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A Hemodialysis Mortality Prediction Model Based on Active Contrastive Learning

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Abstract. Hemodialysis (HD) is the main treatment for end-stage renal disease with high mortality and heavy economic burdens. Predicting the mortality risk in patients undergoing maintenance HD and identifying high-risk patients are critical to enable early intervention and improve quality of life. In this study, we proposed a two-stage protocol based on electronic health record (EHR) data to predict mortality risk of maintenance HD patients. First, we developed a multilayer perceptron (MLP) model to predict mortality risk. Second, an Active Contrastive Learning (ACL) method was proposed to select sample pairs and optimize the representation space to improve the prediction performance of the MLP model. Our ACL method outperforms other methods and has an average F1-score of 0.820 and an average area under the receiver operating characteristic curve of 0.853. This work is generalizable to analyses of cross-sectional EHR data, while this two-stage approach can be applied to other diseases as well.

Keywords. Hemodialysis, active contrastive learning, mortality risk prediction, electronic health records

1. Introduction

End-stage renal disease (ESRD) is the final stage of chronic kidney disease where the kidneys fail to remove waste and excess water, necessitating dialysis or kidney transplantation for survival. In the U.S., 125,984 new ESRD cases were reported in 2020, and 109,107 patients initiated in-center Hemodialysis (HD) , representing 83.9% of individuals with incident ESRD [1]. In China, more than 510,000 patients with ESRD have selected HD as the treatment therapy [2]. The number of HD patients is expected to continuously increase, especially because of the increases in patients with old age, hypertension, and diabetes [3]. Controlling the mortality and identifying risk factors of patients undergoing maintenance HD are of great clinical significance. It can inform patients of their survival prognosis in the early stages of dialysis and allow clinicians to make targeted intervention strategies [4].

In recent years, a number of clinical risk models have been developed to predict early mortality in the dialysis population, and most are based on linear models such as

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logistic regressions and Cox models [5-7]. The performances of these models were not good enough in either the original population or the external validation [8]. Recent studies focused on first-year mortality prediction [2,4]. Machine Learning methods such as long short-term memory (LSTM) [2], and random forest (RF) [9] were proposed to predict first-year mortality in patients undergoing hemodialysis and detect patients with high mortality risk from electronic health record (EHR) data. However, these methods are not generalizable or accurate enough.

Over the past decades, accumulated EHR data and artificial intelligence (AI) technologies have brought new challenges and opportunities for clinical decision support. This study aimed to develop and validate a more accurate and generalized AI model for predicting first-year mortality in patients undergoing maintenance HD.

2. Methods

2.1. Study population

The data involved in this study were obtained from the EHR system of the First Affiliated Hospital of Zhejiang University, PRC. Patients with ESRD who received HD treatment between January 1, 2000, and August 20, 2016, were included, and the cutoff time of observation is August 20, 2017. According to the definition of maintenance HD, patients who died within 3 months after starting dialysis were excluded. Ultimately, we included 1,229 ESRD patients (survival: 1193; death: 36) on maintenance HD.

Demographic information were collected at the start of dialysis. Disease diagnoses, laboratory test results, drugs, surgeries and examinations information were collected 0-3 months after dialysis initiation. A total of 197 variables were included without supervision of prior knowledge and 39 of them were finally selected as candidate features based on correlation analysis and removal of collinearity.

2.2. Model architectures and comparing methods

In this study, we proposed a two-stage protocol based on EHR data to predict mortality risk of maintenance HD patients. First, we developed a multilayer perceptron (MLP) model to predict mortality risk. Second, an Active Contrastive Learning (ACL) method was proposed to select comparing sample pairs and optimize the representation space to improve the prediction performance of the MLP model.

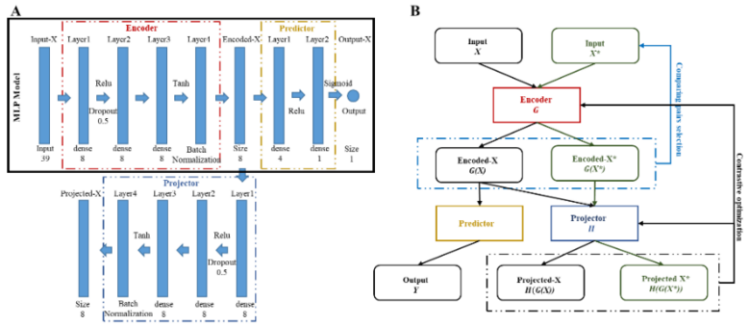

Figure 1. ACL model architecture (A) and flowchart (B).

The ACL model, as depicted in Figure 1, comprises the MLP model and a Projector. And the MLP model consists of an Encoder and a Predictor. In order to simplify the design, the Encoder and the Projector have the same network structure, which consists of three layers of dense net of size 8 and one layer of batch normalization (BN). The activation function between the first and second layers is rectified linear unit (ReLU) with dropout of 0.5. And the activation function between the third layer and the BN layer is hyperbolic tangent (Tanh) function. The Predictor is used to reduce the output dimension to match the outcomes and consists of a dense net of size 4 and a dense net of size 1 with activation functions ReLU and Sigmoid respectively. The inputs to the MLP model is a matrix containing 39 features from 1,229 patients, and the outputs are 0-1 scalars used to fit the outcome labels. The MLP model calculated the first-year risk of mortality in patients undergoing maintenance HD through forward-propagation, and update the model parameters with cross-entropy loss through back-propagation. Popular machine learning methods such as support vector machine (SVM) and RF were compared with MLP model and ACL model for performance evaluation.

2.3. Training and evaluation

The MLP model was trained in the first stage and optimized with a loss function. We set the cross-entropy of the outcome y as the loss function and tried to minimize it in terms of weights of the MLP model. The loss function is as follows:

$$Loss_{cls} = -\frac{1}{N}\sum_{i \in N}(y_i \, log(\hat{y_i}) + (1 - y_i) \, log(1 - \hat{y_i})) \quad (1)$$

Where N is the total number of patients, y_i is the indicator for the ith patient, where 1 indicates death and 0 indicates survival, and $\hat{y_i}$ is the risk score of the ith patient calculated by the MLP model. The ACL model was trained in the second stage and the flowchart is shown in Figure 1B.

After the Encoder and Predictor were trained in the first stage, we passed the original inputs X through Encoder to get Encoded-X. We calculated the Euclidean distance between encoded-X of different samples and actively selected the most representative comparing sample pairs, the ones with the largest, smallest and random distances. We denote sample X* as a positive pair of sample X when they have the same outcome label, and as a negative pair otherwise. Therefore we got 3 positive pairs and 3 negative pairs for each sample respectively. We put Encoded-X and Encoded-X* of comparing sample pairs through Projector to get Projected-X and Projected-X* and calculated a contrastive loss to optimize the Encoder and the Projector. The contrastive loss [10] is as follows:

$$D(x_i, x_i^*) = ||H(G(x_i)) - H(G(x_i^*))||_2 \quad (2)$$

$$Loss_{con} = \sum_{i \in N}(1 - y_i)D(x_i, x_i^*)^2 + y_i\{max(0, 1 - D(x_i, x_i^*))\}^2 \quad (3)$$

Loss minimization can be performed through back-propagation and mini-batch stochastic gradient descent [11]. We used Adadelta [12] to automatically optimize the networks. The gradients were automatically calculated by Keras [13], with TensorFlow [14] as the back end. After the optimization of Encoder and Projector, we froze the Encoder and fine-tuned the Predictor to fit outputs to outcome labels.

The training process was the same for the two-stages. Our data were extremely imbalanced, with approximately 97% of patients surviving and only 3% dying within 1 year. If the model classified all patients as surviving, then the accuracy was approximately 97%, which is unreliable. The F1-score and the area under the receiver

operating characteristic curve (AUROC) were measured as the model performance metrics to illustrate performance differences in the setting of class imbalance.

3. Results

In total, we measured F1-score and AUROC across MLP model, ACL model, SVM and RF by 5-fold cross validation (80% for training, 20% for validation). The comparing results is shown in Table1. We used the t-SNE algorithm to visualize the distribution of features of Input layer, Encoded-X layer and Projected-X layer across training dataset and validation dataset in Figure 2. Two cases of Encoded-X were shown respectively, MLP-Encoded-X represents the results of MLP model, and ACL-Encoded-X represents the projection after ACL optimization. We used red points to represent patients who survived and grey points to represent patients who died within the first year.

Table 1. Model performance across the 5 folds.

Model	F1-score [95% CI]	AUROC [95% CI]
SVM	0.667 [0.667-0.667]	0.561 [0.522-0.600]
RF	0.702 [0.663-0.741]	0.736 [0.680-0.792]
MLP	0.797 [0.752-0.843]	0.830 [0.794-0.866]
ACL	0.816 [0.777-0.855]	0.851 [0.819-0.883]

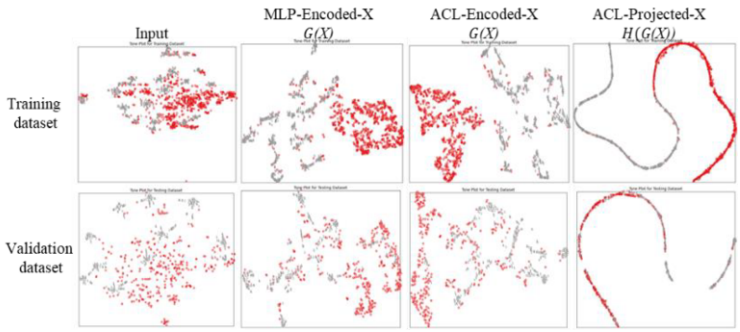

Figure 2. Two-Dimensional t-SNE Projection of features at different layers in ACL model. (Red: Survival, Grey: Death).

4. Discussion

In this paper, we used a two-stage protocol based on EHR data to predict mortality risk of patients undergoing maintenance HD. We proposed a scheme for actively selecting comparison samples for model optimization and named it Active Contrastive Learning (ACL). The F1-score and AUROC of the ACL model outperform SVM, RF and the MLP model. To further illustrate the model performance, we used Two-Dimensional t-SNE to project features at different layers in the ACL model. Compared with the features of Encoded-X layer of the MLP model, the visualization results of features in Encoded-X layer of the ACL model are more discriminative. Since we chose pairwise comparison samples to optimize the model parameters, the imbalance issues may not have much impact. If the model predicted early mortality, the clinician should pay more attention to the individual and may consider various interventions. We will study which counterfactual interventions will give the optimal survivals in the future studies.

5. Conclusions

The ACL model proposed in this study outperformed other models in predicting first-year mortality. The two-stage protocol of ACL can steadily improve the performance of the MLP model. This study has important clinical implications for other studies. This work is generalizable to analyses of cross-sectional EHR data, while this two-stage approach can be applied to other diseases as well.

Acknowledgements

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