RSNA Press Release

Radiomics Shows Cocaine Fuels Coronary Artery Disease Risk

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OAK BROOK, Ill. — Radiomics—the extraction of very detailed quantitative features from medical images—provides a refined understanding of how cocaine use and other risk factors affect the course of coronary artery disease, according to a study published in Radiology. Researchers said the study shows the power of radiomics to improve understanding of not just cardiovascular disease, but cancer and other conditions as well.

Shenghan Lai, M.D., M.P.H.

Coronary artery disease typically develops over time as plaque builds up inside the arteries. This process, known as atherosclerosis, can eventually lead to life-threatening events like heart attack and stroke.

Historically, imaging techniques like coronary CT angiography provided information on atherosclerosis by describing the degree of stenosis, or narrowing, in the coronary arteries. While measures of stenosis are useful, they are not always the most precise way to assess the risk of an adverse event like a heart attack.

“Some people have very bad stenosis where the vessels are 90% blocked and do fine, while others with only 40% to 50% stenosis die suddenly without warning,” said study lead author Shenghan Lai, M.D., M.P.H., professor of epidemiology and public health at the Institute of Human Virology at the University of Maryland School of Medicine and adjunct professor of epidemiology at Johns Hopkins Bloomberg School of Public Health.

At A Glance

- Radiomics provides a refined understanding of how different risk factors affect the course of coronary artery disease.
- Changes in 1,276 radiomic features were analyzed over an average of four years follow-up in 300 individuals with subclinical coronary artery disease.
- The effects of different risk factors may correspond to specific pathways of disease progression providing a more complete picture of the state of cardiac health.
School of Public Health, both in Baltimore. “This shows that not just stenosis but the nature of the plaque itself may play a very important role in risk assessment.”

Radiomics is a tool that goes beyond plaque volume to examine a multitude of features apparent in the image but not visible to the naked eye. To perform radiomics analysis, images are run through software that can analyze thousands of features for a more comprehensive risk assessment.

In the new study, Dr. Lai, Márton Kolossváry, M.D., Ph.D., a pioneer in the use of radiomics in cardiovascular imaging, and colleagues assessed whether different cardiovascular risk factors have distinctive contributions to the changes in plaque over time. Risk factors assessed included cocaine use and HIV infection.

The study group included 300 individuals with subclinical coronary artery disease, or disease not yet severe enough to present any symptoms, as confirmed via coronary CT angiography. Changes in 1,276 radiomic features were analyzed over an average of four years follow-up. The data were derived from the Heart Study, a longitudinal investigation of the effects of HIV and cocaine use on subclinical coronary artery disease, which has been funded by the National Institute on Drug Abuse for 21 consecutive years.

Radiomics-based analysis indicated that conventional risk factors, cocaine use, and HIV-infection each have different effects on changes in coronary atherosclerosis over time. Cocaine use was significantly associated with almost a quarter of the radiomics features. HIV infection, in contrast, was linked to only slightly more than 1% of radiomics features. The study also revealed that HIV infection had a more profound effect on coronary artery disease in younger individuals.

“Cocaine use plays an important role in the pathogenesis of coronary artery disease,” Dr. Lai said. “Cocaine users with HIV should abstain from cocaine use to lower the risk of coronary artery disease.”

The results suggest that rather than having a complex interconnected network of factors contributing to the development of atherosclerosis, the effects of different risk factors may correspond to specific known or unknown pathways of disease progression. This information will likely provide a more complete picture of the state of cardiac health.

“We want to figure out why some people die early, why some die suddenly, and why some people go on and on even if they have very significant fixed disease,” Dr. Lai said. “With radiomics, we can use a CT image or an MR image, because these images have more data than just stenosis.”

Dr. Lai said the radiomics technology used in the study could have applications beyond cardiovascular assessment, such as cancer and diseases of the lungs.

“The technology is there, that’s not the key obstacle,” he said. “The key obstacle is that not enough physician-researchers have access to this information.”
“Contribution of Risk Factors to the Development of Coronary Atherosclerosis as Confirmed via Coronary CT Angiography: A Longitudinal Radiomics-based Study.” Collaborating with Drs. Lai and Kolossváry were Gary Gerstenblith, M.D., David A. Bluemke, M.D., Ph.D., Elliot K. Fishman, M.D., Raul N. Mandler, M.D., Thomas S. Kickler, M.D., Shaoguang Chen, M.S., Sandeepan Bhatia, M.D., and Hong Lai, Ph.D., M.P.H.

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Images (JPG, TIF):

**Figure 1.** Manhattan plot of $P$ values for associations between cocaine use, HIV infection, and elevated atherosclerotic cardiovascular disease (ASCVD) risk and each radiomic parameter. **A–C,** $P$ values for univariate associations between each radiomic feature and cocaine use, HIV infection, and elevated ASCVD risk in univariate models. **D–F,** $P$ values for associations between each radiomic feature and cocaine use, HIV infection, and elevated ASCVD risk in multivariate models corrected for high-sensitivity C-reactive protein level as the most common marker of inflammation, positive family history of coronary artery disease (CAD) as an indicator of potential genetic predisposition for CAD progression, statin use because it is known to modify the composition and development of coronary plaques, and the plaque volume itself because we wished to correct for any potential intrinsic correlation between volume and morphologic characteristic. Radiomic parameters are situated on the x-axis in the same order of each subplot, and the corresponding $P$ values are located on the y-axis. Points above the red line ($P = .00004$) indicate radiomic features in which the given predictor showed a significant association. There was no overlap between radiomic features associated with cocaine use or elevated ASCVD risk, potentially implying different pathways of plaque progression. High-res (TIF) version (Right-click and Save As)

**Figure 2.** A, Hierarchical cluster dendrogram of radiomic features significantly associated with cocaine use, HIV infection, and/or elevated atherosclerotic...
cardiovascular disease (ASCVD) risk. Clusters are color-coded depending on risk factor with which features were associated. B, Heatmap of $R^2$ values for linear regressions between each pair of significant radiomic features ($n = 409$). Elements of the heatmap are color coded depending on risk factor with which features were associated. Clusters are outlined in yellow. C, Corresponding $P$ values for cocaine use, HIV infection, and increased ASCVD for each radiomic feature. Features are reordered based on hierarchical clustering to correspond to the dendrogram. Bars extending farther than the red line ($P = .00004$) indicate significant associations. Results from hierarchical clustering indicate that there are distinct morphologic feature sets that are associated with only specific risk factors. Furthermore, $P$ values for cocaine use among clusters associated with cocaine use were magnitudes lower than for HIV infection and especially elevated ASCVD risk. In addition, $P$ values for elevated ASCVD risk for the three clusters containing only radiomic features associated with elevated ASCVD risk were magnitudes lower than for cocaine use in HIV infection. These results potentially imply distinct pathways of coronary atherosclerosis progression because modifying effects of cocaine use and conventional cardiovascular risk factors are clearly separable.

Figure 3. Corresponding $P$ values for associations between cocaine use, HIV infection, elevated atherosclerotic cardiovascular disease (ASCVD) risk and the significant radiomic features stratified by sex and age. A, B, Corresponding $P$ values for associations between cocaine use, HIV infection, and increased ASCVD for each radiomic feature stratified by sex. C, D, Corresponding $P$ values for associations between risk factors and each significant radiomic feature stratified by age based on the median age of 51 years. The features are reordered according to hierarchical clustering. Bars extending farther than the red line ($P = .00004$) indicate significant associations. The sex-based results indicate sex-specific contributions of the different risk factors on coronary atherosclerosis morphologic features. Furthermore, age stratification indicates that different risk factors may have different contributions to atherosclerosis depending on the individual’s age.

Figure 4. Bar chart of $P$ values for radiomic features affected by cocaine use or elevated atherosclerotic cardiovascular disease (ASCVD) risk stratified by disease subgroups. A, Corresponding $P$ values for cocaine use among the total population, elevated ASCVD risk, and low ASCVD risk subgroups, shown in different shades of blue. B, Corresponding $P$ values for ASCVD risk among the total population and among cocaine user and nonuser subgroups, shown in different shades of green. Bars above the red line ($P = .00004$) indicate significant associations. Results indicate that modifying effects of cocaine use may require a susceptible environment (increased ASCVD risk) to occur. However, once it is present, it modifies the morphologic features of atherosclerosis differently than ASCVD risk. In addition, ASCVD risk
may have a more profound effect among cocaine nonusers, which may imply that
the effects of cocaine use on morphologic changes overwhelm the effects of ASCVD.

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