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Ensemble of heterogeneous classifiers for diagnosis and prediction of coronary artery disease with reduced feature subset

Durgadevi Velusamy[a,*], Karthikeyan Ramasamy[b]

[a] Department of Computer Science and Engineering, M.Kumarasamy College of Engineering, Karur, Tamilnadu, 639 113, India
[b] Department of Electrical and Electronics Engineering, M.Kumarasamy College of Engineering, Karur, Tamilnadu, 639 113, India

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ABSTRACT

Background and Objective: Coronary artery disease (CAD) is considered one of the most prominent health issues causing high mortality in the world population. Hence, earlier diagnosis and prediction of CAD is essential for the proper medication of patients. The objective of this study is to develop a machine learning algorithm that will help in accurate diagnosis of CAD.

Methods: In this paper, we have proposed a novel heterogeneous ensemble method combining three base classifiers viz., K-Nearest Neighbour, Random Forest, and Support Vector Machine for effective diagnosis of CAD. The results of base classifiers are combined using ensemble voting technique based on average-voting (AVEn), majority-voting (MVEn), and weighted-average voting (WAVEn) for prediction of CAD. The random forest-based Boruta wrapper feature selection algorithm and feature importance of SVM are used for relevant feature selection based on attribute importance and rank.

Results: The proposed ensemble algorithm is developed using 5 features selected based on the feature importance and the performance of the algorithm is evaluated using the Z-Alizadeh Sani dataset. Further, the dataset is balanced using Synthetic Minority Over-sampling Technique and its performance is evaluated. The result analysis shows that the WAVEn algorithm achieves better classification accuracy, sensitivity, specificity and precision of 98.97%, 100%, 96.3% and 98.3% respectively for the original dataset. The WAVEn algorithm applied on the balanced dataset achieves 100% accuracy, sensitivity, specificity and precision in diagnosing CAD. To the best of author's knowledge, the accuracy achieved by WAVEn is the highest accuracy when compared with the state-of-the-art algorithms in the literature for both original and balanced dataset.

Conclusions: The statistical results prove the robustness of the WAVEn algorithm in reliably discriminating the CAD patients from healthy ones with high precision, and therefore it can be used for developing a decision support system for diagnosing CAD at an early stage.

1. Introduction

Cardiovascular disease (CVD), also known as Heart disease is one of the clinical disorders that occurs due to the abnormal functioning of the heart [23]. Heart disease can be commonly classified as coronary artery disease (CAD) and heart failure (HF). According to the statistics of world health organization (WHO) [63], it has been estimated that 26 million of world adult population are suffering from heart diseases. Coronary Artery Disease (CAD) occurs due to the accumulation of plaques inside the coronary arteries. Atherosclerosis is a condition where plaque builds up narrowing the artery lumen that limits the flow of oxygenated blood to the heart. This decreased oxygenated blood is inadequate for the heart muscles that cause pain in the chest, pain in the neck, arms, and shoulder called Angina. The complete blockage of oxygenated blood leads to a heart attack.

The various risk factors identified as the cause for CAD are hypertension, stress, diabetes, smoking, unhealthy food intake, physical inactivity, high cholesterol, the genetic history of a person, and so on [45]. The clinical diagnosis of CAD is regarded as a great challenge especially in hugely populated countries like India as it requires lots of medical experts. The death rate due to heart attack is high due to a lack of health awareness and knowledge among the patients, insufficient diagnostic devices, and medical experts

* Corresponding author.
E-mail addresses: mvdurgadevi@gmail.com (D. Velusamy), papkarthik@gmail.com (K. Ramasamy).

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[46]. In such a case, an earlier diagnosis of CAD along with proper medication will drastically decrease the overall deaths in the country.

Coronary angiography, a gold-standard is used for the diagnosis of CAD [8]. However, this approach is expensive and time-consuming. Therefore, a suitable health-care application for automatic CAD diagnosis using intelligent machine learning technique will assist a cardiologist in an earlier diagnosis of the disease. The performance of any diagnostic system greatly depends on the algorithm and the number of feature variables used for disease diagnosis and prediction. The feature selection algorithms can be broadly classified into three categories namely filter methods, wrapper methods, and embedded methods. Various attribute selection algorithms like weights by Support Vector Machine(SVM) [20], correlation [30], Gini index [31], information gain [31], principal component analysis [30], Boruta Wrapper Feature Selection [35], recursive feature elimination [40], and so on are used for identifying important features of CAD. In general, a relevant feature subset selection has the potential to substantially improve the testing performance of any machine learning algorithm on unseen data samples in terms of accuracy and learning ability.

In this study, we have employed Random Forest based Boruta wrapper feature selection algorithm and SVM variable importance measure to select the significant attributes associated with the CAD dataset. To the best of our knowledge, no prior works in literature have applied the Boruta-based attribute selection algorithm on the Z-Alizadeh Sani dataset [55] for the prediction of CAD. Ensemble classification has been proved to be an effective way of improving disease diagnosis accuracy over single classifier models. The main aim of this work is to develop an ensemble of heterogeneous classifiers that will help to detect and predict CAD at an earlier stage. An ensemble of heterogenous classifiers combining the K-Nearest Neighbour [31], Random Forest Ensemble [21], and Support Vector Machine as the base classifiers are used for developing an ensemble model. Further, the class probability of the three base classifiers are combined to develop a voting-ensemble based on the average of the posterior probability (AVEn), a majority vote of the class probability (MVEn) and a weighted average of the posterior probability (WAVEn) to obtain the final classification accuracy of the ensemble method in predicting CAD.

In the proposed work, we have evaluated the performance of the base classifiers and ensemble methods with five significant features on the Z-Alizadeh Sani dataset separated into training and testing datasets. The ten-fold cross-validation is applied to the training set and the testing set is used to test the performance of the classifier on the unseen data. Besides, we have balanced the dataset using Synthetic Minority Over-sampling Technique (SMOTE) and applied the same procedure as that of the original dataset to evaluate model performance on the balanced dataset. Experiments are conducted to evaluate the performance of these algorithms with reduced feature subset in terms of accuracy, sensitivity, specificity, Area under the Curve (AUC), and Matthew's Correlation Coefficient (MCC) for binary classification. The experimental result shows that the proposed WAVEn classification technique has achieved the highest average accuracy of 98.97% with the original and accuracy of 100% for the balanced dataset respectively in the detection of CAD. To the best of our knowledge, these are the highest classification accuracy achieved so far when compared with other state-of-the-art algorithms in the literature.

The significant contributions of this paper are as follows:

(1) We have proposed a heterogeneous ensemble method by combining Random Forest, K-NN and SVM and the result of base classifiers is combined using a voting technique for earlier and effective diagnosis of CAD.
(2) An attribute selection measure is used for selecting relevant features based on their relative importance to minimize classification time and improve accuracy in CAD prediction.
(3) To improve the disease diagnosis accuracy and reduce the false predictions, the weights in the weighted-average voting technique is assigned based on the predictive performance of the base classifier.
(4) The performance of the classifier models are evaluated using the original and SMOTE balanced datasets to analyze the predictive accuracy of each model in identifying the CAD patients as a patients and healthy persons as healthy. The model performance is validated using metrics like accuracy, sensitivity, specificity, precision, F measure, MCC, kappa and *Area under the Curve*.

The rest of the paper is organized as follows. Section 2 describes the related works in the literature, especially for detection of CAD. Section 3 provides details about feature selection algorithms and the proposed heterogeneous ensemble classifiers for prediction of CAD. The experimental results of the classification algorithms for the original and balanced dataset are presented in Section 4. The discussion about the performance of the proposed algorithm in classification of CAD is given in Section 5. Finally, Section 6 summaries the conclusion with future works.

2. Background

2.1. A review of previous research works

Data mining and machine learning algorithms have gained great attention from many researchers in several domains like communication security [59], optimization [60], predictive analytics [22,37], smart grid [61], automatic disease diagnosis and detection and so on. Numerous studies exploiting machine learning algorithms have been reported in the literature for automatic disease diagnosis and classification namely coronary artery disease [1,5–7,19,62], obstructive sleep apnea [57], cancer diagnosis [16,27], Alzheimer diseases [33], chronic kidney disease [40] and so on. In this section, we review some of the significant works reported in the literature for CAD diagnosis using computational intelligence algorithms.

There are several studies reported in the literature for the diagnosis and classification of CAD. Generally, most of the studies reported in [29,34,43,48–52,56,58] have either used Electrocardiogram (ECG) signals or analyzed the heart rate signals for diagnosis of CAD. Nonetheless, data mining and machine learning algorithms are widely used for prediction and classification of CAD. A fuzzy expert system is developed in [42] for CAD prediction using the clinical parameter and the algorithm is able to achieve a sensitivity of 95.85% and specificity of 83.33% with 84.20% classification accuracy. The following are some of the literary works that have applied prediction techniques particularly on the Z-Alizadeh Sani CAD dataset [55] published in 2013. The authors in [5] applied algorithms like Artificial Neural Network (ANN), Naive Bayes (NB), Bagging Algorithm, Sequential Minimal Optimization(SMO) with feature selection and creation algorithms for classification of CAD. The result shows that the SMO achieved a classification accuracy of 94.08% in the prediction of CAD. The disease diagnostic system developed in [6] utilized information gain and Support Vector Machine (SVM) for feature selection and diagnosis of CAD. The algorithm achieved an accuracy of 86.14% for stenosis diagnosis of left anterior descending (LAD), 83.17% for left circumflex (LCX), and 83.50% for right coronary artery (RCA) respectively.

The non-invasive detection of CAD in high-risk patients is proposed [7] for CAD prediction using SVM based on the stenosis of three coronary arteries, namely LCX, LAD, and RCA, respectively. This machine learning algorithm has achieved an accuracy of

96.40%, sensitivity of 100% and specificity of 88.1% in the detection of CAD. The authors in [9] proposed a machine learning algorithm based on SVM with different kernels for diagnosing the stenosis of each individual artery. The PCA and Gini index algorithms are used for feature selection. The proposed algorithm achieved a classification accuracy of 86.43%, 83.67%, and 82.67%, in diagnosing LCA, LCX and RCA stenosis respectively. A hybrid PSO algorithm is proposed in [64] for rule discovery and diagnosing CAD. This study achieved an accuracy of 84.25% using 13 feature attributes in prediction of CAD. An SVM algorithm is presented in [10] for automatic diagnosis of stenosis of LAD, LCX and RCA arteries. The hyper-parameters of SVM kernels are tuned using the genetic algorithm. The SVM with RBF kernel function is utilized for diagnosing individual arteries stenosis and achieved a classification accuracy of 86.64%, 83.47% and 82.85% in diagnosing stenosis of LAD, LCX and RCA arteries respectively. The study in [11] has utilized C4.5, Naive Bayes, and K-NN for diagnosing the stenosis of individual coronary artery. The C4.5 algorithm achieved an accuracy of 74.20% for LAD, 63.76% for LCX and 68.33% for RCA coronary arteries respectively.

The authors in [12,13] employed a cost-sensitive algorithms along with the base classifiers like KNN, SMO, C4.5, SVM and Naive Bayes for classification of CAD with high sensitivity. The SMO algorithm achieved greater sensitivity of 97.22% and 92.09% accuracy, respectively. Utilizing the Bagging and C4.5 classification algorithms, the authors in [14] diagnosed the stenosis of coronary arteries with a classification accuracy of 79.54%, 61.46% and 68.96% in diagnosing stenosis of LAD, LCX and RCA arteries respectively. The authors in [15] utilized the SMO, Naive Bayes and Ensemble algorithm with 16 features for diagnosing CAD. The ensemble method achieved an accuracy of 88.25% in predicting CAD. A heterogeneous hybrid feature selection algorithm is employed [39] for classification of CAD. The authors employed Decision tree, Random Forest, Gaussian Naive Bayes, and XGBoost classifiers on the dataset balanced using SMOTE and Adaptive synthetic (ADASYN) sampling techniques. The XGBoost classifier with SMOTE technique has achieved a classification accuracy of 92.58% in diagnosing CAD.

A machine learning algorithm for diagnosing CAD presented in [2] employs genetic algorithm and particle swarm optimization for feature selection and SVM for identification of CAD. It achieves an accuracy of 93.08% and F1 score of 91.51% in predicting CAD. A hybrid method combining Multi-layer Perceptron (MLP) Neural Network and Genetic Algorithm (GA) is proposed in [19] for the classification of CAD that used 90% of data for training and 10% for testing. The authors have used weights by SVM feature selection method and achieved a classification accuracy of 93.85%, the sensitivity of 97%, and specificity of 92% in predicting CAD. A decision tree-based CAD diagnosis using classification and regression tree (CART) developed in [28] has utilized feature importance measure for relevant feature selection. The algorithm has achieved an accuracy of 100% for 18 and 10 features and an accuracy of 92.41% for five feature using the CART model.

Most of the research works reported in the literature have utilized a single classifier model for CAD diagnosis like Decision Tree (CART) [28], K-Nearest Neighbour (KNN) [5], Artificial Neural Networks (ANN) [5,62], Naive Bayes [5], Support Vector Machine (SVM) [7] and so on. However, a single classifier model cannot assure a high level of accuracy in all contexts, as each classifier model has its own merits and demerits. To the best of the author's knowledge, no prior works except the studies presented in [1,15,47] have used ensemble classification for CAD diagnosis using the Z-Alizadeh Sani dataset [8]. A nested ensemble algorithm (NE-Nu-SVC) with feature selection and multi-step balancing [1] has achieved a classification accuracy of 94.66% on the balanced dataset. An ensemble algorithm for integrating multiple criteria feature selection algorithm is presented in [47] that achieved an accuracy of 93.7% in prediction of CAD. Although several algorithms have been developed for diagnosis and prediction of CAD, only a few works have used random forest ensemble for CAD diagnosis even though it performed well [1]. Moreover, there are several studies in the literature that have applied ensemble methods for prediction task in various fields like agriculture [24], cancer disease diagnosis [16,27,38], attack detection [41], and so on. This motivated us to develop an ensemble classifier for identification and prediction of CAD with a reduced feature set for earlier diagnosis, prediction, and treatment of CAD.

Ensemble techniques can be categorized into two types, namely homogeneous and heterogeneous [27]. When an ensemble method combines a base method with two or more configuration or variants, then it is homogeneous, whereas a heterogeneous ensemble method combines one or more base methods with a meta-ensemble method like Bagging, Boosting or random subspace. Meanwhile, heterogeneous can have a combination of two different base classifiers. An ensemble technique having the capability of accomplishing a favorable trade-off between heterogeneity among base classifiers and diversity in the same training dataset can achieve better accuracy and ability to handle different training errors of base classifiers. In general, an ensemble learning technique enhances the performance and improves the overall accuracy of prediction [24,27,41].

This paper investigates the performance of an ensemble of heterogeneous classifiers with reduced feature subset built with three base classifiers, namely Random Forest ensemble, KNN, and SVM for earlier diagnosis and prediction of CAD. Initially, Random Forest (RF) ensemble classifier along with two single classifiers viz., KNN and SVM are trained as base classifier models to predict the probability of a particular class and perform binary classification. Then, the posterior probability of the individual base classifier algorithms are combined to compute the classification result of the voting ensemble based on average-voting (AVEn), majority-voting (MVEn) and weighted-average voting (WAVEn) techniques.

2.2. *Medical dataset used*

The Z-Alizadeh Sani medical dataset contains information about 303 patients as clinical records with 56 feature attributes freely available in the University of California, Irvine machine learning repository [55]. The dataset consists of 216 records of CAD patients and 87 records of healthy persons with 55 independent feature attributes or predictors and one output or response variable. The medical dataset is the study based on angiography procedure conducted by Alizadeh Sani to measure the stenosis of each artery. The response variable has two values based on an angiographic disease status, namely (i) value 0 for the absence of CAD and (ii) value 1 for the presence of CAD. The target class is set to value 0: When the narrowing diameter of an artery is less than 50% then the person is a non-CAD patient (a person is healthy or normal) and otherwise set to value 1: when the arteries have $\geq$ 50% diameter narrowing, the particular patient record is categorized as CAD patient (a person having CAD).

The dataset is highly imbalanced with 71.29% patient records contributing to CAD patients, and the remaining 28.71% records are normal or healthy persons. The dataset features can be categorized into four groups based on the demography, Echocardiography, symptoms and examination, and laboratory and echocardiography features. The demography consists of 16 parameters, 7 features related to Electrocardiography, symptoms and physical examination results consists of 14 clinical parameters and 17 feature attributes extracted from laboratory tests, and echocardiography results. The details about the features of the Z-Alizadeh Sani dataset along with the range or type of value is given in Table 1.

Table 1
Range value of various features of Z-Alizadeh Sani dataset.

Category	Feature name	Range or type
Demographic Features	Age(yrs)	30 - 86
	Sex	Male, Female
	Weight(kg)	48 - 120
	Body Mass Index (BMI, Kg/m^2)	18 - 41
	Diabetes Mellitus (DM)	Yes, No
	Hyper Tension (HTN)	Yes, No
	Current Smoker	Yes, No
	Ex-smoker	Yes, No
	Family History(FH)	Yes, No
	Obesity	Yes (BMI $\geq$ 25),else No
	Chronic Renal Failure (CRF)	Yes, No
	Cerebrovascular Accident (CVA)	Yes, No
	Thyroid disease	Yes, No
	Airway disease	Yes, No
	Congestive Heart Failure (CHF)	Yes, No
	Dyslipidemia (DLP)	Yes, No
Electrocardiography	Rhythm	Sin,AF
	ST elevation	Yes, No
	ST depression	Yes, No
	Q-wave	Yes, No
	T inversion	Yes, No
	Left Ventricular Hypertrophy (LVH)	Yes, No
	Poor R-wave progression	Yes, No
Symptoms and Physical examination	Blood Pressure (BP, mmHg)	90 - 190
	Pulse Rate(PR)	50 - 110
	Edema	Yes, No
	Weak peripheral pulse	Yes, No
	Lungs rales	Yes, No
	Systolic murmur	Yes, No
	Diastolic murmur (DM)	Yes, No
	Typical Chest Pain	Yes, No
	Dyspnea	Yes, No
	Function Class	1,2,3,4
	Atypical	Yes, No
	Nonanginal Chest Pain	Yes, No
	Exertional Chest Pain	Yes, No
	Low Threshold Angina (LowTH Ang)	Yes, No
Laboratory Tests and Echocardiography	Fasting Blood Sugar (FBS, mg/dL)	62 - 400
	Creatine (Cr mg/dL)	0.5 - 2.2
	Triglyceride (TG mg/dL)	37 - 1050
	Low Density Lipoprotein (LDL, mg/dL)	18 - 232
	High Density Lipoprotein (HDL, mg/dL)	15 - 111
	Blood Urea Nitrogen (BUN, mg/dL)	6 - 52
	Erythrocyte Sedimentation Rate (ESR, mm/h)	1 - 90
	Hemoglobin (HB, g/dL)	8.9 - 17.6
	Potassium (K, mEq/lit)	3.0 - 6.6
	Sodium (Na, mEq/lit)	128 - 156
	White Blood Cell (WBC, cells/mL)	3700 - 18000
	Lymphocyte (Lymph %)	7 - 60
	Neutrophil (Neut %)	32 - 89
	Platelet (PLT, 1000/mL)	25 - 742
	Ejection Fraction (EF-TTE %)	15 - 60
	Region with Regional wall motion abnormality (Region.RWMA)	0,1,2,3,4
	Valvular Heart Disease (VHD)	Normal, Mild, Moderate, Severe

3. Methods

In this section, we discuss about the Boruta wrapper feature selection and embedded feature selection algorithm based on SVM used for selecting relevant feature attributes. After attribute selection, the Random Forest ensemble, K-Nearest Neighbour and Support Vector Machine classifiers are trained as base classifier models using the selected features. The proposed ensemble-method is a heterogeneous ensemble voting technique that combines the posterior probability of base classifiers. The result of the base classifiers are combined with average voting, majority voting and weighted-average voting ensemble techniques to find the final classification result for diagnosing CAD.

3.1. Feature selection algorithms

In this study, we have used a wrapper-based Boruta feature selection algorithm, and embedded algorithm based on SVM feature importance for selecting relevant features from the dataset. We have applied a 10-fold cross-validation technique on the training data for selecting the significant features of importance. The features with higher weights are ranked to find and select a good combination of features. The attribute selection measure helps to identify the subset of attributes that are most relevant, significant, and less redundant. We have selected only those features that have been selected by more than one algorithm based on the feature significance and relevance measure to predict CAD.

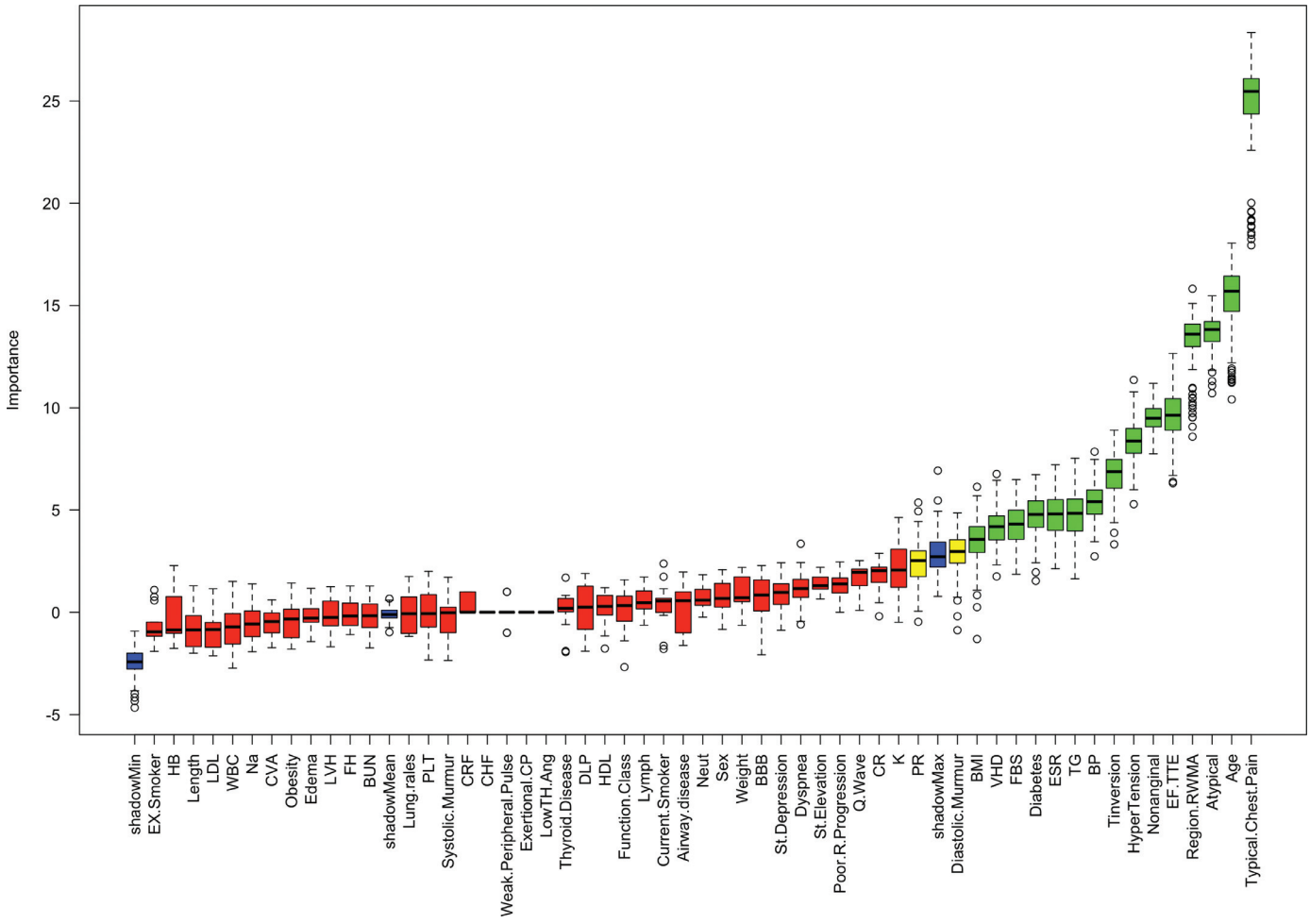

Fig. 1. Feature selection using Boruta wrapper feature selection algorithm.

3.1.1. Boruta feature selection algorithm

Boruta is a random-forest based feature selection algorithm that follows all relevant feature selection method [35]. It works by generating randomness in the dataset by making copies of all features in a shuffled manner (shadow features). Then, the algorithm trains a random forest classifier to evaluate the feature importance based on Mean Decrease of Accuracy or Mean Decrease of Impurity measure as shown in Fig. 1.

During each iteration, the algorithm tries to find significant features by comparing its Z-score with that of the randomly shuffled copies of features (shadow features). An attribute becomes important when higher its Z-score than the maximum Z-score of its shadow features computed using a binomial distribution. Finally, all the attributes are categorized either as confirmed or tentative or rejected based on its importance score. The box plot representation shown in Fig. 1 illustrates that the algorithm has selected 15 features as confirmed (shown in green color), 2 features as tentative (shown in yellow color), and the remaining features are rejected (shown in red color) based on their score.

3.1.2. Feature Selection based on SVM

The feature selection based on variable importance function of SVM shown in Fig. 2. It is based on the model information where the model is trained to incorporate the relation between the predictors for computing the variable importance [20]. In variable importance computation, the feature attributes selected by SVM have the same importance for both the classes and the importance measure ranges from 0 to 100. The main advantage of using the in-built method for model evaluation is that the performance of the model is closely related to it. Fig. 2 shows the top 20 feature variable selected based on its importance using in-built variable importance measure of SVM. However, we have selected only top 12 features viz., Typical.Chest.Pain, Atypical, Age, Region.RWMA, EF.TTE, Nonanginal, HyperTension, FBS, Tinversion,

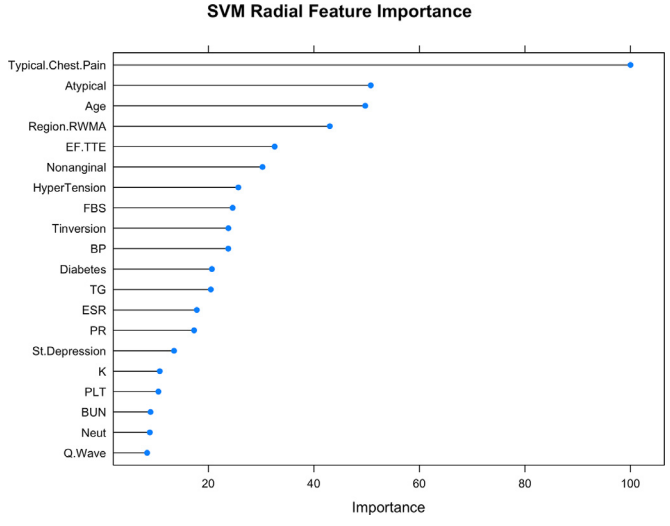

Fig. 2. Feature selection using variable importance measure of SVM algorithm.

BP, Diabetes, and TG having importance measure greater than 20 for our evaluation.

3.1.3. Features selected for model evaluation

This section discusses about the number of features selected for model evaluation for predicting CAD using the base classifier and ensemble models. In this study, we have employed a trial and error procedure to find the number of significant features that can predict CAD more accurately than previous methods reported in the literature. From Figs. 1 and 2, it can be observed that the significant features selected by both the algorithms are the same with some changes in the ranking order. Hence, we initially started with the top seven features that are commonly selected by the two feature selection algorithms namely Typical Chest Pain, Atypical, Age, Region.RWMA, Nonanginal, EF.TTE and Hyper Tension(HTN) for model evaluation. Then, we selected the top five features for model evaluation and diagnosis of CAD. In the present study, the proposed model is developed and evaluated using the five features namely Typical Chest Pain, Atypical, Age, Region.RWMA, and EF.TTE for diagnosis of CAD.

3.2. Data partitioning

The Z-Alizadeh Sani dataset is randomly divided into a training subset and testing subset with the selected features for the development of the three base classifiers. The dataset is split into two parts with 90% of data for training and 10% for testing respectively. In the training process, 10-fold cross-validation with 3 repetitions is utilized with a suitable measure to tune each base classifier according to the training errors and average of results are computed. The data is more efficiently used by taking $k-1$ subsets i.e., 9 subsets for training and one for testing to determine the parameters of the model by repeating the iteration for k times. The parameter tuning is done by exploiting the exhaustive grid search algorithm for predicting CAD using the training subset. Thus, the cross-validation procedure makes available different subsets of samples for training the model to create the model more robust against errors. Once the model is trained and built using ten-fold cross-validation, the testing subset is used to assess the predictive ability of the base classifiers on the unseen test samples during the prediction (testing) process.

3.3. Proposed heterogeneous ensemble classification for CAD prediction

Let us consider for example the dataset D consists of each patient record with n feature variables, m classes and having N number of patient records in the dataset. A classification problem in which sample X is associated with one of the possible classes out of m classes $(C_1, C_2, C_3, \ldots, C_m)$ in the dataset. In our study, the CAD dataset has two classes namely normal or healthy person and abnormal or CAD patient. Let us call it as class C_1 for normal, represented as value 0 and class C_2 for CAD, represented as value 1 in the dataset. Select k most relevant features from D based on feature significance rank and importance measure R, $R(f_1) > Rf_2) > , \ldots, > R(f_k)$. The schematic diagram of the proposed heterogeneous ensemble classification algorithm for diagnosis and prediction of CAD is shown in Fig. 3.

Split the dataset D into two subsets DTR and DTE with k selected features having P training samples and Q testing samples such that $D = DTR \bigcup DTE$. The set DTR is used as a training set and DTE is used as a testing set. The dataset is divided at a ratio of 90% training and 10% testing respectively. Initially, the base classifiers RF, K-NN, SVM are trained on the training samples using the 10-fold cross-validation technique. The hyper-parameters of the base classifiers are tuned to improve the predictive accuracy by reducing training errors. Then, the trained model is tested using the unseen testing samples and a probability score for each class is computed to find the class outcome of sample X. The class with the highest probability score is the final winning class chosen by each classifier. The probability predicted by each classifier is called the posterior probability that is used by the ensemble voting method for prediction of CAD. In final ensemble-based classification, the testing data are classified using the average voting, majority voting and weighted-average voting ensemble techniques.

Algorithm 1 gives a detailed procedure about the flow of the proposed heterogeneous ensemble classification algorithm for the prediction of CAD.

Algorithm 1 Proposed ensemble voting algorithm for CAD prediction.

procedure *Heterogeneous Ensemble Classification*
Input: $D = f_1, f_2, \ldots, f_n$ Training dataset consists of n feature variables, m classes, N number of patient records in the dataset, M Base classifier algorithms $CA_1, CA_2, \ldots, CA_M$.
Output: Prediction results of Ensemble Classifiers.
Select k most relevant features from D based on feature significance rank and importance measure R, $R(f_1) > Rf_2) >, \ldots, > R(f_k)$
Partition the dataset into two sets: Training subset (DTR_k) with P samples and Testing subset (DTE_k) Q samples.
for $i = 1$ to M **do**
Apply 10-fold cross validation on DTR_k using CA_i with the k selected features.
Predict the result of CA_i for all samples in DTR_k
Tune the hyper-parameter of CA_i to improve prediction accuracy and goto step 5.
end for
for $i = 1$ to M **do**
Evaluate the performance of CA_i on DTE_k with the k selected features.
Compute the class probability and predict the result of CA_i for all samples in DTE_k.
end for
Apply average-voting $\widehat{y} = \frac{1}{M}\sum(Pr(CA_1(X)) + Pr(CA_2(X)) + \ldots + Pr(CA_M(X)))$
Apply majority-voting $\widehat{y} = mode(CA_1(X) + CA_2(X) + \ldots + CA_M(X))$
Apply weighted-average voting$\widehat{y} = W_1 \times Pr(CA_1(X)) + \ldots + W_M \times Pr(CA_M(X))$
Compute the Prediction results of Ensemble Voting classifiers.
end procedure

3.3.1. Average voting ensemble (AVEn)

The average voting ensemble is simply summing up the posterior probabilities obtain for each sample from the M classification algorithms $(CA_1, CA_2, \ldots, CA_M)$ and then assigns the sample with a particular class based on the average value of the posterior probabilities obtained from the base classifiers is computed using Eq. (1).

$$\widehat{y} = \frac{1}{M}\sum Pr(CA_1(X)) + Pr(CA_2(X)) + \ldots + Pr(CA_M(X)) \quad (1)$$

if $\widehat{y} > 0.5$ then sample X $\in$ CAD, otherwise Normal.

3.3.2. Majority voting ensemble (MVEn)

The majority voting or hard voting classifies a sample based on the votes received for a particular class from the M different

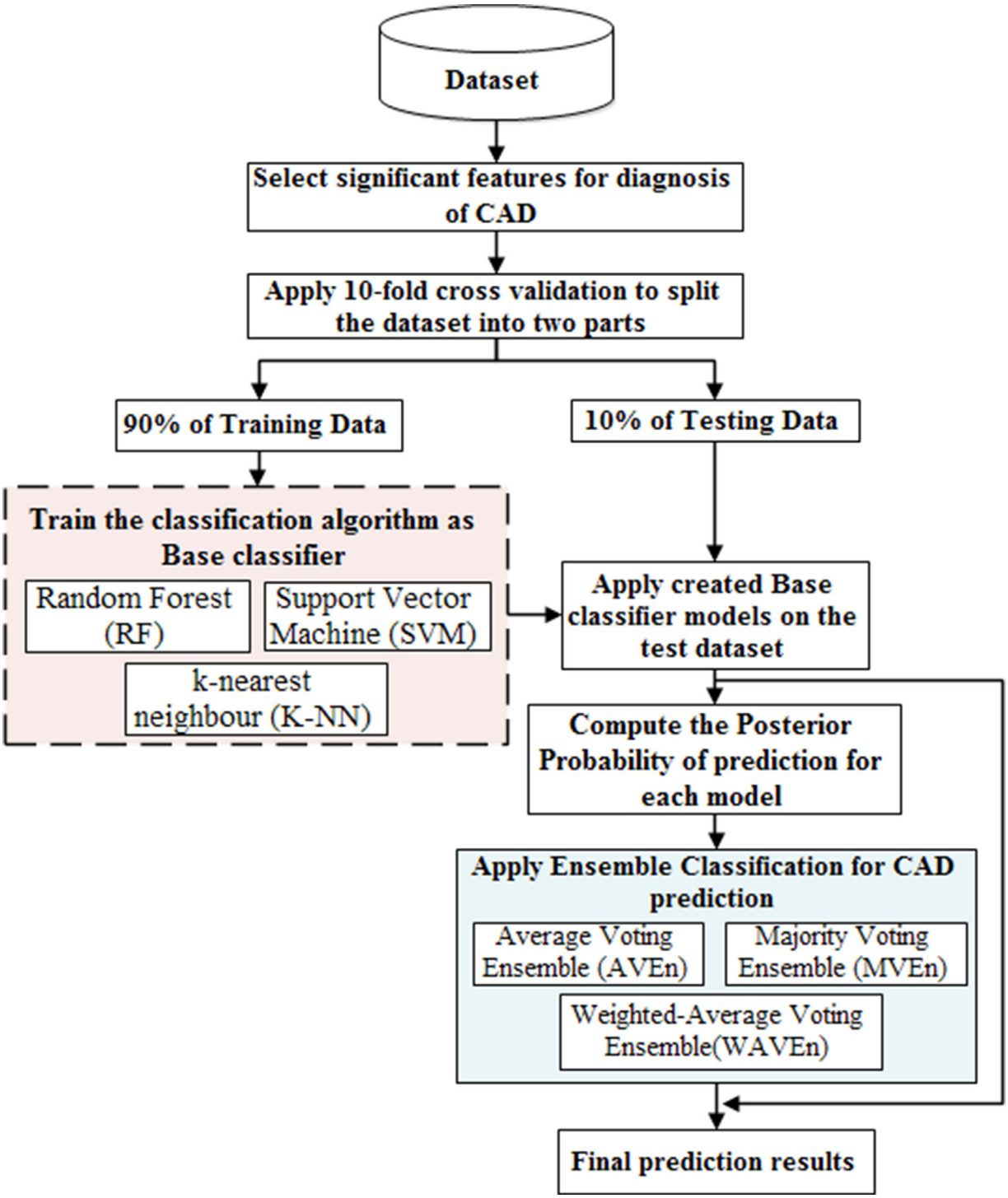

Fig. 3. A typical framework for prediction of CAD.

base classifiers ($CA_1, CA_2, \ldots, CA_M$). The class that gets major votes based on the posterior probabilities is chosen as the final class of the sample is calculated using Eq. (2).

$$\widehat{y} = mode(CA_1(X) + CA_2(X) + \ldots + CA_M(X)) \quad (2)$$

3.3.3. Weighted average voting ensemble (WAVEn)

The weighted average voting ensemble assigns weight to a base classifier based on its performance. The weights are small positive value between 0 and 1 and sum of all weights assigned is equal to 1. The weights are assigned based on the predictive performance of the classifier model on the unseen test data and the weight assigned indicates the percentage of trust on a particular classifier based on its performance and the final classification result is computed using Eq. (3).

$$\widehat{y} = W_1 \times Pr(CA_1(X)) + W_2 \times Pr(CA_2(X)) + \ldots + W_M \times Pr(CA_M(X)) \quad (3)$$

such that $\sum W_1 + W_2 + \ldots + W_M = 1$ if $\widehat{y} > 0.5$, then sample X $\in$ CAD, otherwise Normal.

4. Experimental results

In this section, we discuss the experiments carried out to evaluate the performance of the proposed heterogeneous ensemble technique. The experiments are conducted on a 2.5–4.0 GHz Intel dual-core i7 processors with 16 GB RAM running on Mac-10.13.2 operating system to evaluate the performance of the algorithms. The R-3.6.1 version and RStudio1.2.1335 are used to develop these algorithms for performing classification of CAD. An extensive set of simulation using R to evaluate the performance of base classifiers namely Random Forest Ensemble classifier, K-Nearest Neighbour and Support Vector Machine Radial Basis Kernel are investigated on the original data set. The Ensemble classification approach based on a voting method using average voting, majority voting and weighted-average voting techniques are implemented by combining the result of the base classifiers.

Meanwhile, the classes in the dataset are balanced using Synthetic Minority Over-sampling Technique (SMOTE) and the performance of the base classifier algorithms and Ensemble classifiers are evaluated on the balanced data set. From the experimental results, it is observed that the balanced data improved the overall performance of the algorithm with a considerable amount of improvement in the classification accuracy, sensitivity, specificity and F Measure of the base classifiers as well as for the ensemble classifiers specifically due to the increase in the number of training samples in the balanced data set.

In this study, the experiments are executed for 10 independent trials with the same set of parameters to avoid random errors. The result of all performance evaluation measures is the average value taken from 10 independent simulations with different random seed values. These results are reported for the base classifiers and ensemble methods.

4.1. Performance evaluation measures

This section presents the performance evaluation of the base classifiers and the ensemble of heterogeneous classifiers in effectively diagnosing and predicting CAD. The performance of any classification algorithm is measured in terms of accuracy. However, relying only on classification accuracy, especially for an imbalanced medical dataset could be misleading sometimes. Hence, in addition to the accuracy, model evaluation metrics like sensitivity, specificity, precision, F measure, Kappa, MCC and area under the curve (AUC) are computed to assess the performance of the classifier models. The effectiveness of the classifier is experimentally evaluated using the parameters obtained from the confusion matrix namely True Positive (TP) i.e., CAD predicted as CAD, True Negative (TN) i.e., Normal predicted as Normal, False Positive (FP) i.e.,Normal predicted as CAD and False Negative (FN) i.e., CAD predicted as Normal.

Accuracy is defined as the metrics that determine the number of correctly classified class out of the total samples in the testing database. The accuracy is mathematically computed using the Eq. (4).

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN} \tag{4}$$

Sensitivity or True Positive Rate (TPR) and Specificity or True Negative Rate (TNR) of a classifier model is computed using the Eqs. (5) and (6) respectively.

$$Sensitivity = \frac{TP}{TP + FN} \tag{5}$$

$$Specificity = \frac{TN}{TN + FP} \tag{6}$$

Table 2
Average testing results of 10 runs obtained by the base classifiers (RF, K-NN, and SVM) and ensemble classifiers (AVEn, MVEn, and WAVEn) using the selected five feature performed on the original Z-Alizadeh Sani dataset.

Algorithm	ACC%	Kappa	Sen	Spe	Prec	F1	MCC
RF	98.3	0.96	1.00	0.94	0.98	0.989	0.96
K-NN	86.21	0.655	0.905	0.75	0.905	0.905	0.655
SVM	95.17	0.87	1.00	0.825	0.94	0.969	0.88
AVEn	92.76	0.8	1.00	0.74	0.91	0.953	0.82
MVEn	96.9	0.92	1.00	0.89	0.96	0.98	0.922
WAVEn	98.97	0.973	1.00	0.963	0.987	0.994	0.974

ACC - Accuracy, Sen - Sensitivity, Spe - Specificity, Prec - Precision, MCC - Matthew's Correlation Coefficient

Precision and F measures are computed to measure the algorithm performance using Eqs. (7) and (8) respectively.

$$Precision = \frac{TP}{TP + FP} \tag{7}$$

$$F1 = 2 \times \frac{precision \times sensitivity}{precision + sensitivity} \tag{8}$$

Matthew's Correlation coefficient (MCC) is a measure used to evaluate the quality of a binary classifier for diagnosing CAD in a patient is computed using Eq. (9)

$$MCC = \frac{TP \times TN + FP \times FN}{\sqrt{(TP + FP)(TP + FN)(TN + FP)(TN + FN)}} \tag{9}$$

The kappa coefficient measure takes into account the random classifier accuracy to evaluate the achieved classification accuracy as given in Eq. (10).

$$\kappa = \frac{acc - rand}{1 - rand} \tag{10}$$

where acc - is the accuracy achieved by an algorithm and rand - is the accuracy achieved by the algorithm with random outputs.

4.2. Classification results

In this section, the classification performance of the proposed heterogeneous ensemble classifier models and the three base classifiers using five features namely Typical Chest Pain, Age, Atypical, Region.RWMA and EF-TTE to predict CAD is reported for the original Z-Alizadeh Sani dataset and the dataset balanced using the SMOTE sampling techniques.

4.2.1. Original dataset

This section describes about the performance results of the ensemble models and three base classifiers for prediction of CAD in terms of classification accuracy, Kappa, sensitivity, specificity, precision, F1 measure and MCC is reported for original dataset. The developed model applies 10-fold cross-validation on the training samples and the testing data do not affect model training. The test samples are independently tested to evaluate the performance of the models on the unseen data.

The original dataset consists of 303 samples out of that 216 samples are diseased and 87 samples are healthy. The dataset consists of 274 training samples and 29 test samples. The average testing result of 10 runs in terms of accuracy, kappa, sensitivity, specificity, Precision, F measure and MCC obtained by the base classifiers namely Random Forest (RF), K-Nearest Neighbour (K-NN), Support Vector Machine (SVM) and ensemble classifiers based on average voting (AVEn), Majority Voting (MVEn) and Weighted-Average Voting (WAVEn) for the original Z-Alizadeh Sani dataset is reported in Table 2.

Table 3
Average testing results of 10 runs obtained by the base classifiers (RF, K-NN, and SVM) and ensemble classifiers (AVEn, MVEn, and WAVEn) using the selected five feature performed on the SMOTE balanced Z-Alizadeh Sani dataset.

Algorithm	ACC%	Kappa	Sen	Spe	Prec	F1	MCC
RF	100	1.00	1.00	1.00	1.00	1.00	1.00
K-NN	88.34	0.767	0.905	0.862	0.868	0.886	0.767
SVM	97.62	0.952	1.00	0.952	0.955	0.977	0.953
AVEn	97.62	0.952	1.00	0.952	0.955	0.977	0.953
MVEn	97.86	0.957	1.00	0.957	0.959	0.979	0.958
WAVEn	100	1.00	1.00	1.00	1.00	1.00	1.00

ACC - Accuracy, Sen - Sensitivity, Spe - Specificity, Prec - Precision, MCC - Matthew's Correlation Coefficient

From the experimental results, it can be seen that the WAVEn model shows better performance in terms of accuracy, kappa, sensitivity, specificity, precision, F measure and MCC. From the three ensemble models developed for prediction, the Weighted-Average Voting Ensemble (WAVEn) technique is able to achieve better performance with a classification accuracy of 98.97% having a sensitivity value of 100% and specificity value of 96.3% on the original Z-Alizadeh Sani dataset with 303 patient records. This shows the efficiency of the model in predicting all patients with CAD as positive cases which is required for any medical diagnostic system. However, the result shows that there are some false predictions say some of the healthy persons are classified as CAD patients.

From the result, it can be inferred that WAVEn algorithm significantly identifies all CAD patients as patients and sometimes it has little degradation in its discriminative power of identifying all healthy persons as healthy. It should be noted that the previously developed models for diagnosing CAD using Z-Alizadeh Sani dataset have not achieved this accuracy level.

4.2.2. Balanced dataset

In this section, we discuss about the performance results of the ensemble models and three base classifiers for prediction of CAD in terms of classification accuracy, Kappa, sensitivity, specificity, precision, F1 measure and MCC for the dataset balanced using Synthetic Minority Over-sampling Technique (SMOTE). We have evaluated the performance of the classifier models and reported the results obtained by the base classifiers and ensemble classifier models for the testing samples.

We have balanced the dataset to improve the robustness of the algorithm and achieve better performance by correctly classifying CAD patients as patients and healthy persons as healthy. The balanced dataset consists of 432 samples with 216 diseased samples and 216 healthy samples. In developing our classifier models, we have used 390 samples for training and 42 samples for testing. The average testing result of 10 runs in terms of accuracy, kappa, sensitivity, specificity, Precision, F measure and MCC obtained by the base classifiers namely RF, K-NN, SVM and ensemble classifiers based on Average Voting (AVEn), Majority Voting (MVEn) and Weighted-Average Voting (WAVEn) for the balanced Z-Alizadeh Sani dataset is reported in Table 3.

From the experimental results, it can be observed that RF and WAVEn show superior performance for all performance evaluation measure with an average accuracy of 100% and zero false positive and false negative rate. This shows the efficiency and robustness of the developed model in predicting CAD with less time and cost.

In addition, the performance of the proposed heterogeneous ensemble classifier model was compared with the results of the previous studies reported in the literature for the Z-Alizadeh Sani dataset. From the Table 4, it can be observed that the proposed methodology has obtained better performance when compared with all the existing works. It should be noted that we have used only five features selected based on the importance score using Boruta and SVM feature importance algorithms that significantly improved the performance of the proposed algorithm. Moreover, our research is different from the previous works reported in the literature as we have studied the performance of our algorithms on both the original unbalanced and SMOTE balanced datasets. It is important to mention that in this research optimization algorithms such as evolutionary or nature inspired techniques are not utilized for tuning the hyper-parameters of the base classifiers.

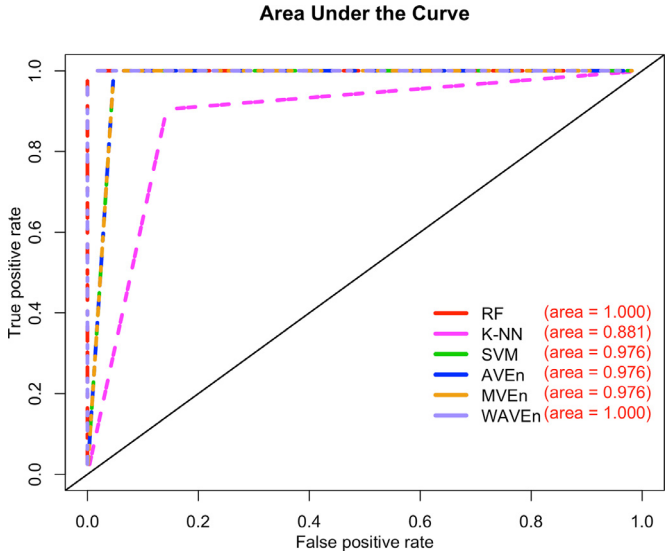

Fig. 4. ROC curve of the three base classifiers and ensemble models for the SMOTE balanced Z-Alizadeh Sani dataset on 90% training and 10% testing ratio.

4.3. Receiver operating characteristics (ROC) analysis

The Receiver Operating Characteristics (ROC) curve was plotted against the true-positive rate against the false-positive rate. The relationship between the True positive rate (Sensitivity) and False positive rate (1-Specificity) helps to visualize the strength of the classification performance of a classifier model with a Receiver operating characteristics (ROC) curve. When the ROC curve is closer to the ideal coordinate then the classifier is more accurate in predicting the CAD. The ROC graph is plotted against the true positive rate (TPR) in y-axis against false positive rate (FPR) in x-axis for different cut-points starting from the coordinate (0,0) to (1,1).

The Z-Alizadeh Sani dataset is balanced using SMOTE to analyze the performance of the classifiers. The ROC curve for the three base classifiers and ensemble models is given in Fig. 4 for the SMOTE balanced Z-Alizadeh Sani dataset. From the figure, it is observed that the ROC curve raises up to (0,1) and then horizontally reaches (1,1) indicates Weighted-Average Voting Ensemble (WAVEn) identifies both positive instances and negative instances more effectively than other classifiers. The RF and WAVEn Model achieves higher predictive accuracy in identifying CAD effectively when compare with other classifier models. The ROC curve shows that RF and WAVEn approaches achieve a 100% classification accuracy in detecting CAD. The value of the *Area under the Curve* (AUC) for each classifier is given in red color nearer to each classifier model in the figure.

4.4. Experimental results of proposed method on the Cleveland dataset

In this section, we discuss about the experimental results of our proposed method on other datasets. To analyze the performance of our proposed method on other dataset, we have selected

Table 4
Comparison of the proposed method with other methods in literature on the Z-Alizadeh Sani dataset.

Method	#Features	Accuracy(%)	Sensitivity	Specificity
Information Gain + SMO [5]	16	94.08	0.963	0.885
Information Gain + SVM [6]	24	86.14 (LAD) 83.17 (LCX) 83.50 (RCA)	NR	NR
SVM+Feature Engineering on Extended Dataset* [7]	32	96.4	1.00	0.88
Gini Index+SVM [9]	26	86.43 (LAD) 83.67 (LCX) 82.67 (RCA)	NR	NR
Hybrid PSO [64]	13	84.25	NR	NR
SVM+GA [10]	40	86.64 (LAD) 83.47 (LCX) 82.85 (RCA)	NR	NR
Information Gain+C4.5 [11]	37	74.2 (LAD) 63.76 (LCX) 69.33 (RCA)	NR	NR
SMO [12]	34	92.09	0.97	NR
SMO [13]	34	92.09	0.97	NR
Bagging-C4.5 [14]	20	79.54 (LAD) 61.46 (LCX) 68.96 (RCA)	NR	NR
Ensemble::Naive Bayes+SMO [15]	16	88.52	0.91	0.82
Hybrid FSA+FA+ETCA +XGBoost+SMOTE[39]	27	92.58	0.93	NR
N2GC-nuSVM + balancing [2]	29	93.08	NR	NR
NN-GA [19]	22	93.85	0.97	0.92
CART [28]	5	92.41	0.986	0.77
Proposed WAVEn Ensemble+Ori	5	98.97	1.00	0.937
Proposed WAVEn Ensemble+Bal	5	100	1.00	1.00

#Features-Number of Features selected, NR- Not Reported, Ori-Original Dataset, Bal- SMOTE Balanced Dataset, Extended Dataset* has 500 patient records

the Cleveland dataset for experimental evaluation as it is widely used by the researchers for heart failure identification and prediction. The Cleveland dataset is a famous heart failure dataset taken from University of California, Irvine machine learning repository with 303 records [25]. This dataset consists of 14 features with 13 independent feature attributes namely Sex, Age, resting Blood Pressure (RBP), serum cholesterol (CHO), Fasting Blood Sugar (FBS), Rest Electrocardiogram (RECG), Maximum achieved Heart rate (THA), Angina induced by exercise (EXA), old peak (OP), peak exercise slope (SLO), major blood vessels coloured by Fluoroscopy (CA), Thallium Scan (THAL), Chest Pain Type (CPT) and one target class (NUM). The target class has two values: value 0 represents the absence of disease and value 1 represents the presence of disease.

In the dataset, we have selected only 297 records from 303 records and removed 6 records having missing values. Finally, the dataset consists of 160 normal or healthy records and 137 CAD or unhealthy records with a class distribution of 53.87% normal and 46.13% abnormal or CAD patients. The dataset is divided into training and testing subsets with 90% for training and remaining 10% of the data is used for testing. A 10-fold cross-validation technique is utilized for training the model using seven significant features namely Sex, THA, EXA, OP, CA, THAL, and CPT selected using the Boruta feature selection algorithm.

Experiments are conducted to evaluate the performance of the proposed algorithm on both original and SMOTE balanced dataset. From the experimental results, it can be observed that the WAVEn model shows better performance in terms of accuracy, kappa, sensitivity, specificity, precision, F measure and MCC. The WAVEn technique achieves a classification accuracy of 96.55% with a sensitivity value of 100%, specificity value of 93.75%, 92.86% precision and F1 score of 96.3% on the original Cleveland dataset. The quality of binary classification measured using MCC score has a value of 0.933 with a kappa value of 0.931. In addition, the 100% sensitivity shows the efficiency of the WAVEn model in predicting all positive cases which is required for any medical diagnostic system that make it practically applicable. From the results, it can be inferred that WAVEn algorithm significantly identifies all CAD patients as patients and sometimes it has little degradation in its discriminative power of identifying all healthy persons as healthy.

Similarly, the experimental results of the SMOTE balanced dataset shows that the proposed WAVEn algorithm achieved 100% for all metrics. This shows the effectiveness of the proposed model in significantly identifying all heart failure persons as CAD patients and normal persons as healthy. Nonetheless, the previously developed models for identification and prediction of heart failure disease using Cleveland dataset have not achieved this accuracy level. Table 5 shows the performance result of various algorithms and number of feature selected for predicting CAD using the Cleveland dataset. The proposed WAVEn algorithm improved the predictive accuracy with only 7 features and achieved a better classification accuracy when compared with all the existing techniques [3,4,17,18,26,32,36,44,53,62], except one that has slightly better performance than ours only in terms of accuracy and specificity for unbalanced dataset [54]. However, it should be noted that high sensitivity is required for any medical diagnosis system to accurately identify the diseased data from healthy data. Hence, our proposed algorithm is effective than [54] as it has the ability in discriminating the diseased data more accurately.

5. Discussion

In the proposed work, we achieved the maximum achievable accuracy, sensitivity, specificity, and precision in diagnosis and prediction of CAD. The main objective during the diagnosis of CAD is that a CAD patients should be reported as having CAD and a

Table 5
Comparison of the proposed method with other methods in literature on the Cleveland dataset.

Method	#Features	Accuracy(%)	Sensitivity	Specificity
CFS + PSO + MLP [62]	7	90.28	NR	NR
ANN + F-AHP [53]	13	91.10	1.00	0.84
Logistic Regression[26]	13	85	0.89	0.81
Adaptive FDSS [44]	8	92.13	0.92	0.92
HRFLM [36]	13	88.4	0.93	0.826
RSA-RF [32]	7	93.33	0.95	0.898
Voting [17]	9	87.41	NR	NR
Stacked SVM [4]	9	92.22	0.829	1.00
DNN [3]	11	93.33	0.85	1.00
HNCL+AMLN [54]	13	97.80	0.955	1.00
NE-nu-SVC+GA+balancing [18]	7	98.60	0.986	NR
Proposed WAVEn Ensemble +Ori	7	96.55	1.00	0.937
Proposed WAVEn Ensemble +Bal	7	100	1.00	1.00

#Features-Number of Features selected, NR- Not Reported, Ori-Original Dataset, Bal- SMOTE Balanced Dataset

healthy person should not be reported as a patient. Also, it is essential to identify a person having CAD correctly as a patient is more important than identifying a healthy person. In this aspect, the WAVEn algorithm always correctly identifies a person having CAD as a patients with some false predictions say some of the healthy persons are classified as CAD patients in original dataset. However, the WAVEn and RF algorithms have the ability to predict patients having CAD as well as always identifies and reports a healthy person as healthy without any error for the balanced dataset. With compliance to these experimental results, the developed model can be used to test a patient initially to find whether he/she is having CAD or not. When the test results are negative no further diagnostic measures are required for the patient, otherwise, recommend angiography procedure for identification of the stenosis.

Experimental results clearly shows the robustness of our algorithm in diagnosis and prediction of CAD. To the best of author's knowledge, no prior works in literature have obtained these highest result using only five features in CAD diagnosis with an average accuracy of 98.97%, 100% sensitivity and 96.3% specificity for the original dataset and similarly 100% average accuracy, 100% sensitivity and 100% specificity rate for a balanced dataset. Comparing both original and balanced dataset performance, it is found that the proposed WAVEn ensemble model shows better performance with zero false-negatives ensures that the algorithm identifies the CAD patients more accurately than identifying a healthy person. Furthermore, the WAVEn model has zero false predictions for a balanced dataset. Obviously, the performance result shows the reliability of the WAVEn model in distinguishing CAD patients from healthy persons that makes it more suitable for practical implementation.

6. Conclusion

In this study, a heterogeneous ensemble method is proposed to facilitate effective diagnosis and prediction of CAD disease in a patient. We have evaluated the performance of the proposed ensemble technique and base classifiers to analyze the predictive or diagnostics performance of the model to correctly classify CAD data using original and balanced Z-Alizadeh Sani dataset. We have employed feature selection algorithm and selected five features based on feature importance and rank. Then, 10-fold cross-validation is applied on the training subset and the performance of the algorithm is independently assessed on the unseen test data. Compared with all classifier models, the WAVEn algorithm shows better performance and able to identify CAD with 98.97% accuracy with a precision of 98.3% for the original dataset. Moreover, the WAVEn method is able to discriminate the diseased data from healthy data on the balanced dataset to achieve the highest precision of 100% and no prior works have achieved this reliability with only 5 features. Hence, the proposed model can be used effectively to predict CAD in a patient without using angiography procedure that will greatly reduce the side-effects of angiography, saves time and cost for the patients.

In this study, the highest classification accuracy of WAVEn with zero false negatives strongly emphasize on the practical implementation of a diagnostic system in hospitals that can be helpful for a cardiologist to diagnose CAD at the earlier stage. Finally, the algorithm can be applied on the extended version of Z-Alizadeh Sani dataset with 59 features and its performance in predicting stenosis using LAD, LCX and RCA arteries can be taken as future research work.

Declaration of Competing Interest

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