Are Neural Networks the ultimate risk prediction models in patients at high risk of acute myocardial infarction?

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In the current issue of European Journal of Preventive Cardiology, Mitrovic et al<sup>1</sup> investigated the role and predictive capacity of an artificial neural network for acute myocardial infarction (AMI) in patients within 5 years following their coronary artery bypass grafting. The authors aimed to compare a form of machine learning with traditional statistical techniques, while it is emerging as a novel method in predictive modelling.

There is evidence that the development of AMI is associated with increased mortality, acute kidney injury, hospital stay and increased costs.<sup>2</sup> These adverse outcomes are further augmented by the association of cardiogenic shock.<sup>3</sup> It is thus, a research priority to develop more powerful risk prediction tools to aid in the prevention and management of AMI.

Machine learning (ML) aims to address important clinical questions, inherently difficult to tackle through classical approach. One of the most common algorithms used is pattern recognition. An eloquent example is the diagnosis of obstructive coronary disease on computed tomography angiography.<sup>4</sup>

Another type of ML is reinforcement learning, which is reward-based learning, while some algorithms are focused on discriminative learning rather than generative learning. Machine learning algorithms frequently employed in practice include linear and logistic regression, artificial neural networks (ANN), support vector machines (SVM), and tree-based methods. When training neural networks, an optimal fit is usually desired, but under-fitting and over-fitting may be present due to the selection of data for inclusion in the analysis.

Datasets used in ML projects are typically partitioned into training, validation, and test subsets: the training set, which encompasses the bulk of all available data, is used for the primary development of the model; the validation set is used to estimate overall model performance or to fine-tune its "hyperparameters". The performance benchmarks and metrics are problem dependent and are tested against existing dataset benchamrks.

The implementation of the ML model within a clinical setting could help automate the process of selecting appropriate candidates for further diagnostic evaluation, while circumventing more cumbersome routine clinical steps. The current evidence suggests that neural networks can find hidden features in input patterns that are not visible by conventional statistical methods.

The current European Guidelines on cardiovascular disease prevention in clinical practice<sup>5</sup> recommends (Class I, Level C) the systematic risk assessment for cardiovascular disease in individuals at high risk, and the repeat of this assessment every 5 years (Class I Level

C). Patients that underwent previous coronary artery bypass grafting are considered at very high risk.<sup>5</sup> Furthermore, the use of validated scores and strategies for prevention of cardiovascular disease is recommended (Class I Level C).

Existing scores (e.g. GRACE) have a limited discriminatory power. The role of neural networks may be to address the need of a powerful discriminatory risk stratification tool, which is an essential requisite of management in these patients. These have been shown to perform better when compared to established risk prediction algorithms (e.g. AHA/ACC).<sup>6</sup> This may be explained by the inclusion by the ML of emerging biomarkers, which are not routinely included in existing risk scores.

There is emerging evidence that neural network models are useful in predicting mortality post CABG<sup>7</sup>, the need for revascularisation<sup>8</sup>, or the detection of arrhythmias<sup>9</sup>. ML has been shown recently to be superior to predict cardiovascular or all-cause mortality by combining clinical or imaging modalities and comparing to clinical and imaging metrics alone.<sup>6,10</sup> This has an added importance in the context of emerging standard electronic health records, which may be used following consent to predict adverse outcomes.

This study addressed an important question that may pre-empty re-admission, a quicker revascularisation and aid the prognosis of these patients.

In this study, the authors have shown that the neural network could predict AMI, time interval from CABG, localisation of AMI, type of AMI with an accuracy of over 85%. This was achieved by allocating randomly the data sets to training and validations sets, Mitrovic et al have demonstrated higher specificity, sensitivity, positive and negative predictability when comparing the neural network with the linear regression model. The sensitivity was overall the lowest outcome, and reflected the lower prediction of new coronary events by this network.

One of the inherent limitations of ML models is the high number of variables and interactions, which may preclude the identification of specific therapeutic targets. Another limitation of neural networks may be the lack of standardisation across datasets, which hinders the selection of optimal models for clinical integration. This may be mitigated by regular and systematic reviews of these algorithms by humans to avoid traditional biases. One of the ongoing ethical considerations is the accountability of the output generated through machine learning.

In conclusion, neural networks have shown promising utility in improving risk stratification and guide management, but there is still a lack of understanding on how and the extent by which these tools can be integrated in clinical practice. The scientific community is excited to learn of further developments and the implementation of these ultimate risk stratification tools.

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