**Coronary arteries and aortic valve calcifications in COVID-19**

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**Abstract**

**Purpose** High coronary artery calcium score (CACS) and aortic valve calcifications (AC) increase cardiovascular risk. Our purpose is to evaluate CACS, measured by Weston score (WS), and the presence of AC in chest CT of COVID-19 patients and possibly investigate their prognostic role.

**Methods** This retrospective case–control study includes 150 hospitalized COVID-19 patients who underwent a chest CT at admission. The case group (group A) was formed by 50 in-patients in intensive care unit (ICU) under invasive ventilation (IV), while the control group (group B) was formed by 100 in-patients in non-ICU units, not under IV. After, a second case–control selection was originated from these two groups: the case group (group A1) composed by 30 patients, and the matching control group (group B1) composed by 60 patients. WS and the presence of AC were compared between groups A and B, and between groups A1 and B1. Moreover, lung severity score (LSS) and WS were correlated.

**Results** LSS was 7.5 ± 3.9, and WS was 6.4 ± 3.0; AC was present in 97/150 (64.7%). WS was significantly higher in group A than in group B, respectively, 7.4 ± 4.0 and 5.7 ± 2.6 (p = 0.0146), and also the presence of AC, respectively, 41/50 (82.0%) vs 56/100 (56.0%) (p = 0.0016). Finally, WS and AC were significantly higher in group A1 compared to group B1.

**Conclusion** Both WS and AC were higher in ICU COVID-19 patients than in non-ICU COVID-19 patients.

**Keywords** COVID-19 · Chest CT · Coronary artery calcium score · Aortic valve calcifications

**Introduction**

Lower respiratory tract disease is the leading clinical manifestation of the COVID-19 pathology, and diffuse alveolar damage represents the histopathological condition of the severe acute respiratory syndrome (SARS) related to the new coronavirus (CoV-2) [1–3].

However, mortality in COVID-19 is often caused by major cardiovascular events, whose exact pathophysiological mechanisms are not well-understood [4]. COVID-19 might cause injuries to the cardiovascular system with different mechanisms: the SARS-CoV-2 host cell receptors, the angiotensin-converting enzyme 2, are expressed in the myocardial and endothelial cells; this could possibly be a reason of direct damage; moreover, the excessive production of proinflammatory cytokines, induced by the virus, can lead to widespread cardiac and endothelial indirect damage [5–8]. As a matter of fact, in 8–28% of COVID-19 patients, troponin increases in the early course of the disease, due to acute myocardial injury [9–11]. The comorbidity or a new onset of cardiac disease can worsen the prognosis of severe COVID-19, causing admission to the intensive care unit (ICU), invasive ventilation (IV), and death [12–14].

Some papers show that coronary artery calcium score (CACS) is a strong independent predictor of mortality from cardiac disease [15, 16]. Moreover, aortic valve calcification (AC) is an important risk factor for cardiac events [17, 18]. A visual CACS system, the Weston score (WS), applied to non-gated chest CT, strongly correlates with the Agatston score (AS), which is the traditional and most reliable method to evaluate CACS [19].

Up to now, pericardial effusion and cardiomegaly in chest CT have been reported as a possible cardiac involvement in COVID-19 patients [20]; however, to our knowledge, no studies have described the presence of CACS and AC in these patients yet.

The purpose of our study is to evaluate the association of CACS and AC to COVID-19 infection.
Materials and methods

Study population

Our study protocol was approved by the Institutional Review Board of our Hospital. Informed consent was waived due to the COVID-19 emergency.

In this retrospective case–control study, we selected from our Hospital Database 150 COVID-19 patients who were hospitalized between March and May 2020. COVID-19 was confirmed by RT-PCR with oropharyngeal swab and chest CT performed at admission time. All chest CTs were performed because of severe clinical conditions, sudden clinical deterioration, or mismatch between clinical and chest X-ray findings. For each patient, we recorded sex, age, body mass index (BMI), troponin value, presence of chronic pulmonary obstructive disease, hypertension, chronic renal disease, diabetes, and oncologic conditions.

The case group (group A) was composed of 50 inpatients admitted to ICU and under IV (Fig. 1); the matching control group for sex, age, and BMI (group B)
was composed by 100 in-patients in a non-ICU unit and not under IV (Fig. 2) (e.g., Infective Disease or Pulmonology Units).

After, from these two groups, we originated another case–control selection: the case group (group A1) composed by 30 patients selected from group A, and the matching control group for age, sex, BMI, and CT lung severity score (LSS) (group B1) composed by 60 patients selected from group B.

**Chest CT protocol**

All CT examinations were performed on a 64-row CT scanner (LightSpeed VCT; GE Healthcare, Chicago, USA). Chest CTs were carried out without contrast medium, in a single inspiratory breath-hold, from the lung apices to the costophrenic recesses, using the following parameters: tube voltage 120 kVp; tube current 90–130 mAs; collimation 64×0.625. The CT images were reconstructed with slice increment and thickness of 0.625 mm. MPRs and MIPs images were also generated.

*Fig. 2* Sixty-year-old male patient, in ordinary unit without invasive ventilation and with a troponin value of 0.15 ± 0.08 ng/dL. The images show the absence of aortic valve calcification (full yellow arrow) (A), and the calcium score of 0 in right coronary artery, left anterior descending artery, and left circumflex artery (full yellow arrows) (B, C, D) and for the left main trunk (dotted yellow arrow) (C) because the calcium was no visually detected. The WS was 0. The upper right lobe of the lung parenchyma was diffusely involved by extensive areas of consolidations, and the other lung lobes were characterized by multiple focal areas of ground glass and consolidation. The LSS was 13 (E–F)
Chest CT evaluation

Two radiologists reviewed in consensus chest CT images for lung evaluation and for CACS and AC assessment.

Lungs were analyzed with pulmonary parenchyma window setting (width/level: 1300/−600 HU). A semiquantitative CT lung severity score (LSS) was used; for each patient, percentage of involvement in each lobe was recorded as follows: 0, none (0%); 1, minimal (1–25%); 2, mild (26–50%); 3, moderate (51–75%); 4, severe (76–100%). Total LSS was obtained adding the five lobes scores (range 0–20) [21].

WS was employed for CACS evaluation; a mediastinal window setting (width/level 400/40 HU) was used. We assigned to each patient a score for any of the major coronary vessels (left main trunk, left anterior descending artery, left circumflex artery, right coronary artery), as follows: 0, no visually detected calcium; 1, only a single high-density pixel was detected; 3, calcium was dense enough to create blooming artifact; and 2, calcium density between 1 and 3. The WS was calculated by adding the score of each vessel (range 0–12) [19]. When motion artifacts were considerable, a third radiologist with 30 years of experience in cardio-radiology reviewed the images and assigned the score. Finally, the absence or presence of AC was evaluated in each patient.

Statistical analysis

Statistical analysis was performed with a dedicated software (MedCalc v19.1.6, MedCalc Software, Ostend, Belgium). Continuous variables were displayed as mean ± standard deviation (SD) and categorical variables were reported as count and percentage. Sex, age, BMI, troponin value, LSS, WS, and AC were compared between groups A and B and, then, between groups A1 and B1. Moreover, LSS and WS were correlated both in our study population and in groups A and B. Student’s T test was used to compare continuous variables. Chi-square or Fisher’s exact test was used to compare categorical variables. Pearson’s test (r) was used to correlate WS with LSS. A statistically significant value (p) of 0.05 or less indicated a statistically significant difference.

Results

Study population

The patient’s characteristics are reported in Table 1. There were more men than women (70% vs. 30%), the average age was 70.2 ± 13.3 years (range 31–89 years), and troponin values averaged 0.27 ± 0.11 ng/dL (range 0–1.1 ng/dL, normal values < 0.4 ng/dL). The most prevalent comorbidities were hypertension (39.3%) and diabetes (29.3%). There was a linear positive correlation between LSS and WS.

Comparison between groups A and B

There was a statistically significant difference in LSS between groups A and B, 10.0 ± 5.3 vs. 6.4 ± 3.4 (p = 0.0002), and troponin levels, 0.37 ± 0.17 ng/mL vs. 0.19 ± 0.07 ng/mL (p = 0.0001). The WS was significantly higher in group A, 7.4 ± 4.0 vs 5.7 ± 3.3 (p = 0.0146). The presence of AC was higher for group A (p = 0.0016). The linear positive correlation of LSS to WS did not hold true for group A (r = 0.0238, p = 0.8806) but was persisted in group B (r = 0.2240, p = 0.0405). See Table 2 for comparisons.

Comparison between groups A1 and B1

The WS was significantly higher for group A1, 7.9 ± 3.7 and 4.4 ± 2.6 (p = 0.0007). The presence of AC was significantly higher for group A1. The comparison between groups A1 and B1 is reported in Table 3.

Discussion

Acute myocardial injury, detected by troponin increase in the early course of the disease, may be one of the clinical consequences of COVID-19 [7, 8]. This event could be due to cardiac ischemia secondary to COVID-19 [8] and could be related to inflammatory activation, microvascular dysfunction, and a pro-coagulatory state secondary to SARS-CoV-2 infection [9–11]. The onset and/or the presence of cardiac disease are related to a more severe prognosis in COVID-19 patients, often leading to ICU admission, IV, or death [12–14]. CACS and AC are strong independent predictors of cardiac mortality and therefore they add incremental prognostic information to estimate cardiac disease [15–19].
The purpose of our study was to evaluate CACS by use of WS in non-gated chest CT, and the presence of AC in COVID-19 patients.

In our study, WS was significantly higher in in-patients with IV than without IV. Our results seem to be supported by previous works [17, 20, 21], in which the authors concluded that a WS > 7 (as it proved to be in group A of our study) well correlates with an AS > 400, and this value indicates a high risk of cardiac disease, independent from underlying risk factors [24]. Conversely, a WS between 2 and 7 (as it proved to be in group B of our study) well correlates with an AC between 100 and 400 [22, 23], which is associated with moderate cardiovascular risk [24, 25]. These results agree with the assumption that COVID-19 patients, who are also at increased risk for cardiac disease, carry a higher risk of worse COVID-19 evolution, related to ICU admission and IV support [12–14], and that CACS may be an indicator of this risk. Moreover, cardiovascular morbidity and mortality are higher in patients with AC [6]. In our study, the higher rate of AC in group A (82.0%) compared to group B (56.0%) well correlates with this assumption: AC could be a second indicator of higher risk of cardiac disease and worse evolution in COVID-19 patients. Then, to prove if CACS and AC could be independent factors of greater risk of ICU admission, we carried out a further selection of patients in two groups who had comparable LSS (groups A1 and B1). It is noteworthy that both CACS and AC values are also different in these further groups. Especially, in ICU patients compared with patients in non-ICU units, the WS and AC were significantly higher. Finally, we correlated the LSS and WS, to verify if CACS could be related to lung involvement severity in COVID-19 patients. Interestingly, a statistically significant correlation was found both in all our study population and in patients in non-ICU units (group B). A possible explanation of these results could be that CACS is a surrogate marker of subclinical atherosclerosis, which is associated with inflammatory markers [27].

The limitations of the study are numerous. First, it is a retrospective mono-centric study. Second, the WS, AC, and LSS were evaluated in consensus by two radiologists and the inter-observer agreement was not calculated. Third, the sample size is relatively small, especially for the subgroups. Fourth, the exams were evaluated on 0.625 mm images and the slice thickness used in daily clinical practice is at least 1.25 or 2.5. Fifth, a multi-variable analysis that includes WS, LSS, AC, comorbidities, and troponin was not performed.

In conclusion, this was an observational study that showed that WS and the presence of AC were significantly higher in sicker COVID-19 patients, and that this result persisted after controlling for LSS. The chest CT that it is necessary for the diagnosis and for the evaluation of COVID-19 progression could be used to evaluate the presence of CACS and AC. However, further work needs to be done to confirm

### Table 2: Comparison between groups A and B

|                | Group A (case, n = 50) | Group B (control, n = 100) | p     |
|----------------|------------------------|---------------------------|-------|
| Sex—M/F       | 35 (70%)/30 (30%)      | 70 (70%)/30 (30%)         | 1.0000|
| Age (years)    | 68.6 ± 13.5            | 71.0 ± 13.4               | 0.5740|
| Body mass index (kg/m²) | 25.4 ± 3.5          | 24.9 ± 4.0               | 0.3870|
| Troponin value (ng/dL) | 0.37 ± 0.17          | 0.19 ± 0.07               | 0.0001|
| LLS            | 10.0 ± 5.3             | 6.4 ± 3.4                | 0.0002|
| WS             | 7.4 ± 4.0              | 5.7 ± 2.6                | 0.0146|
| AC—Y/N        | 41 (82%)/9 (30%)       | 56 (56.0%)/44 (44.0%)    | 0.0016|

**Abbreviations:** n number; M male; F female; LLS lung severity score; WS Weston score; AC aortic valve calcification; Y yes; N no

### Table 3: Comparison between groups A1 and B1

|                | Group A1 (case, n = 30) | Group B1 (control, n = 60) | p     |
|----------------|-------------------------|---------------------------|-------|
| Sex—M/F       | 21 (70%)/9 (30%)        | 38 (63.3%)/30 (36.7%)     | 0.6401|
| Age (years)    | 67.4 ± 13.7             | 70.6 ± 13.8               | 0.3014|
| Body mass index (kg/m²) | 25.2 ± 4.2           | 24.7 ± 4.1               | 0.5899|
| LLS            | 5.5 ± 2.3               | 4.1 ± 2.6                | 0.4771|
| WS             | 7.9 ± 3.7               | 4.6                     | 0.0007|
| AC—Y/N        | 27 (90.0%)/3 (10.0%)    | 35 (58.3%)/25 (41.7%)    | 0.0032|

**Abbreviations:** n number; M male; F female; LLS lung severity score; WS Weston score; AC aortic valve calcification; Y yes; N no
these results and determine whether these findings have prognostic value or can be considered for risk stratification.

**Declarations**

**Ethics approval and consent to participate** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study. Institutional review board approved the study.

**Conflict of interest** The authors declare no competing interests.

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