**Oxidative Stress Markers identify Cardiac Autonomic Neuropathy Progression: Applying Machine Learning Methods.**

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**Aims:** This study aimed to highlight the association between oxidative stress and cardiac autonomic neuropathy using machine learning algorithms for risk prediction. Oxidative stress is a significant factor in chronic diseases, including cardiorespiratory, renal, and neuropathology, with cardiac autonomic neuropathy commonly linked to diabetes mellitus because of autonomic nervous system impairment.

**Methods:** 2621 participant data were provided by the DiabHealth diabetes complications screening clinic at Charles Sturt University (CSU) for analysis from year 2002 till 2015. The machine learning methods used to develop models for the prediction of CAN on oxidative stress markers were Random Forest, Logistic Regression, K-Nearest Neighbours, Support Vector Machines, Gradient Boosting, Stacking and Multiple Linear Regression. In order to enhance accuracy and performance, tuning hyperparameters and multi-class models were implemented. For model evaluation, accuracy, precision, recall, F1-score, and ROC-AUC measures were used.

**Results:** Of the total number of patients, 805 have Diabetes Mellitus (DM). Five different multi-class models were defined and tested. Based on our findings, the model with the best performance turned out to be the stacking classifier for the binary model. This was with an accuracy of 80.89%, precision of 79.35%, recall of 80.89%, F1-score of 78.30%, and AUC of 77.88%.

**Conclusion:** The results show that the stacking binary model can effectively predict the severity of CAN in the presence of oxidative stress markers at a satisfactory level.