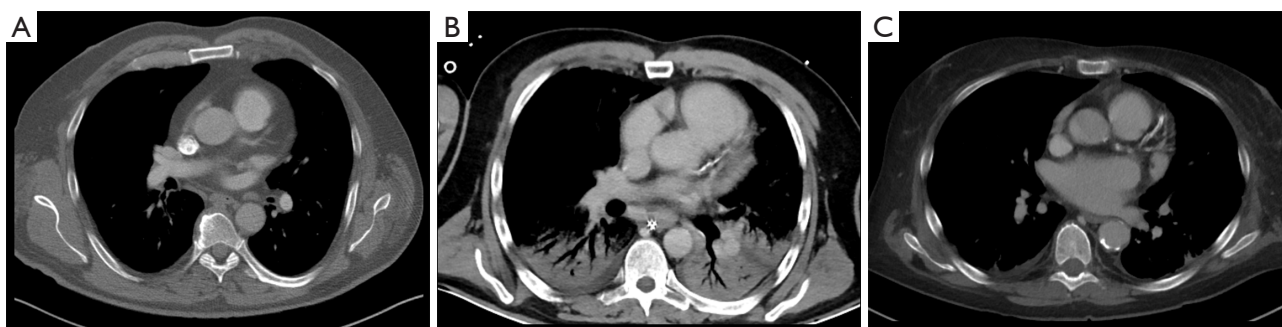


Figure 1 Representative patients of the patient sample. (A) A patient without any calcifications, CA score 0; (B) a patient with moderate calcifications in the left descending artery and circumflex artery, CA score of 5; (C) a patient with severe calcifications of all coronary arteries with a CA score of 12. CA, coronary artery calcification.

for every case without any form of previous treatment.

CT imaging was acquired during clinical routine on a multidetector CT scanner (Siemens Somatom Definition AS+; Siemens Healthcare, Erlangen, Germany). At the beginning of the pandemic, the CT scanner was solely used for patients suspected or confirmed of COVID-19. The CT protocol the following technical parameters: slice thickness 1 mm with 5 mm reconstructions, tube voltage 120 kV, automatic tube current modulation, pitch factor 1.2, and collimation 0.6 mm. *Figure 1* provides representative cases of the investigated cohort for illustration purposes.

CA scoring

Weston scoring was performed by an experienced radiologist with 7 years of experience in cardiovascular radiology. The four coronary arteries comprising of the left main, the left anterior descending, left circumflex and right coronary artery were each scored for the amount of calcification of the vessel. For this purpose, a 4-point scale was used ranging from 0= no calcification to 3= extensive calcifications indicated by blooming artefacts. The exact score was described in detail previously (17). The score can therefore range from 0 to 12.

Statistical analysis

SPSS (IBM SPSS Statistics for Windows. version 225.0: IBM corporation, Armonk, NY, USA) and GraphPad Prism 5 (GraphPad Software, La Jolla, CA, USA) were utilized for the statistics. The figures were created with GraphPad Prism 5. Collected data were first evaluated by means of descriptive statistics). Spearman's correlation coefficient (r)

was performed to elucidate the associations between the CA score and the clinical parameters. Group differences were calculated with Mann-Whitney test and Fisher exact test, when suitable. Uni- and multivariable logistic regression analyses were conducted to identify the associations between CA scoring with 30-day mortality. Receiver operating characteristics (ROC) analysis was performed to elucidate the diagnostic accuracy. The threshold of a P value below <0.05 was used to demonstrate statistical significance.

Results

Clinical signs and scores

Overall, 61 patients (25.3%) of the patient sample died within the 30-day period. *Table 1* provides an overview between survivors and non-survivors.

In survivors, the mean CA score was 2.3 ± 3.0 and in non-survivors, it was 4.2 ± 4.1 , $P=0.002$ (*Figure 2*). CA score correlated with age ($r=0.55$, $P<0.0001$, *Figure 3*).

Furthermore, there was a weak inverse correlation between CA score and duration of intubation ($r=-0.14$, $P=0.03$).

Overall, 94 patients (41.1%) had no presence of calcifications (CA score of 0). In this group, 17 patients died (18.1%). In the group with calcification in the coronary vessels ($n=147$, 58.9%), 43 patients died (29.3%). There was no difference regarding 30-day mortality between these groups ($P=0.13$).

However, CA score was associated with 30-day mortality [odds ratio (OR) =1.15; 95% confidence interval (CI): 1.06–1.25; $P<0.001$; *Table 2*]. This remained statistically significant in multivariable regression analysis adjusted for age and sex with CA score influencing 30-day mortality (OR

Table 1 Comparison between survivors and non-survivors

Parameter	Survivors (n=180)	Non-survivors (n=61)	P value
CA score	2.3±3.0	4.2±4.1	0.002
Age (years)	62.8±15.7	65.9±14.2	0.2
Gender (female)	62	23	0.77*
Need for intubation	60	55	<0.0001*
Intubation duration (hour)	182.4±344.2	376.0±311.9	<0.0001
Need for ICU admission	88	54	0.01*

Data are presented as mean ± standard deviation or number. *, Fisher's exact test. CA, coronary artery calcification; ICU, intensive care unit.

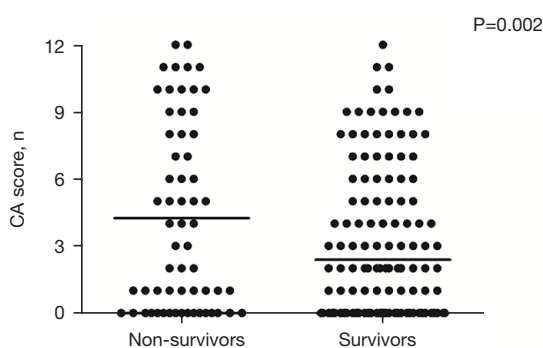


Figure 2 Scatter plot of the survivors and non-survivors according to the CA score. The CA score was statistically significantly lower in surviving patients compared to the non-survivors ($P=0.002$). CA, coronary artery calcification.

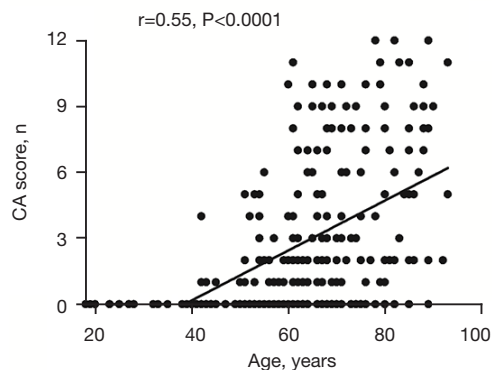


Figure 3 Spearman's correlation analysis between CA score and the patient's age in years ($r=0.55$, $P<0.0001$). CA, coronary artery calcification.

=1.28; 95% CI: 1.08–1.4, $P=0.002$; Table 2).

CA score was not associated with ICU admission with an OR of 0.96 (95% CI: 0.89–1.03, $P=0.31$) and with need for

intubation with an OR of 0.98 (95% CI: 0.91–1.05, $P=0.38$).

ROC analysis

The diagnostic accuracy for CA scoring to predict 30-day mortality was elucidated by ROC analysis. The AUC was 0.62 (95% CI: 0.54–0.71). Employing a threshold value for the CA of 3, a sensitivity of 0.49 with a specificity of 0.74 was achieved.

Discussion

Risk stratification is crucial for patients with COVID-19 in clinical care. Several clinical parameters and different scores were investigated and employed to predict an unfavorable course and mortality in patients with COVID-19 (2,5,6).

During the first months of the pandemic, it was shown that cardiovascular disorders, especially coronary heart disease are risk factors for an unfavorable course of COVID-19 (18).

The present analysis can corroborate these predominantly clinical anamnestic based studies with the significant association between coronary calcification quantified on CT image as an imaging biomarker of coronary heart disease. However, it should be acknowledged that there are also patients with coronary heart disease with no calcified plaques, which are not detected by the current analysis.

That is why the diagnostic gold standard of coronary stenosis is the contrast enhanced cardiac-gated CT imaging.

However, an important aspect of the present study is that the sole presence of calcified plaques identified on CT image can be predictive for an unfavorable outcome in patients with COVID-19. Moreover, it has been shown that plaque quantification is more sensitive to predict

Table 2 Univariable and multivariable regression analysis to predict 30-day mortality

Parameter	Univariable			Multivariable		
	OR	95% CI	P value	OR	95% CI	P value
CA score	1.15	1.06–1.25	<0.001	1.28	1.08–1.4	0.002
Age	1.01	0.99–1.03	0.17	1.009	0.98–1.04	0.58
Gender	1.1	0.61–2.0	0.70	1.2	0.55–2.61	0.63
Need for intubation	18.0	7.3–44.2	<0.001	62.1	7.1–541.3	<0.001
Intubation duration (h)	1.001	1.0–1.002	0.01	1.0	0.99–1.01	0.49
Need for ICU admission	8.0	3.4–18.6	<0.001	0.48	0.05–4.0	0.48

OR, odds ratio; CI, confidence interval; CA, coronary artery calcification; ICU, intensive care unit.

unfavorable outcome than only the sole presence of calcification in a stratified manner (19,20). This can be underlined by the present results.

A previous meta-analysis could already demonstrate the clinical importance of coronary artery calcifications in patients with COVID-19 (21). In this analysis, the data of 5 studies comprising 3,500 patients were investigated and reported an OR of 2.68 (95% CI: 1.78–4.04) (21). Noteworthy, the included patients were of the first wave of the pandemic with a different severity course and outcomes compared to the recent days and the presented results in this study.

Another recent meta-analysis reported an OR of 2.19 (95% CI: 1.36–3.52) for the effect of detectable coronary calcifications on mortality based upon 2,875 patients (22).

The importance of CA scoring was also demonstrated in other diseases.

Until recently, only cardiac-gated CT studies were solely used and investigated for quantification of CA. Due to advances in technology including larger numbers of detectors and faster gantry speeds in current CT scanners, even non-gated studies can provide either semiquantitative scores as the investigated Weston score and even quantitative CA, similar to the established Agatston scoring (17). This was demonstrated by high correlations with cardiac CT gated CT images and was also associated with relevant cardiovascular disease outcomes (17). This is the rationale, why the analysis used in the present study can be assumed as reliable. Notably, this allows to use the low dose CTs performed for the detection of infectious foci in patients with COVID-19 to provide a prognostic imaging marker as a by-product.

The possible prognostic benefit of CA scoring beyond the anamnestic presence of cardiovascular diseases was

demonstrated in several analyses (22–26).

One strength of the present CA scoring is that is semiquantitatively and easily performed in clinical routine. Compared to the standard Agatston score, there is no need for cardiac gated CT, which is not routinely performed for thoracic CT in patients with COVID-19.

Presumably, the inclusion of CA scoring into the proposed risk scores should be further investigated in multivariable analyses. In the current state, the severe overlap between the patient groups cannot justify the benefit in clinical routine.

Notably, even if CA score can be considered as a prognostic imaging marker, it could not change the management of the patient. To this date, a patient with high calcification status of the coronary arteries could not be treated differently compared to a patient with no calcifications.

The present analysis is not free from limitations. First, it is a retrospective study with possible known inherent bias. However, the reader was blinded to the clinical outcome to reduce possible bias. Second, the patient sample is relatively small caused by the single center design. Noteworthy, there might be selection bias, which can have an influence of the present results, as patients without the need for hospital admission were not included into the present analysis. Notably, the present patient sample has a relatively high mortality rate compared to other reported patient samples. Therefore, the identified associations might not transferrable to patient samples with a lower mortality rate. Third, the CA scoring was performed on non-cardiac gated CT. The gold standard is the Agatston score calculated on cardiac gated CT. However, the Weston score, which was used in the present study is highly correlated with this established score and is considered almost as reliable as the

Agatston score (17). Moreover, the reading was performed by one radiologist without a test for interreader variability. However, it was shown in previous analyses that the Weston score has low interreader variability, which reduces this limitation of the present work (17). Forth, the patient history for known coronary heart disease and metabolic diseases was not available for all patients. Therefore, we could not address for this factor in the multivariable analysis. It remains elusive, whether CA scoring adds prognostic relevance beyond the anamnestic presence of CA scoring in patients with COVID-19.

Conclusions

CA score derived from native CT images was associated with 30-day mortality in patients with COVID-19. However, the identified overlap between the patient groups might be too large for translation into clinical routine. Therefore, CA scoring should be further investigated as a potential imaging marker in patients with COVID-19.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://jtd.amegroups.com/article/view/10.21037/jtd-23-728/rc>

Data Sharing Statement: Available at <https://jtd.amegroups.com/article/view/10.21037/jtd-23-728/dss>

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://jtd.amegroups.com/article/view/10.21037/jtd-23-728/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are

appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The retrospective analysis was approved by the Ethics Committee of Otto von Guericke University Magdeburg, Magdeburg, Germany (No. 25/21). Individual consent for this retrospective analysis was waived.

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