Results COVID-19 patients were characterised by significantly higher C19-RS values (adjusted odds ratio of 2.97 [95%CI: 1.43–6.27], $p=0.004$), while patients infected with the new B.1.1.7 variant (“UK variant”) were also found to have higher C19-RS values compared to those with the original variant, evidence suggestive of higher degrees of vascular inflammation. C19-RS had prognostic value for in-hospital mortality in COVID-19, with hazard ratios of 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 external testing cohorts respectively, after correction for clinical factors and biochemical biomarkers of inflammation (WBC, CRP) and myocardial injury (troponin). Importantly, 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 after the test, suggesting that anti-inflammatory treatment may be modifying the natural history of COVID-19 infection by improving outcomes specifically in those patients with high vascular inflammation.

Conclusions Our study introduces a new radiotranscriptomic signature, C19-RS, extracted from routine CTPAs, trained to detect cytokine-driven arterial inflammation, and demonstrates that vascular inflammation determined in this way has prognostic value in patients with COVID-19. The “UK variant” leads to higher vascular inflammation measured in this way, and the risk associated with COVID-19 arteritis is modifiable by dexamethasone.

E ABNORMAL RESTING ECG T-WAVE MORPHOLOGY PREDICTS VENTRICULAR ARRHYTHMIC RISK IN A LARGE “LOW-RISK” COHORT

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Introduction Early identification of individuals in the general population at high sudden cardiac death (SCD) risk remains a major challenge. The T-wave morphology reflects ventricular repolarization dispersion, one of the main contributors to ventricular arrhythmias (VAs) leading to SCD. Deviations of traditional T-wave indices, like the corrected QT (QTc) interval or the T-peak-to-T-end (Tpe) interval, from standard thresholds indicate increased risk. However, there is currently no index

quantifying overall T-wave morphological deviations from a normal reference, even though it could be a more robust VA risk marker. The aim of this study is to test the predictive value of a novel index quantifying T-wave morphology deviations from a normal reference.

Methods sex-, heart rate-, and electrocardiogram (ECG) lead-specific T-wave morphology references were extracted from standard 10-s 12 leads ECGs from 23,962 participants in the UK Biobank imaging study. We, then, calculated the difference between the T-wave morphologies from 51,794 independent participants without a previous history of cardiovascular events in the UK Biobank and their corresponding sex-, heart rate- and ECG lead-specific T-wave morphology using time-warping metrics. In particular, we derived the TMT index, quantifying T-wave morphology deviations in time, and its predictive power was compared to that of traditional risk factors and standard T-wave indices for two endpoints. The primary endpoint was VA mortality or hospitalizations for VA reasons. The secondary endpoint was major adverse cardiovascular events, defined as either hospitalization or death due to myocardial infarction heart failure or ventricular arrhythmia. The median follow-up time was 122 months.

Results A total of 220 (0.4%) individuals reached the primary endpoint, and 4,786 (9.2%) was significantly higher in individuals meeting the primary endpoint compared to controls (median 1.8 versus 1.6, $P = 0.003$). Multivariable Cox analysis revealed that TMT was significantly associated with the primary endpoint (hazard ratio (HR) 1.13, 95% confidence interval [CI] of 1.04 – 1.25, $P = 0.007$) independently of standard cardiovascular risk factors, as well as resting heart rate, T-wave inversions, resting Tpe interval and QTc interval. TMT was also significantly associated with the secondary endpoint (HR 1.06, 95% CI of 1.03 – 1.08, $P < 1 \times 10^{-3}$).

Conclusion This study shows that an abnormal T-wave morphology at rest is associated with VA risk in a cohort from the general population without previous cardiovascular conditions independent of standard cardiovascular risk factors and a better predictor than traditional ECG risk markers. Our findings support the hypothesis that the overall morphology of the T-wave is able to capture increased dispersion of ventricular repolarization than traditional T-wave indices, identifying a high-risk substrate for malignant VAs that could lead to SCD.