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A Deep-Learning Neural Network-Based Predictive System for the Occurrence of Major Adverse Cardiovascular Events (MACE) in Patients with Acute Myocardial Infarction

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Abstract—**Deep-learning is an emerging technology in health informatics nowadays. Therefore, this paper proposes a novel Deep Neural Network (DNN)-based diagnosis system for Cardiovascular Disease (CVD) in patients with Acute Myocardial Infarction (AMI). In this research, Korea Acute Myocardial Infarction Registry (KAMIR-IV) dataset is used and 11,189 subjects are extracted after data pre-processing, and then divided into two subdatasets such as males' and females' datasets. Later, all datasets are splitted into training and test datasets, and consequently, the Synthetic Minority Oversampling Technique (SMOTE) on training data for data imbalance problem has been applied. The proposed prediction model is trained on oversampled training data, and hyperparameters are tuned using grid search approach. Following, the performance of proposed model is evaluated using performance measures such as accuracy, precision, recall, F1-score, and the Area under the ROC Curve (AUC). The proposed DNN-based prediction model achieved an accuracy of 0.9835, a precision of 0.9835, a recall of 0.9835, an F1-score of 0.9834, and an AUC of 0.9943 on a complete dataset whereas, the accuracy of 0.9713, a precision of 0.9710, a recall of 0.9713, an F1-score of 0.9710, and an AUC of 0.9989 on males' subdata and an accuracy of 0.9607, a precision of 0.9701, a recall of 0.9613, an F1-score of 0.9720, and an AUC of 0.9985 on females' subdata. In addition, a web-based decision support system is developed and deployed on the local server for physicians, doctors, and CVD patients. Consequently, our finding was that the proposed diagnosis system is predicting efficiently for all patients and diagnosing the major adverse cardiovascular events' (MACE) occurrences accurately in order to select the proper treatment for patients with AMI**.

Index Terms—**Cardiovascular disease, deep neural network, machine learning, diagnosis system, Major adverse Cardiovascular Events (MACE), Acute Myocardial Infarction (AMI)**

I. Introduction

Cardiovascular Disease (CVD) is the top death-causing disease around the globe [1, 2]. The death ratio is still increasing not only for Korean nation, but all over the world which is the threatening situation [3]. Therefore diagnosis and prognosis of CVD in patients with Acute Myocardial Infarction (AMI) is necessary so that we can save their lives from this deadly and dreadful disease. There are already developed prediction tools for CVD but have some challenges for the prediction of CVD occurrences. First, traditional tools are unable to provide significant details about Major Adverse Cardiac Events (MACE) such as Cardiac Death (CD), Non-Cardiac Death (NCD), Myocardial Infarction (MI), repeated Percutaneous Coronary Intervention (re-PCI), and Coronary Artery Bypass Grafting (CABG), resulting in undergoing unnecessary treatments [4, 5]. Second, there is the possibility of misclassification and wrong prediction of CVD occurrence due to limited number of risk predictors [6]. Third, the traditional prediction tools are based on Cox model or regression model [7], and are inefficient for the complex decision problems. These prediction tools are based on few risk factors and obviate the important risk factors such as obesity, cholesterol level, medical history, etc, resulting in failure of proper decisions for patients.

Therefore, this paper proposes a Deep Neural Network (DNN)-based diagnosis system for the prediction of MACE occurrences in AMI patients and highlight the latest prediction techniques for MACE. Our research contents can be summarized as follows. Firstly, the proposed prediction model will diagnose the occurrences of MACE using the cutting edge technology of Deep Learning (DL). Secondly, Korean Acute Myocardial Infarction Registry (KAMIR-IV) dataset is used and 11,189 patients' record is extracted from 13,104 records [8], and divided into maleand female subdatasets. Later on, the datasets are divided into training and test datasets after applying preprocessing rules. Thirdly, we applied the Synthetic Minority Oversampling Technique (SMOTE) [9] to overcome the data imbalance problem and trained the proposed DNN-based model using oversampled training data. Fourthly, we evaluated the performance of the proposed DNN-based diagnosis system using performance measures such as accuracy, precision, recall, F1-score, and AUC using three datasets named as complete dataset, males dataset, and femaledatasets. Finally, we have developed and deployed the local server-based web application for physicians, paramedical staff and patients as well. Consequently, the proposed diagnosis system will accurately predict the MACE occurrences and help the physicians to select the necessary treatment for AMI patients.

The research contributions and practical aspects of this article can be summarized as follows:

- The deep neural network-based predictive system is proposed for the occurrence of major adverse cardiovascular events (MACE) in male and female patients with acute myocardial infarction.
- For the proposed predictive system, we preprocessed the data using various preprocessing methods, followed by

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the data division into complete, male and female datasets and then, into training and test datasets, and then trained the model on an oversampled data. Later on, we evaluated the performance using performance measures such as accuracy, precision, recall, F1-score, and AUC for all datasets.

- For the imbalanced dataset, we applied the Synthetic Minority Oversampling Technique (SMOTE) on training data to overcome the class imbalance issues.
- Regarding the use of the predictive system for patients as well as paramedical staff, we also developed and deployed the local-server based web-application so that timely prediction can be done and proper treatment can be recommended.

II. Materials and Methods

This section will explain our experimental materials and research methods more in details.

A. Architecture of Proposed Diagnosis System

The architecture of the proposed diagnosis system is elaborated in Fig. 1. The workflow is categorized into the following steps. First, we collected the KAMIR-IV dataset and applied preprocessing rules to make it AI-friendly data. Second, we applied the extra tree classifier for obtaining relevant and highly correlated feature extraction [10]. Third, we divided the dataset into two subgroups classified as males' and females' datasets, and then, divided the dataset into 80% of the training dataset and 20% of the test dataset. Fourth, to deal with the data imbalance problem, we applied the SMOTE [9] and standard scaler techniques [11] to oversample the experimental dataset. Fifth, we designed the DNN-based diagnosis system for the prediction of MACE occurrences and tuned the hyperparameters of the system using grid search method [12]. Sixth, we used all the datasets such as complete dataset, males' dataset, and females' dataset to measure the performance of the proposed model for the prediction of MACE occurrences on accuracy, precision, recall, F1-score, and AUC [13]. At the end, we designed and deployed the local-server based web application for the diagnosis and prediction of MACE occurrences. The overall process of the diagnosis system is shown in Fig. 1.

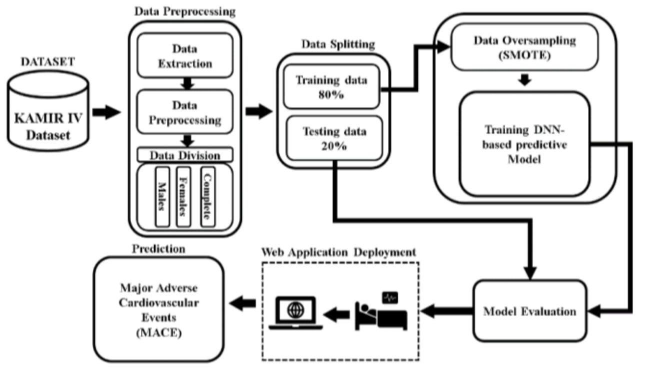

Fig. 1. Overall workflow of proposed MACE diagnostic system.

The architecture of DNN-based diagnosis system is highlighted in Fig. 2, which consists of three hidden layers and 128 nodes. We applied the rectified linear unit (ReLU) as an activation function [14], "adam" optimizer is used for the weight optimization [15], and "categorical cross entropy" as the loss function [16]. The input layer gets the selected features (e.g., age, gender, Killip class, hypertension, diabetes mellitus, smoking, neutrophil, platelet, creatinine, HDL, LDL, SBP, DBP, and HR) and forwards it to the next layer where features are feeded in feedforward mechanism and model training is refined by backpropagation mechanism [17]. Finally, the output layer gives the final prediction results by using the SoftMax activation function [18].

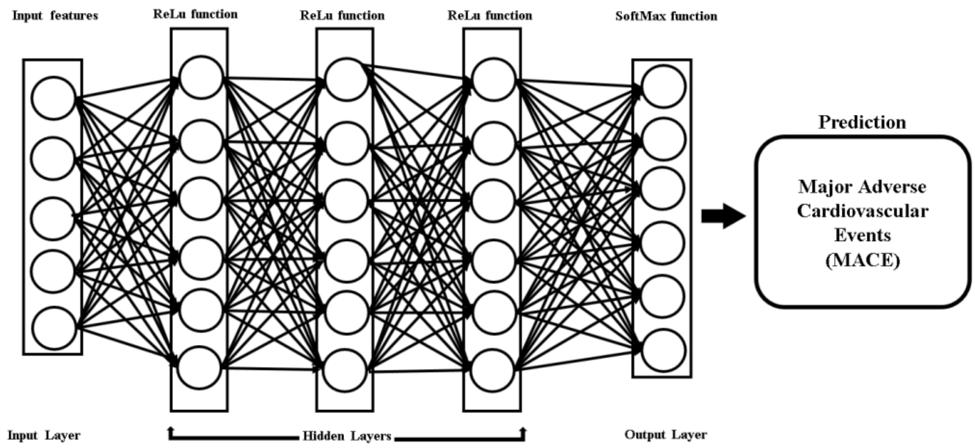

Fig. 2. A DNN architecture for MACE predictive system.

B. Data Source and Experimental Data Extraction

Korean Acute Myocardial Infraction Registry (KAMIR-IV) dataset is used for the experiment which is a multi-centered registry, and associated with 52 hospitals in Korea. It has medical records, previous medical history, drugs information, and follow-ups records of the AMI patients. Our target is MACE which is defined as CD, NCD, MI, re-PCI, and CABG [19] as per dataset provided by the KAMIR. The dataset provided was the raw dataset so that we have to go through the data extraction and preprocessing to utilize it for the DNN-based diagnosis system. It consists of 550 features, and has 13,104 records of CVD patients. First of all, we applied the extra tree classifier-based features selection method [10] and extracted the important features with high correlation. After that, we excluded the records of the patients who did not go through the 2-year followups and also the ones which have more than 70% missing values. After that, we obtained the 11,189 patients records on which we applied the mean value imputation method to deal with missing values. The dataset is subdivided into male and femaledatasets and then, further subdivided into MACE (CD, NCD MI, re-PCI, CABG) and No-MACE groups.

C. Data Preprocessing and Sampling

In the experimental dataset, we applied the mean value imputation method [20] on the data with less than 70% missing values as it gave us good results as compared with the k-nearest neighbors imputation method [21], and median value data imputation [22]. We applied zero imputation method on the entries with special characters and outbound values. We also applied the American Heart Association's and Korean Heart Association's [12, 19, 23] rules for the preprocessing of experiment dataset accordingly. The dataset consisted of categorical and continuous variables so that we applied one hot encoding [24] on categorical variables and keep the continuous values same as it is. We applied the extra tree classifier-based feature selection method and considered the 14 highly correlated and important features such as age, gender, Killip class, hypertension, diabetes mellitus, smoking, neutrophil, platelet, creatinine, HDL, LDL, SBP, DBP, and HR.

The experiment dataset was highly imbalanced because it had 10,578 No-MACE records and only 611 MACE records. Therefore, we applied the synthetic minority oversampling technique (SMOTE) to overcome the data imbalance problem. This oversampling method does not generate the duplicates of the original dataset. Instead, it creates the synthetic data points which are different from the original ones. It moves the data points in the direction of its neighbours so that the synthetic data points are not exactly same as original data, as well as, not completely from the original data.

D. Evaluation Method and Performance Measures

The experimental data is divided into two subgroups such as males' data and females' data and then divided all experimental datasets into training data (80%) and testing data (20%). 10-fold cross validation is applied and hyper-parameters are tuned using grid-search method. The performance evaluation of the proposed DNN-based diagnosis system is evaluated on accuracy, precision, recall, F1-score, and AUC as shown in Eqs. (1)–(4) and Table I as follow:

$$Accuracy = \frac{TP + TN}{TP + FP + FN + TN} \quad (1)$$

$$Recall\ (Sensitivity) = \frac{TP}{TP + FN} \quad (2)$$

$$Precision = \frac{TP}{TP + FP} \quad (3)$$

$$F1 - Score = 2 \times \frac{(Recall \times Precision)}{(Recall + Precision)} \quad (4)$$

where TP, TN, FP, FN denoted as true positive, true negative, false positive, false negative, respectively. Note, in information retrieval, object detection and classification (machine learning) fields, precision index or positive predictive value (how many retrieved items are relevant?) is the fraction of relevant instances among the retrieved instances. However, "recall" or "sensitivity index" (how many relevant items are retrieved?) is the fraction of relevant instances that were retrieved. Both "precision" and "recall" indexes are therefore based on relevance. F1-Score is the measure of model's accuracy which is the harmonic mean of precision and recall.

TABLE I: CONFUSION MATRIX FOR MACE

		Predicted MACE	
		Yes	No
Actual MACE	Yes	TP	FN
	No	FP	TN

E. Implementation Environments

The implementation was performed on 64-bit WindowsOS with Intel(R) Core i5-3230M CPU @ 2.60 GHZ processor and 8GB RAM, and used Jupyter Notebook was used as development tool. Python language (Version 3.7.3) with Tensor flow [25], Scikit-learn [26], and Keras (Version 2.3.1) [27] libraries are used for coding and experiment.

III. EXPERIMENTAL RESULTS AND DISCUSSION

This chapter will describe the detailed overview of our experimental results and finally the discussion of the results.

A. Comparison of Experimental Results

In this research, DNN-based diagnosis system for the prediction of MACE occurrences in AMI patients is proposed and the performance of the proposed model is measured using three kinds of datasets such as males' dataset, females' dataset, and complete dataset. We evaluated the performance of the proposed model using performance measures such as accuracy, precision, recall, F1-score, and AUC. The results of the proposed model on three different datasets are shown in Tables II–IV, whereas Table II shows the performance on males' dataset, Table III on females' dataset, and Table IV on the complete dataset.

Table II shows the performance results of the proposed DNN-based prediction model on males' dataset on AUC, precision, recall and F1-score. In this table, the results for each target variable such as No-MACE, CD, NCD, MI, re-PCI, and CABG are measured on AUC, precision recall, and F1-score.

TABLE II: EVALUATION RESULTS OF THE PROPOSED DNN-BASED PROPOSED MODEL ON MALES DATASET

Class labels	Performance Measures			
	AUC	Precision	Recall	F1-score
No-MACE	0.9613	0.9456	0.9032	0.9245
Cardiac death	0.9959	0.9804	0.9606	0.9959
Non-cardiac death	0.9985	0.9794	0.9967	0.9844
MI	0.9875	0.9894	0.9867	0.9844
Re-PCI	0.9866	0.9381	0.9782	0.9514
CABG	0.9999	0.1000	0.1000	0.1000

***Note:** MACE denotes major cardiac adverse event; MI myocardial infarction; re-PCI repeated percutaneous coronary intervention; CABG coronary artery bypass grafting.

In Table III, the results for each target variable is calculated on AUC, precision, recall, and F1-score using females dataset, whereas Table IV shows the results of performance measures on complete dataset.

TABLE III: EVALUATION RESULTS OF THE PROPOSED DNN-BASED PREDICTION MODEL ON FEMALES DATASET

Class labels	Performance Measures			
	AUC	Precision	Recall	F1-score
No-MACE	0.9504	0.9832	0.8745	0.9286
Cardiac death	0.9929	0.9704	0.9906	0.9800
Non-cardiac death	0.9974	0.9594	0.9962	0.9741
MI	0.9831	0.9881	0.9852	0.9834
Re-PCI	0.9866	0.9537	0.8857	0.9747
CABG	0.9998	0.9946	0.1000	0.1000

***Note:** MACE denotes major cardiac adverse event; MI myocardial infarction; re-PCI repeated percutaneous coronary intervention; CABG coronary artery bypass grafting.

TABLE IV: EVALUATION RESULTS OF THE PROPOSED DNN-BASED PREDICTION MODEL ON COMPLETE DATASET

Class labels	Performance Measures			
	AUC	Precision	Recall	F1-score
No-MACE	0.9643	0.9619	0.9495	0.9557
Cardiac death	0.9914	0.9834	0.9930	0.9882
Non-cardiac death	0.9943	0.9919	1.00	0.9959
MI	0.9957	0.9921	1.00	0.9960
Re-PCI	0.9780	0.9741	0.9985	0.9862
CABG	0.9999	0.9990	0.9610	0.9796

***Note:** MACE denotes major cardiac adverse event; MI myocardial infarction; re-PCI repeated percutaneous coronary intervention; CABG coronary artery bypass grafting.

TABLE V: OVERALL EVALUATION RESULTS OF THE PERFORMANCE MEASURES FOR THE PROPOSED DNN-BASED PREDICTION MODEL

Experimental Datasets	**Performance Measures**				
	Accuracy	**AUC**	**Precision**	**Recall**	**F1-score**
Males Dataset	0.9713	0.9989	0.9710	0.9713	0.9710
Females Dataset	0.9607	0.9985	0.9701	0.9613	0.9720
Complete Dataset	0.9835	0.9814	0.9835	0.9835	0.9834

Table V shows the oveall evaluation results of the performance measures for the proposed DNN-based prediction model using all datasets such as males dataset, female dataset, and complete dataset. The results of the proposed system is measured on accuracy, precision, recall, F1-score, and AUC.

The proposed DNN-based diagnosis system for the prediction of MACE occurrences is designed and validated by 10-fold cross validation. We applied the Synthetic Minority Oversampling Technique (SMOTE) to oversample the highly imbalanced data and measured the performance of the proposed model on accuracy, precision, recall, F1-score, and AUC indexes. The experimental results are calculated using three different kinds of datasets such as males' dataset, females'dataset, and a complete dataset. The results showed that the proposed model was efficient and had an accuracy of 0.9713, a precision of 0.9710, a recall of 0.9713, a F1-score of 0.9710, and an AUC of 0.9989 on males' dataset, and an accuracy of 0.9607, a precision of 0.9701, a recall of 0.9613, an F1-score of 0.9720, and an AUC of 0.9985 on females' dataset, and an accuracy of 0.9835,a precision 0.9835, a recall of 0.9835, an F1-score of 0.9834, and an AUC of 0.9943 on a complete dataset.

The precision value shows the correct results from the positive predictions. Recall describes the total number of positive results that are correctly predicted by the DNN-based predictive system. AUC validated the model's performance by measuring the area under the ROC curve and shows the model's ability in classification of final outputs. The higher the accuracy value, the higher the correct predictions from overall prediction results and vice versa.

The experimental results for No-MACE class are comparatively lower than those of the other classes, but we are considering MACE occurrences more than No-MACE class. In the dataset, the CABG class has least number of records (N = 13), so the experimental dataset for the CABG class is an oversampled data, and therefore, the results on this class are comparatively higher.

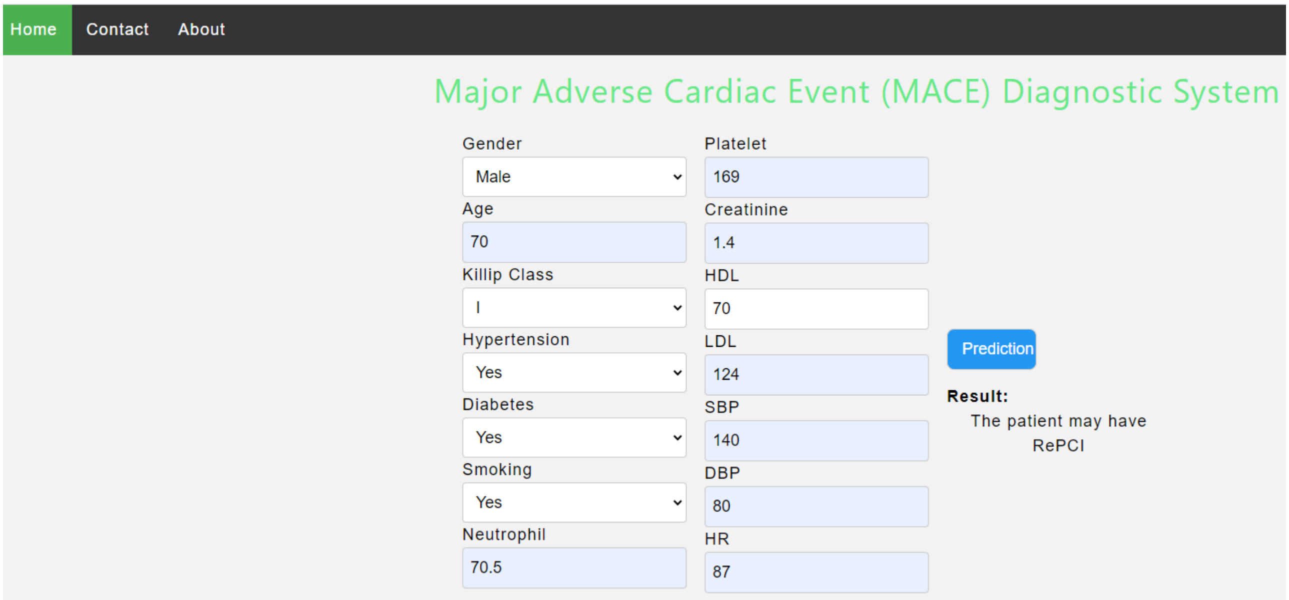

Fig. 3. Example of diagnosis and decision support system for the classification of no MACE and MACE occurrences.

B. Deployment Example

We have also designed and deployed the DNN-based MACE diagnostic system on local host which is an important step of this research. This MACE diagnostic system is developed on REST API based flask application which is a web development framework. The basic purpose of this MACE diagnostic system is to help out the doctors, paramedical staff, and patients by providing the quick diagnosis results of MACE so that they can timely choose the appropriate treatment. The diagnostic system is shown in Fig. 3 which is the homepage of the web application system and collects the clinical record of the patients. After collecting the details from the AMI patients, it will classify the medical condition of the patient and predict the upcoming MACE whether the patient will have No-MACE tracks, or will have CD or NCD in future, or suffer from MI, or get the re-PCI or CABG.

IV. CONCLUSIONS

This paper proposed a DNN-based diagnosis system for the prediction of MACE in AMI patients having cardiovascular disease. The performance of the proposed system is evaluated on performance measures using three different datasets. Our finding in this research was that the proposed system is efficient for the prediction of MACE occurrences. The web-based MACE diagnostic system is facilitating the doctors, paramedical staff, and patients to timely diagnose the occurrence of MACE so that early precautions can be done and save the life of the patients. There's the possibility that with the further improvements in the proposed DNN-based diagnosis system and web-application based MACE diagnostic system , it will surely help to lower the mortality rate of the patients suffering from this deadly disease. Sharma *et al*. proposed a more in-depth analysis of sensitivity and specifity [28].

There were some limitations in this research. First, the experimental dataset limited for the Korean nation and predict more accurately for Korean people. Second, the web-based MACE diagnostic system is still under process and needs more improvements to overcome the flaws in early diagnosis and prognosis stages. Third, the MACE diagnostic system is not officially released and hopefully, it will be released soon.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

AUTHOR CONTRIBUTION

Syed Waseem Abbas Sherazi performed the method design, data collection and analysis, data preprocessing, deep neural network-based predictive system design and implementation, manuscript preparation, and all revisions. Huilin Zheng designed the diagnosis and decision support system framework, implementation and revision of system, and performed the data preprocessing. Saba Arif helped in system framework, implementation and manuscript writing. Malik Muhammad Waqar helped in manuscript writing, data preprocessing, implementation and designing of predictive system. Gyeongtae Kim performed the data preprocessing, model design, and helped in manuscript revision. Jong Yun LEE performed the method design, framework design, experiment coordination, and manuscript preparation. All authors give their final approval of the submitted manuscript.

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