**DEEP-LEARNING-BASED CAD RISK STRATIFICATION VIA RETINA FUNDUS IMAGES: PROGNOSING HEART ATTACK AND STROKE RISKS IN A BLINK OF AN EYE**

**Keywords: Deep-learning (DL), Convolution Neural Network (CNN), Retinal Fundus Imaging, Coronary Artery Disease (CAD), Survival Analysis**

**ABSTRACT**

**The branch of medicine used to determine the future health of a patient (prognosis)**

**Assessment in evaluation a risk of developing CAD (CAD risk stratification)**

Remarkable advances in biomedical research have led to the generation of large amounts of data. Using artificial intelligence, it has become possible to extract meaningful information from large volumes of data, in a shorter frame of time, with very less human interference. In effect, convolutional neural networks (a deep learning method) have been taught to recognize pathological lesions from images. Diabetes has high morbidity, with millions of people who need to be screened for diabetic retinopathy (DR). Deep neural networks offer a great advantage of screening for DR from retinal images, in improved identification of DR lesions and risk factors for diseases, with high accuracy and reliability. This review aims to compare the current evidences on various deep learning models for diagnosis of diabetic retinopathy (DR)

**Survival model will be the key to reduce heart attack deaths**

Convolutional neural network (CNN) models provide us the opportunity to extract meaningful hierarchical features to characterize cancer subtype and prognosis outcomes. On the other hand, feature selection can mitigate overfitting and reduce subsequent model training computation burden by screening out significant genes from redundant genes. To accomplish model simplification, we developed a concise and efficient survival analysis model, named CNN-Cox model, which combines a special CNN framework with prognosis-related feature selection cascaded Wx, with the advantage of less computation demand utilizing light training parameters. Experiment results show that CNN-Cox model achieved consistent higher C-index values and better survival prediction performance across seven cancer type datasets in The Cancer Genome Atlas cohort, including bladder carcinoma, head and neck squamous cell carcinoma, kidney renal cell carcinoma, brain low-grade glioma, lung adenocarcinoma (LUAD), lung squamous cell carcinoma, and skin cutaneous melanoma, compared with the existing state-of-the-art survival analysis methods. As an illustration of model interpretation, we examined potential prognostic gene signatures of LUAD dataset using the proposed CNN-Cox model

In clinical practice, medical imaging plays an increasingly important role in informed decision making of clinicians for disease management. Radiomics is a systematic approach to study the latent information in medical imaging for improved accuracy in prognosis.

1. **INTRODUCTION**

Coronary Artery Disease (CAD) is a non-communicable and the most prominent heart disease without a cure. It emerges from atherosclerosis—the thickening or hardening of heart blood vessels: when fatty material (atheroma) or plaque build-up inside coronary arteries and blocks the flow of oxygen-rich blood to the heart muscles and the brain [1]. The disease is globally leading in mortality rate due to heart attack and stroke concerns [2], [3]—contributing to 85% of cardiovascular diseases (CVDs) that caused 32% of global death in 2019—where three-quarters of victims were in low and middle-income countries [4].

Although CAD is estimated to catalyze the mortality rate from 17.9 million in 2019 to 23 million in 2030, risk stratification remains a challenging endeavor [5], [6]. Despite computing and sensor technologies enhancing decision-making and CAD disease management through Cardiac imaging, the prognosis is still illusive. The methods are impotent to perform deeper quantification of imaging phenotype—as they are limited to quantitative measures and qualitative visual assessments of cardiac structure and functions [7]—as expensive, time-consuming, risky (invasive or radioactive), and susceptible to human errors [8]. The risk calculators (such as the Pooled Cohort equations, Framingham, and SCORE) also might be inaccurate estimators in pregnancy or early menopause situations, cholesterol levels management, metabolic syndrome, autoimmune disease, and inflammatory disorder [9]–[11].

The capacity of Machine Learning to influence effective decision-making and predict accurate outcomes without being explicitly programmed has optimized the limitations of cardiac imaging by advancing comprehensive analysis techniques: for quality visual assessments and deeper extensive image quantification without the cardiologists’ hand [12], [13]. However, the best linear classifiers such as Naive Bayes, SVM, and Decision tree are also limited to accuracy and training complexity (processing time and hyper-parameter tuning): whenever vast (high-dimensionality) data or complex features are available for training [14], [15].

With the capability to mimic human brain behavior and handle numerous unstructured data (high-dimensional spaces) with automatic feature engineering, Deep learning (DL) through the CNN algorithm has become a breathtaking AI innovation for CAD risk stratification—as it trains an artificial neural network to perform self-learning and recognize complex cardiac image phenotype via multiple computations—at high speeds without compromising accuracy [16]–[18]. Nevertheless, a convenient mode of achieving multimodal and high-quality data in a quick, easy, non-invasively, and non-radioactive means remains challenging [19], [20].

Since eye vasculature and coronary heart arteries have associated characteristics, studies highlight the retinal fundus as a reliable CAD biomarker since the risk factors: modifiable (smoking, hypertension, cholesterol, diabetes, and obesity) and non-modifiable (sex and age)—can be non-invasively and quickly manifested in an eye by analyzing and evaluating retinal microvascular abnormalities: through examining the alteration of retinal characteristics (texture features, values, and patterns) and variability of blood vessels diameter at the instance of body's systemic or neurological diseases [21]–[23]. Hence, we propose retinal fundus imaging as a convenient approach to incorporate the CNN algorithm in achieving a versatile and intelligent prognostic tool: to stratify CAD risks at easy, safe, and high speed with accuracy.

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