Subclinical coronary artery disease in COVID-19 patients

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Online publish-ahead-of-print 16 July 2020

Patients with cardiovascular disorders are particularly vulnerable to coronavirus disease (COVID-19).1 We aimed to investigate the impact on COVID-19 patients’ outcome of subclinical coronary artery disease (CAD), as evaluated by coronary calcium score (CCS) at chest high-resolution computed tomography (HRCT).

Consecutive patients with confirmed COVID-19 infection undergoing HRCT on admission at Padua University Hospital (Italy) were retrospectively evaluated. Subjects with known CAD were excluded. CCS was calculated at HRCT as described elsewhere.2 A composite endpoint (CE) including in-hospital mortality and intensive care unit (ICU) admission was assessed in patients with high (>400) and low–intermediate (<400) CCS.

Fifty-three hospitalized COVID-19 patients, mean age 65.3 ± 14.6 years, were considered for analysis. CCS >400 was found in 15.1% (Table 1). The CE was observed in 75% of patients with high vs. 20% with low–intermediate CCS (P = 0.004). In-hospital mortality was 50% vs. 8.9% (P = 0.003). After adjustment for age and gender, CCS >400 was associated with occurrence of CE [odds ratio (OR) 7.86, 95% confidence interval (CI) 1.16–53.01, P = 0.034], as it was in a model including age and oxygen saturation on admission (OR 10.7, 95% CI 1.19–68.01, P = 0.035). Peak high-sensitivity (hs)-troponin was higher in non-survivors vs. survivors (1229.7 vs. 43.7 ng/L, P = 0.031).

The main finding of our study, the first to examine the potential impact of subclinical CAD on COVID-19 patients, is that CCS >400 is a marker of higher risk of worse in-hospital outcome. In our cohort, half of patients with CCS >400 died during hospitalization as compared with 8.9% with CCS <400. Moreover, myocardial infarction (MI) was more frequent in patients with high CCS. These findings add to previous results from Wuhan,1 showing that subjects with cardiovascular disease and evidence of MI had >60% mortality.

The mechanism of MI in COVID-19 patients is unclear, but our preliminary experience suggests that the presence of significant subclinical CAD correlates with higher hs-troponin and worse outcome. We acknowledge that this is an early report on a relatively small population and that we were not able to include all potential confounders, thus the independent predicting role of CCS could not be definitively determined. Accordingly, we cannot exclude that the presence of high CCS is a marker of increased baseline risk rather than having a pathophysiological role in contributing to a worse prognosis. However, our data suggest that inclusion of CCS as part of routine HRCT evaluation might provide useful prognostic information in COVID-19 patients at no additional cost. It also remains to be further assessed whether MI is secondary to worsening of myocardial ischaemia in the setting of hypoxaemia or to plaque erosion/rupture triggered by systemic inflammatory response.

In conclusion, our preliminary, hypothesis-generating results suggest that evaluation of subclinical CAD at HRCT in COVID-19 patients might help in identifying subjects at higher risk of worse in-hospital outcome.

Author contributions: All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

Conflict of interest: none declared.

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Table 1  Characteristics of patients with COVID-19 according to coronary calcium score

| Clinical characteristics                  | Total (53) | Calcium score <400 (45) | Calcium score ≥400 (8) | P-value |
|-------------------------------------------|------------|-------------------------|------------------------|---------|
| Age, years                                | 65.3 ± 14.6| 62.9 ± 14.5             | 78.6 ± 4.9             | 0.004   |
| Female                                    | 18 (34%)   | 16 (36%)                | 2 (25%)                | 0.561   |
| Hypertension                              | 28 (53%)   | 20 (46.5%)              | 8 (100%)               | 0.005   |
| Diabetes mellitus                         | 13 (24.5%) | 11 (25%)                | 2 (25%)                | 1.00    |
| Smoking                                   | 10 (19%)   | 3 (7%)                  | 7 (87.5%)              | 0.001   |
| ACEi/ARB use history                      | 14 (26%)   | 10 (22%)                | 4 (50%)                | 0.120   |
| White blood cells, /μL                    | 7.64 ± 5.12| 7.31 ± 5.18             | 9.44 ± 4.55            | 0.282   |
| Neutrophils, /μL                          | 5.19 ± 3.29| 5.02 ± 3.15             | 6.19 ± 4.17            | 0.393   |
| Lymphocytes, /μL                          | 1.76 ± 3.09| 1.81 ± 3.32             | 1.49 ± 1.00            | 0.821   |
| Creatinine, mg/dL                         | 1.15 ± 1.20| 1.15 ± 1.31             | 1.16 ± 0.34            | 0.993   |
| D-dimer, μg/L                             | 566.48 ± 1124.16 | 618.12 ± 1210.47 | 264.00 ± 78.24 | 0.447   |
| CRP, mg/L                                 | 126.76 ± 96.91 | 115.53 ± 98.10 | 182.87 ± 71.55 | 0.072   |
| Procalcitonin, μg/L                       | 1.41 ± 3.29 | 1.02 ± 2.10             | 3.15 ± 6.36            | 0.099   |
| SpO2, %                                   | 90 ± 10.35  | 91 ± 8.75               | 88 ± 11.65             | 0.704   |
| Lactic acid, mmol/L                       | 1.79 ± 0.97 | 1.79 ± 1.03             | 1.82 ± 0.82            | 0.956   |
| Hs-Troponin I on admission, ng/L          | 175 ± 450   | 23 ± 48                 | 754 ± 642              | 0.057   |
| Hs-Troponin I peak, ng/L                  | 660 ± 1396  | 419 ± 1092              | 1424 ± 2139            | 0.084   |
| Imaging features                          |             |                         |                        |         |
| Consolidation, %                          | 16 (30%)    | 13 (29%)                | 3 (37.5%)              | 0.685   |
| Ground-glass opacity, %                   | 24 (45%)    | 19 (42%)                | 5 (62.5%)              | 0.444   |
| Bilateral infiltration, %                 | 40 (75.5%)  | 33 (73%)                | 7 (87.5%)              | 0.662   |
| Medical treatment                         |             |                         |                        |         |
| Antibiotic therapy                        | 53 (100%)   | 45 (100%)               | 8 (100%)               | 1.00    |
| Antiviral therapy                         | 5 (9%)      | 4 (9%)                  | 1 (12.5%)              | 0.911   |
| Hydroxychloroquine                        | 37 (70%)    | 30 (67%)                | 7 (87.5%)              | 0.579   |
| Corticosteroid                            | 35 (66%)    | 29 (64%)                | 6 (75%)                | 0.937   |
| Tocilizumab                               | 9 (17%)     | 6 (13%)                 | 3 (37.5%)              | 0.186   |
| Outcomes                                  |             |                         |                        |         |
| Composite endpoint                        | 15 (28%)    | 9 (20%)                 | 6 (75%)                | 0.004   |
| Intensive care unit admission             | 13 (24.5%)  | 8 (18%)                 | 5 (62.5%)              | 0.028   |
| Invasive mechanical ventilation           | 10 (19%)    | 7 (15.5%)               | 3 (37.5%)              | 0.218   |
| Death                                     | 8 (15%)     | 4 (9%)                  | 4 (50%)                | 0.003   |

Values are mean ± SD or n (%). The values in bold represent statistical significant differences between groups. ACEI, angiotensin converting-enzyme inhibitor; ARB, angiotensin receptor blocker; CRP, C-reactive protein Hs-Troponin, high-sensitivity troponin.