Prediction of insulin resistance in depression is associated with long-term clinical outcome

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Background

Insulin resistance is a physiological state characterized by the attenuated response of peripheral receptors to insulin.[1] Insulin resistance frequently co-occurs with depression, and depression may be a risk factor for insulin resistance and type 2 diabetes.[2] Dysfunctional metabolism such as insulin resistance may facilitate neuro-progression in patients with depression.[3] Also, comorbid depression and diabetes are associated with an increased mortality risk.[4] Therefore, identifying insulin resistance in patients with depression may be important for treatment strategy and clinical outcomes. We developed and validated machine learning models to predict patients with insulin resistance and assess long-term outcomes in patients with depression.

Methods

Clinical data were extracted from the electronic health records of the Ajou University Medical Center in South Korea. The study population included patients with depression, and the outcome was insulin resistance within 12 months after diagnosis of depression. Insulin resistance was measured by Hba1c and fasting glucose. Demographic variables, diagnoses, medications, procedures, and laboratory tests were used to develop machine learning models to predict insulin resistance. We used the extreme gradient boosting (XGBoost) machine, logistic regression, and random forest as an algorithm for the model. The area under the receiver operating characteristic curves (AUC) was calculated for the performance metric. An algorithm with the best performance, according to the value of AUC, was selected as the final model. The patient data was randomly split to train set (75%) and test set (25%) for model development. We performed an internal validation using test set and conducted the external validation using other hospital databases. The cut-off value of predicted probability for the decision was based on Youden's index. Using the predicted outcome for each patient, we assessed the association between the risk of insulin resistance and the incidence of long-term outcomes through the survival analyses. Long-term outcomes were relapse of depression within one year or five years after the index date. Relapse was defined as emergency department visits or hospitalization due to exacerbation of a patient with depression. The Cox proportional model was developed for calculating the hazard ratio and the Kaplan-Meier method was applied for plotting the survival curve.

Results

A total of 6,822 patients with depression were included, and 503 (7.4%) were insulin resistance within 12 months after diagnosis of depression. And 1,704 patients were used for internal validation. The XGBoost model had a higher performance that other models in the internal validation dataset (XGBoost: AUC of 0.722, Logistic regression: AUC of 0.711, and random forest: AUC of 0.639, respectively) (Figure 1). The external validation of Wonkwang University Hospital (WKUH), Daegu Catholic University Medical Center (DCMC), and Kyung Hee University Medical Center at Gangdong (KHNMC) in South Korea was performed, and the AUROC was 0.603, 0.694, and 0.590, respectively. During the one-year follow up, diagnosis of insulin resistance occurred more frequently for patients predicted to have insulin resistance ($P = 0.01$) (Figure 2). During the one year and five years of follow-up, relapse occurred more frequently for patients predicted to have insulin resistance ($P < 0.01$, and $P = 0.04$, respectively).

The survival analyses showed that the hazard ratio of relapse was 1.61 during one-year follow up (95% CI 1.20–2.17; P < 0.01) and 1.27 during five-year follow up (95% CI 1.02–1.59; P = 0.04) when predicted of insulin resistance.

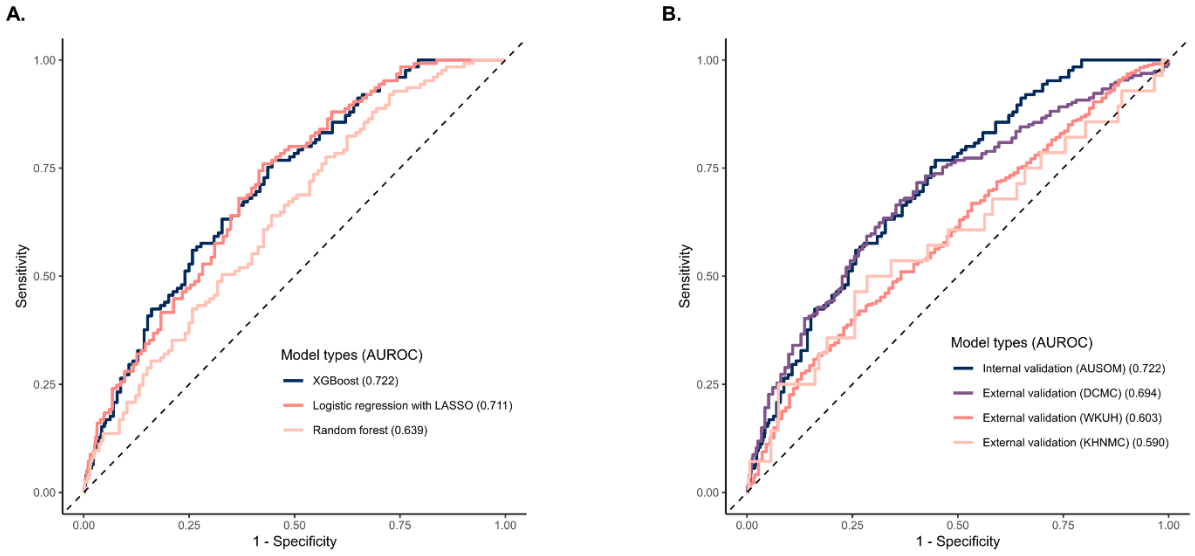

Figure 1. Performance of machine learning models for insulin resistance using internal and external validation dataset

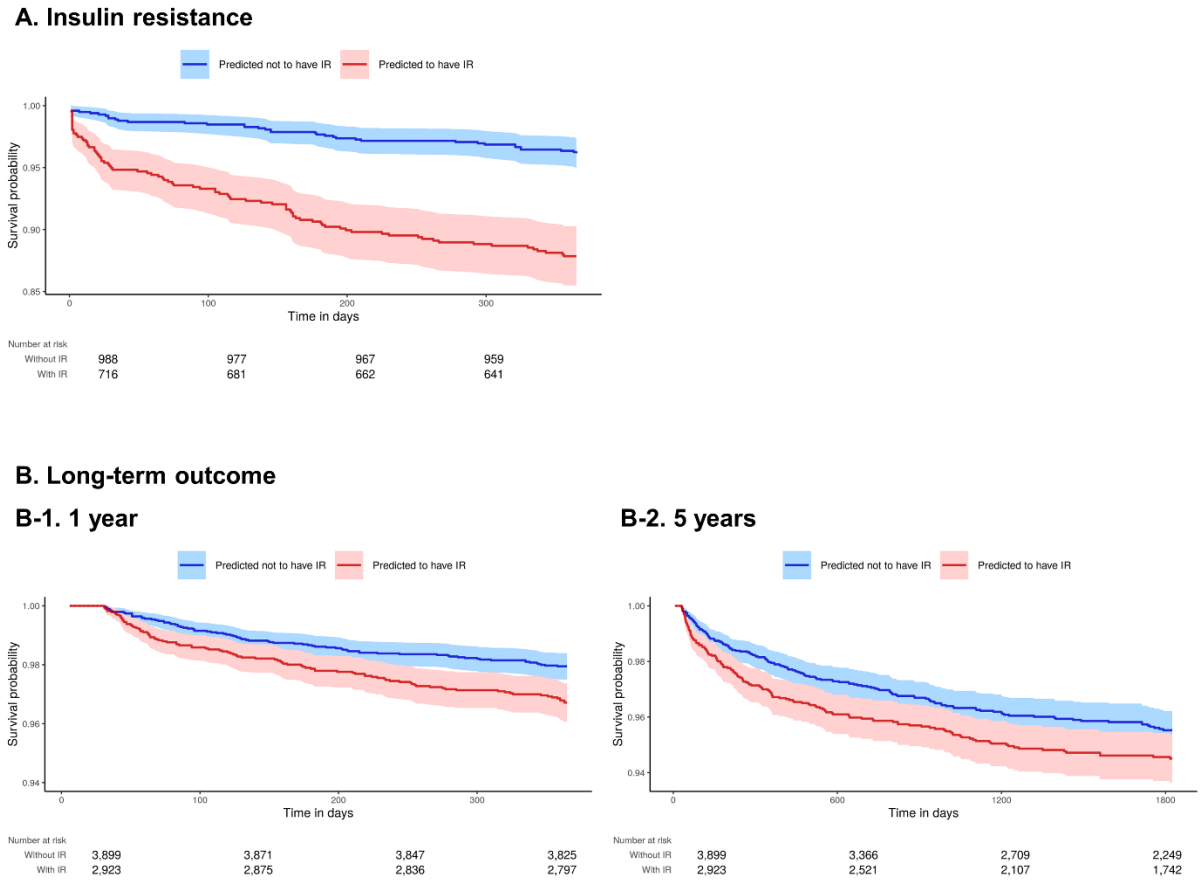

Figure 2. Kaplan–Meier survival analysis of insulin resistance and long-term outcome in patients predicted by the machine learning models to have insulin resistance.

Conclusion

We demonstrated that machine learning may help identify insulin resistance in patients with depression. Long-term outcome was also associated with prediction results.

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