Constructing custom-made radiotranscriptomic signatures from CT angiograms: an application in COVID-19 vascular inflammation

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Background: Advances in computational methodologies have enabled processing of large datasets originating from imaging studies. However, most imaging biomarkers suffer from a lack of direct links with underlying biology, as they are only observationally correlated with pathophysiology.
Purpose: To develop and validate a novel AI-assisted image analysis platform, by applying quantitative radiotranscriptomics that quantifies cytokine-driven vascular inflammation from routine CT angiograms (CTA) performed as part of clinical care in COVID-19.
Methods: We used this platform to train the radiotranscriptomic signature C19-RS, derived from the perivascular space around the aorta and the internal mammary artery in routine chest CTAs, to best describe cytokine-driven vascular inflammation, defined using transcriptomic profiles from RNA sequencing data from human arterial biopsies (A). This signature was validated externally in 358 clinically indicated CT pulmonary angiograms from patients with or without COVID-19 from 3 different geographical regions.
Results: First, 22 patients who had a CTA before the pandemic underwent repeat CTA <6 months post COVID-19 infection (B). Compared with 22 controls (matched for age, gender, and BMI) C19-RS was increased only in the COVID-19 group (C). Next, C19-RS was calculated in a cohort of 331 patients hospitalised during the pandemic, and was higher in COVID-19 positives (adjusted OR=2.97 [95% CI: 1.43–6.27], p=0.004, D). C19-RS had prognostic value for in-hospital mortality in COVID-19, with HR=3.31 ([95% CI: 1.49–7.33], p=0.003) and 2.58 ([95% CI: 1.10–6.05], p=0.028) in two testing cohorts respectively (E, F), adjusted for clinical factors and biochemical biomarkers of inflammation and myocardial injury. The corrected HR for in-hospital mortality was 8.24 [95% CI: 2.16–31.36], p=0.002 for those who received no treatment with dexamethasone, but only 2.27 [95% CI: 0.69–7.55], p=0.18 in those who received dexamethasone subsequently to the C19-RS based image analysis, suggesting that vascular inflammation may have been a therapeutic target of dexamethasone in COVID-19. Finally, C19-RS was strongly associated (r=0.61, p=0.0003) with a whole blood transcriptional module representing dysregulation of coagulation and platelet aggregation pathways.
Conclusion: We present the first proof of concept study that combines transcriptomics with radiomics to provide a platform for the development of machine learning derived radiotranscriptomics analysis of routine clinical CT scans for the development of non-invasive imaging biomarkers. Application in COVID-19 produced C19-RS, a marker of cytokine-driven inflammation driving systemic activation of coagulation, that predicts in-hospital mortality and identifies people who will have better response to anti-inflammatory treatments, allowing targeted therapy. This AI-assisted image analysis platform may have applications across a wide range of vascular diseases, from infections to autoimmune diseases.