Machine learning using cardiovascular magnetic resonance to predict cardiovascular events in patients with acute myocarditis

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**Background:** In patients with acute myocarditis (AM), current prognostic risk assessment is based on a limited selection of clinical, biological, and imaging findings using cardiovascular magnetic resonance (CMR). While the potential value of a stratification risk score in these patients is not well established, machine learning (ML) methods could provide accurate score for prediction.

**Purpose:** To investigate the feasibility and accuracy of ML to predict major adverse cardiovascular events (MACE) in patients with AM, and compare its performance with traditional statistical methods.

**Methods:** Between 2008-2017, all consecutive patients with diagnosis of AM based on CMR and without hemodynamic compromise were recruited in two centres (Hospital 1, N=203 and Hospital 2, N=185) to constitute the derivation cohort. The external validation cohort of the ML score was performed in another centre (N=218, Hospital 3, APHP). The primary composite outcome was major adverse cardiac events (MACE) defined by: cardiac death, cardiac transplantation, ventricular arrhythmia, hospitalization for heart failure, recurrence of AM, and unplanned hospitalization for cardiac reason. Least absolute shrinkage and selection operator (LASSO) regression was used to select variables and prevent model overfitting. Several ML models (Elastic Net, Random Forest, Multi-Layer Perceptron [MLP], Support Vector Machine [SVM], and XGBoost) were then trained on 70% of patients and evaluated on the other 30% as internal validation. Their performance was compared against standard logistic regression model, using receiver operating characteristics (ROC) and precision-recall (PR) curves and area-under-the curves (AUC).

**Results:** Of the 388 AM patients (mean age 39 years, 77% male) included in the derivation cohort, 71 experienced a MACE (18%) after a median follow-up of 7.5 [IQR 6.6–8.9] years. Among those, 30 patients (7.7%) had a recurrence of AM. CMR was performed 4 ± 2 days after index presentation. Out of 56 clinical, biological, and CMR variables, 7 variables were selected as being the most important in predicting MACE: age, initial presentation with syncope, LV ejection fraction, myocardial extent of LGE, mid-wall pattern of LGE, septal location of LGE, and number of segments with T2-hypersignal (T2-STIR). The Random Forest model showed the best performance compared with the other ML models (AUROC=0.74, PR-AUC=0.33). This ML model exhibited a higher AUC compared with a traditional model using logistic regression analysis (AUROC 0.74 vs 0.70; p<0.001). The ML score also exhibited a good performance for predicting MACE in the external validation cohort (AUROC 0.73).

**Conclusions:** A machine learning score using Random Forest including clinical and CMR data exhibited a better performance than traditional statistical methods to predict MACE in patients with acute myocarditis.