Unsupervised machine learning improves risk stratification of patients with visual normal SPECT myocardial perfusion imaging assessments


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Background: Unsupervised machine learning has the potential to identify new cardiovascular phenotypes and more accurately assess individual risk in an unbiased fashion.

Purpose: We aimed to use unsupervised learning to identify, analyze, and risk-stratify subgroups of patients with normal perfusion by visual interpretation on single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI).

Methods: We included consecutive patients with visual normal clinical assessment (summed stress score of 0) from the multicenter (9 sites), RE-FINE SPECT registry. We considered 23 clinical, 17 image-acquisition, and 26 imaging variables. Optimal dimensionality reduction (Uniform Manifold Approximation and Projection), clustering (Gaussian Mixture Model), and number of clusters were selected to maximize the silhouette coefficient (how similar a patient is to those in their own cluster compared to other clusters). Risk stratification for all-cause mortality (ACM) and major adverse cardiac events (MACE) was assessed within these clusters and compared to risk stratification by quantitative ischemia (>5%, 5–10%, >10%) using Kaplan-Meier curves and Cox Proportional-Hazards analysis.

Results: In total, 17,527 (of 30,351) patients in the registry had visually normal perfusion, 49.7% female, median age of 64 [55, 72] years. There were 1,138 ACM events and 2,091 MACE events with a median follow-up of 4.1 [2.9, 5.7] years. Unsupervised learning provided better risk stratification for both ACM and MACE compared to quantitative ischemia (Figure). Notably, the high-risk cluster by unsupervised learning had a hazard ratio (HR) of 9.5 (95% confidence interval [CI]: 7.7–11.7) compared to 1.4 (95% CI: 1.1–1.9) for quantitative ischemia >10%. The high-risk cluster had proportionally more women (45% [low-risk], 51% [medium-risk], 57% [high-risk], all p < 0.001), higher body mass indices (26.9, 27.4, 29.6, all p < 0.001), prevalence of diabetes (17%, 22%, 33%, all p < 0.001), and abnormal rest ECGs (30%, 43%, 64%, p < 0.001); with lower rates of family history of coronary artery disease (40%, 33%, 24%, p < 0.001). Patients in the low-risk cluster were more likely to undergo exercise stress (100%, 38%, 0%, all p < 0.001), had lower rest peak systolic blood pressure (130, 131, 140 mmHg, all p < 0.001), and higher stress peak systolic blood pressure (164, 150, 131 mmHg, all p < 0.001). Patients in the high-risk cluster had higher left ventricular mass (129, 135.45, 143.9 g, all p < 0.001) and stress volume (57, 59, 66 ml, all p < 0.001).

Conclusion: Unsupervised learning identified new phenotypic clusters for SPECT MPI patients with visual normal assessments which provided improved risk stratification for ACM and MACE compared to SPECT ischemia. Such individualized risk assessment may allow better targeted management of patients with visually normal perfusion.