CT-based radiomics and machine learning for the prediction of myocardial ischemia: Toward increasing quantification

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Current clinical interpretation of coronary computed tomography angiography (CTA) is limited to anatomical assessment of stenosis severity,¹ which alone does not determine the hemodynamic significance of coronary lesions.^{2,3} The addition of static CT myocardial perfusion significantly increases the diagnostic performance of CTA for detecting flow-limiting coronary artery disease with stress single-photon emission computed tomography myocardial perfusion imaging (SPECT-MPI) as the reference standard.⁴ However, the clinical implementation of CT perfusion is limited by an increased radiation dose for patients and a lack of standardized scanning protocols.⁵ Visual assessment of perfusion deficits on standard coronary CTA images is also challenging due to the relatively poor contrast resolution.⁶ Radiomics is the process of extracting a large number of quantitative features from medical images to create big data in which each abnormality is characterized by hundreds of parameters indiscernible to the human eye.⁷ Computational techniques such as data mining and machine learning can then be used to identify new imaging patterns or biomarkers that associate with clinical features or outcomes.⁸ In cardiac magnetic

resonance imaging, radiomic texture analysis has been used for characterizing myocardial scar,⁹ distinguishing between acute and chronic infarction,¹⁰ and diagnosing myocarditis.¹¹ The application of radiomics to coronary CTA has predominantly been in plaque analysis, where it has demonstrated superior accuracy to conventional qualitative and quantitative parameters for the identification of high-risk plaque.^{12,13} Few studies have performed CT-based radiomic analysis of cardiac structures such as the myocardium.

In this issue of *Journal of Nuclear Cardiology*, Shu et al.¹⁴ used machine learning to develop and validate a coronary CTA-derived radiomics nomogram for the prediction of chronic myocardial ischemia by SPECT-MPI. They retrospectively studied patients who underwent both imaging modalities within a one-week interval, allocated into training (n = 107) and testing (n = 47) cohorts. An independent cohort of 49 patients was used for external validation. Myocardial ischemia was defined as fixed or reversible perfusion defects on SPECT-MPI by visual assessment. Using CCTA images, a total of 378 textural radiomic parameters were calculated from three-dimensional myocardial segmentations, and feature dimensionality reduction was used to select 8 parameters which constituted a ‘radiomics signature’ for each patient. This was then input into a machine learning model along with clinical factors and stenosis severity grade to compute a ‘radiomics nomogram’; essentially an individualized risk score for myocardial ischemia. The accuracy of the machine learned nomogram for predicting SPECT-MPI-determined ischemia was 0.839, 0.832, and 0.816 for the training, testing, and validation cohorts, respectively. Using decline curve

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analysis, the investigators showed good clinical net benefit in using the nomogram to predict ischemia in all three cohorts. In the entire study population, the radiomics nomogram (area under the receiver operator curve [AUC] 0.824) outperformed the radiomics signature (AUC 0.736, $P = .026$) and stenosis severity grade (AUC 0.708, $P < .0001$) for the discrimination of myocardial ischemia.

While this represents a proof-of-concept study with small training and validation cohorts, Shu et al.¹⁴ are to be commended for their novel work in the field of cardiac CT radiomics. Given the challenges of CT perfusion and difficulties in evaluating myocardium on routine CTA, the investigators sought to provide a quantitative surrogate measure of the risk of myocardial ischemia. Radiomic analysis can be performed on standard coronary CTA images without the need for additional iodinated contrast or radiation exposure to the patient. The present study calculated only textural (gray level co-occurrence matrix and run-length matrix) radiomic parameters, with the aim of characterizing the heterogeneity of myocardial tissue via the spatial distribution of voxels. However, as conventional CT perfusion assessment relies on attenuation differences between normal and ischemic myocardium,⁵ it is likely that first-order (intensity-based) radiomic metrics would also be of value. Further, their CT-based radiomic nomogram was developed and validated using subjective visual, not quantitative, assessment of ischemia on SPECT-MPI as the reference standard. Importantly, a global 'radiomic signature', as a representative biomarker of ischemia anywhere in the myocardium, should be validated by quantitative measure of myocardial ischemia by SPECT or PET.¹⁵ Myocardial ischemia is also typically vessel-specific, with perfusion deficits localizing to the associated myocardial segments; this is true for both SPECT-MPI and CT perfusion. Future studies should also assess whether radiomic analysis according to myocardial vascular territories can predict vessel-specific quantitative measures of ischemia. Finally, the 'radiomic nomogram' in this study requires validation in larger, independent cohorts.

With the rapid generation of big data by cardiovascular imaging, there is a demand for increasingly sophisticated and efficient computational techniques to interpret these datasets. Advancements in radiomic feature extraction and machine learning methods will enable the identification of new quantitative imaging biomarkers that may enhance current coronary CTA

assessment, by accurately predicting the risk myocardial ischemia or future adverse events.

Disclosures

The authors declare that they have no conflicts of interest.

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