Hindawi
International Journal of Intelligent Systems
Volume 2023, Article ID 6442756, 19 pages
https://doi.org/10.1155/2023/6442756

Review Article

Towards Diagnostic Aided Systems in Coronary Artery Disease Detection: A Comprehensive Multiview Survey of the State of the Art

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Received 3 January 2023; Revised 10 June 2023; Accepted 28 July 2023; Published 9 August 2023

Academic Editor: Said El Kafhali

Introduction. Coronary artery disease (CAD) is one of the main causes of death all over the world. One way to reduce the mortality rate from CAD is to predict its risk and take effective interventions. The use of machine learning- (ML-) based methods is an effective method for predicting CAD-induced death, which is why many studies in this field have been conducted in recent years. Thus, this study aimed to review published studies on artificial intelligence classification algorithms in CAD detection and diagnosis. *Methods*. This study systematically reviewed the most cutting-edge techniques for analyzing clinical and paraclinical data to quickly diagnose CAD. We searched PubMed, Scopus, and Web of Science databases using a combination of related keywords. A data extraction form was used to collect data after selecting the articles based on inclusion and exclusion criteria. The content analysis method was used to analyze the data, and based on the study's objectives, the results are presented in tables and figures. *Results*. Our search in three prevalent databases resulted in 15689 studies, of which 54 were included to be reviewed for data analysis. Most studies used laboratory and demographic data classification and have shown desirable results. In general, three ML methods (traditional ML, DL/NN, and ensemble) were used. Among the algorithms used, random forest (RF), linear regression (LR), neural networks (NNs), support vector machine (SVM), and K-nearest networks (KNNs) have the most applications in the field of code recognition. *Conclusion*. The findings of this study show that these models based on different ML methods were successful despite the lack of a benchmark for comparing and analyzing ML features, methods, and algorithms in CAD diagnosis. Many of these models performed better in their analyses of CAD features as a result of a closer look. In the near future, clinical specialists can use ML-based models as a powerful tool for diagnosing CAD more quickly and precisely by looking at its design's technical facets. Among its incredible outcomes are decreased diagnostic errors, diagnostic time, and needless invasive diagnostic tests, all of which typically result in decreases in diagnostic expenses for healthcare systems.

1. Introduction

With the industrialization of societies and the surge in urban populations, cardiovascular diseases (CVDs) are recognized as the main cause of death in the world. CVDs include coronary artery disease (CAD), pulmonary embolism, peripheral arterial disease (PAD), cerebrovascular disease, rheumatic and congenital heart disorders, and deep vein thrombosis. However, CADs are the most prevalent CVD diseases, wherein atherosclerosis causes arterial ducts to narrow. CAD is a serious health problem that develops due to the buildup of plaque in the coronary arteries, impeding the transfer of oxygen-rich blood to the heart. Patients with this disease may experience no symptoms, feel pain or discomfort in their chests (angina), or have heart attacks [1–3]. The permanence of this condition enfeebles the heart muscles and leads to arrhythmias, heart failure, and even sudden death. Thus, the blood flow reaching the distal myocardium decreases in CAD and, finally, gives rise to ischemia. The prevalence of CAD, the main cause of death in the world, has increased in low- and middle-income countries in recent years. The statistics of patients and deaths caused by this disease are increasing every day, such that CAD is the primary cause of mortality among men and women in the United States. CAD treatments and interventions impose high economic burdens on healthcare systems. Hence, early detection and faster diagnosis of CAD can accompany remarkable outcomes concerning patient survival, reduction in treatment costs, and surgical interventions. Besides, early detection of CAD can facilitate clinical interventions and save the patient's life. Coronary angiography, or catheterization, is among the primary CAD detection procedures. This golden standard for CAD detection is an invasive approach that needs a Cardiac Catheterization Laboratory (Cath Lab), where angiography or angioplasty is applied with the injection of contrast agents into vessels and the visualization of vessels and blood flows. However, this method is invasive and requires anesthesia, and the side effects of the contrast agent on patients are not negligible, such that this substance negatively impacts patients and elderlies. On the other hand, the lack of Cath Lab sites in many geographical regions and clinical sectors and the long lines of angiography-needing patients are among the main reasons for this detection method. Therefore, numerous clinical specialists and researchers look for alternative, noninvasive CAD detection approaches [3–7]. Machine learning (ML) algorithms are among the principal approaches attracting the attention of many clinical researchers, such that a bulk of studies has employed ML methods in the past decade. These algorithms use various markers for CAD detection and classification. Every one of these studies has employed a specific group of features (markers) to diagnose CAD and applied different ML algorithms. Likewise, these studies have applied (traditional) machine learning and deep learning approaches to predict, detect, and classify CADs. However, no systematic literature review (SLR) inclusively addressing ML uses and various influential features in these algorithms has been published for CAD detection. Thus, the present SLR identifies and examines studies that have employed different ML methods to determine CAD severity. This SLR commits as follows:

(i) Design an ontology to classify ML uses in CAD detection
(ii) Discuss the uses of different ML methods in CAD detection
(iii) Discuss the application of various features in CAD detection
(iv) Present suggestions for future models on CAD detection

This SLR is organized in the following order:

Section 2 presents the related works, Section 3 discusses the SLR methodology, and Section 4 tackles the applications of different ML algorithms in CAD detection.

2. Related Works

Several review studies have addressed the use of ML and AI methods in detecting cardiac and CAD diseases. Alizadehsani et al. [8] reviewed all studies published in the 1992–2019 interval based on different ML algorithms, extracted applied ML algorithms, and displayed their degree of usage. This study disregarded the type of markers and features. In another survey, Alizadehsani et al. examined artificial intelligence techniques in CAD detection and probed trends, diagnostic features, and geographical differences in these studies. Yet, AI methods and algorithms were not explored in this review study.

Concerning the other cardiac diseases, there were several published review papers that the present SLR refrained from reviewing. Therefore, by meticulously examining the databases, the researchers found that no comprehensive review study has targeted different dimensions of ML uses for CAD detection and classification.

3. Review Protocol and Strategy

This section describes the phases of the review protocol, including the research questions, the search strategy, inclusion and exclusion criteria, and the quality assessment and data extraction processes. This SLR has been registered in the International Prospective Register of Systematic Reviews (PROSPERO) with the CRD42022340726 number. The early detection of CAD with ML and DL methods has considerably increased since 2016. Hence, this review study should be registered as intellectual property to provide researchers with a concise perspective and a glance at CAD detection by reviewing past studies.

3.1. Search Questions. After searching for the review papers on CAD detection and applying the paper-searching methodology, we should raise the research questions not discussed and answered in these studies. These questions are presented as follows:

(1) In what countries and years did researchers probe CAD diagnosis and classification?
(2) What features and markers have been used to detect CAD?
(3) Which feature extraction techniques are used for marker and biomarker reduction?
(4) Which machine learning methods have been used to detect and classify CAD?

(5) Which machine learning algorithms have been effective for detecting CAD?

(6) What suggestions can be made for better detection and classification of CAD using learning algorithms?

3.2. Search Strategy. By concisely investigating the electronic databases publishing scientific papers in the medical and computer fields, the researchers discovered that the PubMed, WOS, and Scopus databases contained numerous articles related to this research. By focusing on the early November 2017 to late April 2022 interval, this search employed keywords and logical phrases included in Table 1 and extracted the respective papers published in this area. Google Scholar and IEEE publications were excluded from the search domain due to their proximity.

3.3. Quality Assessment. In systematic studies, a step towards supporting data analysis and preventing evidence bias and poor results is the quality assessment of the search, which is as crucial as other phases, such as data extraction and analysis. As the closest guide to the scope of our study, we carried out the present SLR based on the quality assessment (QUADAS-2) [9] for systematic reviews of diagnostic accuracy studies. This tool has been designed with seven criteria, four of which examine the risk of bias, while the others pertain to applicability-related concerns.

3.4. Data Extraction. The data extraction phase included different issues related to the design of the research questions. Every study was initially examined by the first reviewer (M.G.) and then by an expert review team (A.G.) for likely errors in data extraction. Table 1 presents the list of items with their definitions in the data extraction form. The differences in the searches were removed by discussions with an independent author (A.B.) The elements of the extracted data, including the author's name, country of the research, examined population, applied data, purpose, method, the role of mobile applications, and assessment methods, were evaluated.

4. Results

The researchers searched the valid databases according to the search strategies, extracted 15689 papers, and selected 52 full-text papers by studying the abstracts and bodies of papers, applying inclusion and exclusion criteria, and choosing articles commensurate with the topic of the present research. Figure 1 displays the PRISMA flowchart of the mentioned process.

After extracting the searched studies from the research population, investigating their details, and comparing their CAD results, we presented the operational metrics of the machine learning algorithms in the obtained detection and classification in four sections, endeavoring to answer the research questions in every section.

4.1. Characteristics of the Included Studies. A large number of studies have employed ML methods to detect cardiovascular diseases. However, many of these studies have targeted the early detection and prediction of CAD. Numerous studies have utilized different terminologies for CAD. While many researchers have used ACS as the primary type of CAD, others have utilized other terms such as obstructive CAD, SCAD, and varying ischemic heart diseases, including AIHD (coronary atherosclerosis) and CIHD (ACS). Despite the different ICD-10 codes for these cardiac diseases, many care centers use CAD instead of these terminologies. Figure 2 illustrates the sunburst of studies applying various AI methods to diagnose and classify different CAD types.

In the studies conducted in this domain, 33 used the CAD title in their research transparently, 13 applied ACS, and others employed types of obstructive CADs and SCADs.

A further investigation of the studies revealed that researchers were more engrossed in using ML to detect different CAD types during the past five years. Presumably, many studies have attempted to predict a spectrum of CAD diseases using various ML methods due to the increased international attention of healthcare organizations to cardiovascular health and the prevention of cardiac diseases. In the last four years ending in 2021, we witnessed an uptrend in these studies, except for 2021, when the number of these studies became fewer. It is likely that the outbreak of COVID-19 and the wave of research on this disease have distracted researchers from CAD detection and made them focus on other aspects of cardiac disorders, such as their association with COVID-19, the effect of the coronavirus, infections resulting from corona, and the impacts of various vaccines on heart function and coronary diseases. To answer the first research question, we can refer to Figures 3 and 4, which display the number of studies on detecting different CAD diseases in the past five years.

America, with eleven studies, and China, with nine studies, possessed the maximum number of studies applying machine learning to predict the conditions of CAD patients. The next rank belonged to Iran and South Korea, each with six studies in this domain. Figure 4 depicts the researchers of countries that have employed deep learning to process CAD data with the intention of fast detection and prediction of this disease.

The researchers of the present study presume that countries with the highest rate of cardiovascular diseases have conducted more studies on CAD diagnosis, such that some surveys have categorized America, China, India, and Iran into the group of countries with the highest number of cardiac patients. On the other hand, the datasets of Iranian CAD patients are among the most prevalent in Kaggle. It can be a justification for researchers to test different ML methods and algorithms on these datasets [10–14].

4.2. Overview of the Types of Features (Markers) Used for CAD Diagnosis. Various datasets have been presented for developing models that can rapidly predict and diagnose vascular diseases, especially CAD. The investigations showed that 67 applicative datasets were presented in different

Table 1: Search keywords and database query.

Keywords		Logical combination of keyword
Coronary artery disease, CAD; acute coronary syndrome, ACS; coronary heart disease, CHD	#1	"Coronary artery disease" OR "CAD" OR "acute coronary syndrome" OR "ACS" OR "coronary heart disease" OR "CHD"
Machine learning, classification, data mining, decision tree, neural network, support vector machine, ensemble, Bayesian	#2	"Machine learning" OR "classification" OR "data mining" OR "data-mining" OR "decision tree" OR "artificial neural network" OR "support vector machine" OR "ensemble" OR "Bayesian"
Final search strategy		#1 AND #2

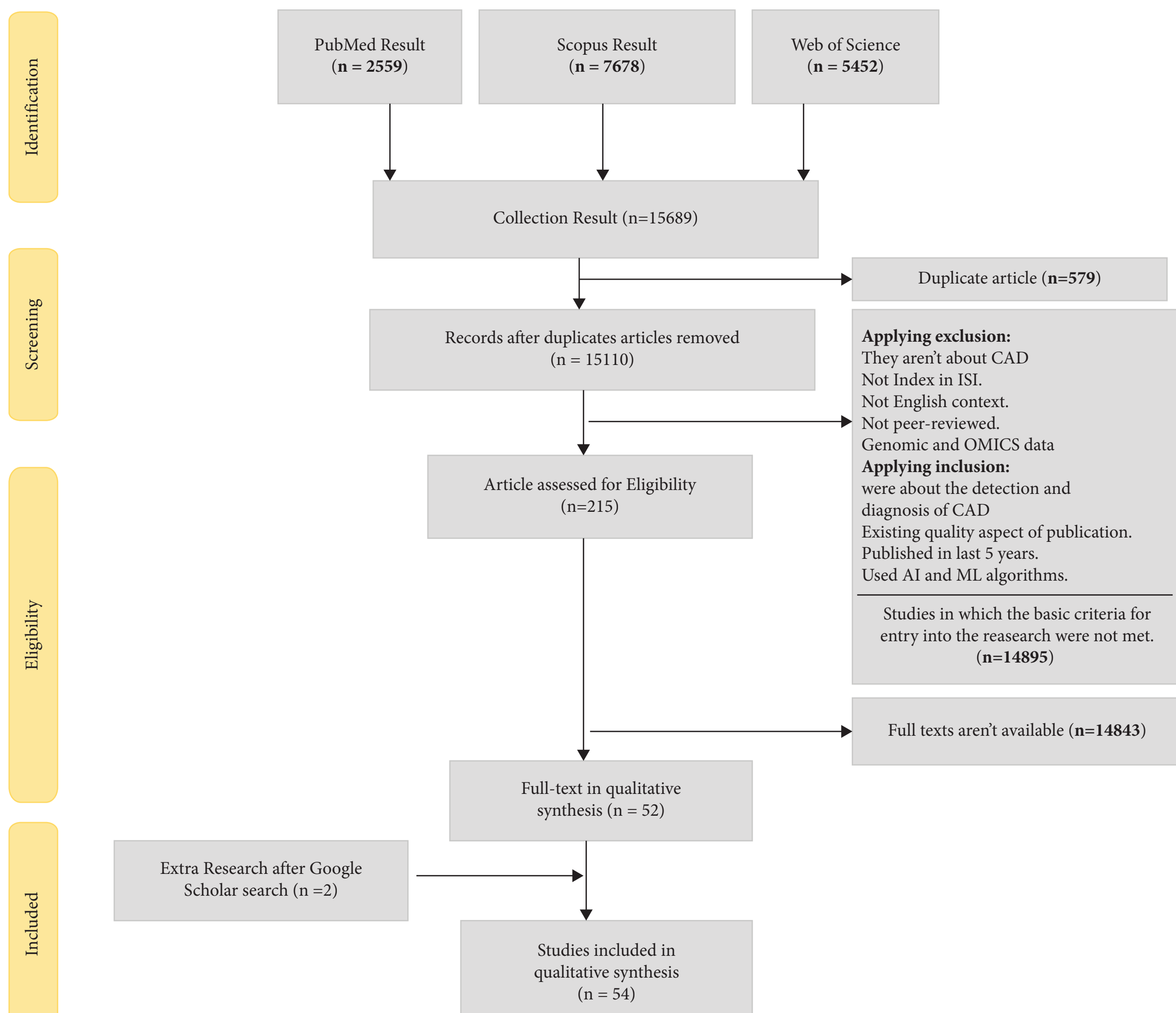

Figure 1: PRISMA flowchart of search and exclusion process. Out of 15689 retrieved studies, 54 studies were selected for data analysis.

scientific datasets from 18 countries for CAD prediction and detection with data mining (DM) techniques. These datasets had different dimensions and features, such that the smallest and biggest datasets with 20 and 24000 samples possessed 9 and 11 features from India, respectively [8].

By examining these datasets and those used by studies in the research population, we could provide two answers to the research question. The probed data were generally of three kinds: clinical data (data associated with patients' biographies, underlying diseases, physical and somatic information, and so on), laboratory data, and data acquired from diagnostic procedures and measures, such as ECGs. Figure 5 displays the number of studies using various data.

Some studies have applied more than one data type. One of the most famous and known datasets in CAD diagnosis is the SZ-Alizadeh Sani dataset [15], which contains different data on demographics, symptoms and examination, laboratory echo features, and ECGs. However, some studies have employed an integration of laboratory data, signs and symptoms, and demographics but ignored ECG data and invasive and noninvasive diagnostic procedures [16, 17]. Some researchers have utilized a broad spectrum of clinical

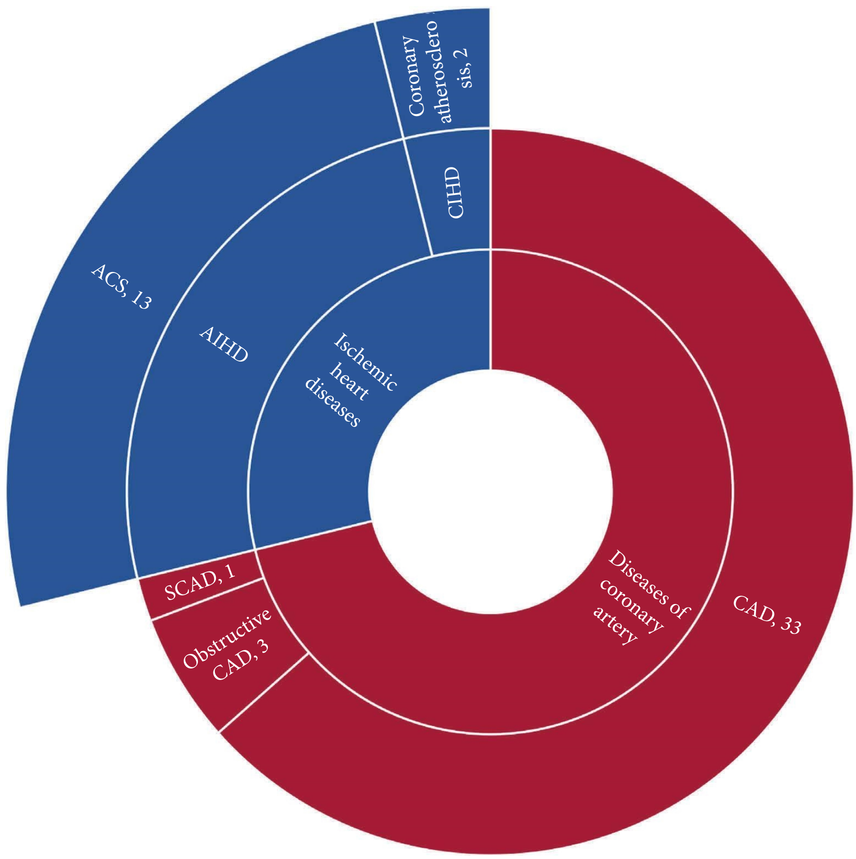

Figure 2: Number of studies using machine learning to detect and classify various CADs.

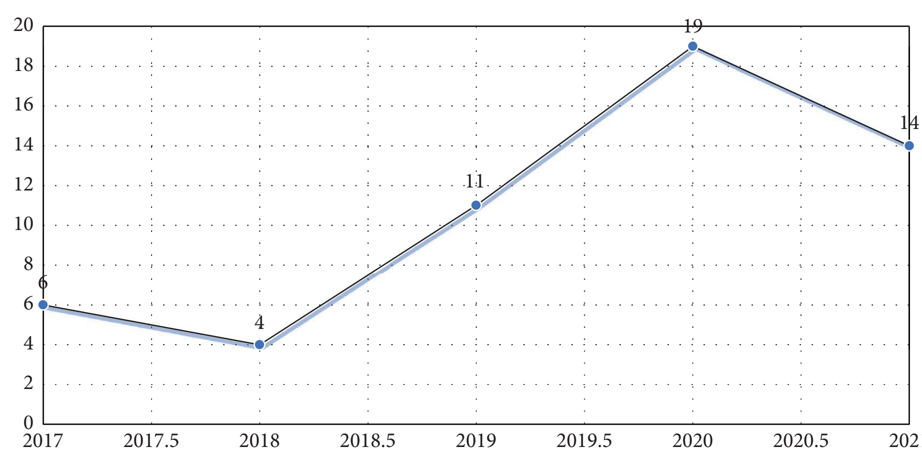

Figure 3: Research included in this SLR, broken down by year of publication.

and demographic data, besides physical diagnostic tests, such as the stress test and echocardiography, in their examined datasets [18, 19]. Some introduced models have only used laboratory and demographic data to estimate the risk of ACS and CAD incidence and neglected the data provided with physical diagnostic tests and symptoms [20].

Demographics mostly mean using data about age, weight, body mass index (BMI), and indices influencing cardiovascular diseases, such as smoking. Table 2 displays the most significant and prevalent features influencing the risk of cardiovascular diseases (CADs). All studies have employed some of these features according to feature selection algorithms or clinical findings.

4.3. Feature Engineering. Feature engineering, a crucial and significant task in preparing data for ML- and AI-based modeling, aims to fabricate fit and optimum features from available features and improve the performance of the mathematical model or artificial model [21–23]. Feature engineering involves applying transfer functions like arithmetic operators to given features to create new

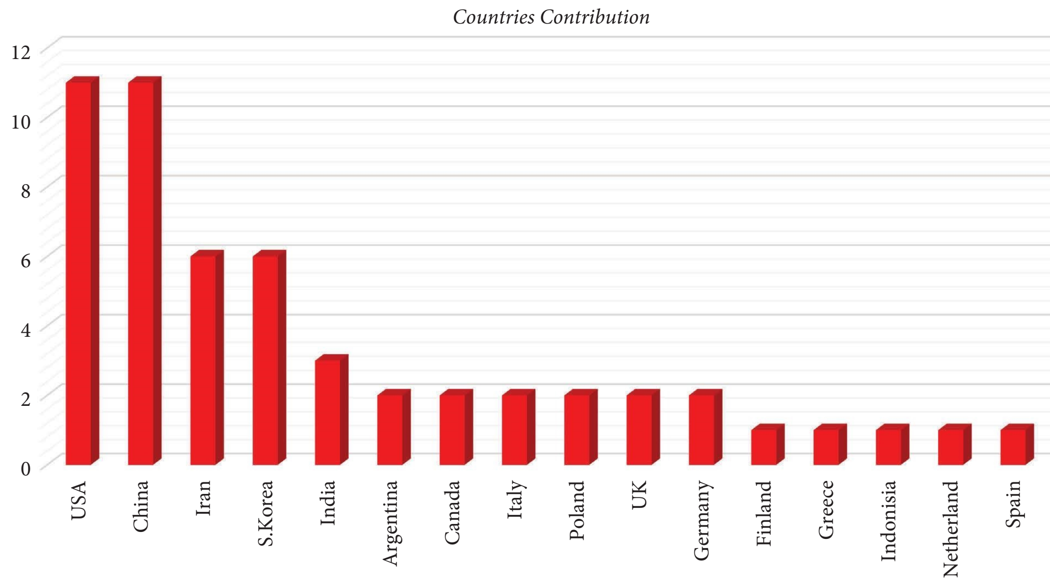

FIGURE 4: Contribution of various countries to research that employed ML to diagnose CAD.

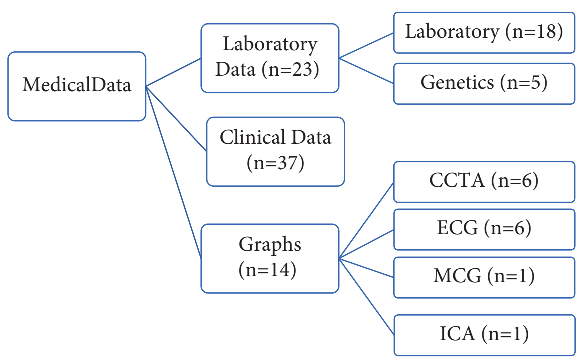

FIGURE 5: The rate of various medical data used for CAD diagnosis.

functions. Feature engineering includes feature selection and extraction, though many studies subsume these two phases under a single feature selection stage [24–26]. Various statistical, mathematical, and intelligent algorithms, e.g., swarm intelligence, genetic, and evolutionary, are used to select and extract these features. In some ML-based models, features are selected automatically (deep learning methods), such that studies working with visual and auditory data have employed these methods for feature selection and extraction. However, numerous investigations have selected features manually using various mathematical methods (traditional ML algorithms). Nevertheless, many approaches have been used to opt for more influential features of CADs in machine learning algorithms. Since almost countless studies have applied nonvisual and nonaudio data in detecting CAD, statistical and mathematical methods were used for feature selection, and feature extraction techniques like convolution were not employed. To answer the third research question, we presented the extent to which feature extraction methods were used in the examined studies in Figure 6.

As Figure 6 depicts, statistical methods have been frequently used for feature selection. Twenty-eight studies have employed these methods to limit the number of features to the most influential ones. This reduction in feature dimensions eliminates irrelevant features and decreases the memory size allocated to the model's computations.

Before implementing ML algorithms, some articles have used feature selection and data reduction methods, classified in this section, to enhance the accuracy of algorithms over data. For feature selection, the papers have used various approaches, the most significant and applied of which is recursive feature elimination (RFE). Likewise, some studies have employed statistical analyses for feature selection. Figure 7 illustrates to what extent the dimension reduction methods of features have been utilized.

Principal component analysis (PCA) is one of the most applied methods for reducing data dimensions. Seven studies have employed PCA to reduce data dimensions [27–33].

4.4. Overview of Machine Learning Methods in CAD Diagnosis and Classification. Studies aiming to diagnose and classify CADs via ML have applied several methods. To answer the fourth research question, we examined studies using ML for CAD detection and classification and concluded that three

Table 2: Most prevalent features in detection and diagnosis CAD using ML methods.

Feature category	Feature name
Demographic data	Age Weight Length Sex BMI Smoking status Family history Pacemaker rhythm
Diseases and physical indicators	Diabetes mellitus Thyroids diseases Edema Systolic murmur Typical chest pain Dyslipidemia Airway disease Hyper tension Congestive heart failure Cerebrovascular accident Atypical Weak peripheral pulse Exertional chest pain Nonanginal CP Dyspnea Chronic angina Peripheral arteriopathy Lung rales Diastolic murmur Low threshold angina Blood pressure (BP) Function class Right bundle branch block Left bundle branch block Pulse rate (PR) (ppm) Previous myocardial infarction Previous CABG surgery Beta-blocker treatment Calcium blocker treatment ACE inhibitor treatment
Genetic features	GCPII C1561T RFC1G80A cSHMT C1420T TYMS 5′-UTR MTHFR C677T MTR A2756G MTRR A66G CYP1A1 m1, CYP1A1 m2, CYP1A1 m4
ECG features	Poor R wave progression (poor R progression) T Inversion Q wave LVH (left ventricular hypertrophy) ST depression\ST elevation Rhythm ST-deviation Combination of ECG features BBB Rhythm
Laboratory feature and biomarkers	VHD (valvular heart disease) Erythrocyte sedimentation rate (ESR) (mm/h) Neutrophil (neut) (%) High density lipoprotein (HDL) (mg/dl) Hemoglobin (HB) (g/dl) Platelet (PLT) (1000/m) Maximum creatine kinase-MB level in IU/l Maximum troponin level in IU Fasting blood sugar (FBS) Sodium (Na) White blood cells (WBS) Maximum creatine kinase-MB level in IU Serum creatinine level in mg HB ESR LDL, BUN K, Lymph, EF, region RWMA, serum glycemia level (used frequently)
Echo features	Ejection fraction (EF) Regional wall motion abnormality Creatine kinase level

ML methods were significant and frequent in analyzing CAD features. They were traditional machine learning methods, ensemble methods, and neural networks (NNs) deep learning (DL) methods, used in 25, 21, and 10 studies, respectively. To answer this research question in detail, we provided supporting documents as follows.

4.4.1. Traditional Machine Learning (TML). TML methods with numerous algorithms allocate the highest portion of the respective research to themselves. The outnumbering algorithms of this method have been used to process the data in various health domains. These algorithms have developed from the emerging concepts of AI and are founded on statistical and mathematical formulas. TML algorithms encompass a broad spectrum of algorithms recurrently used for CAD diagnosis in the past decade. Table 3 presents the extent to which these algorithms have been used to detect and classify CAD against other cardiovascular abnormalities.

4.4.2. Ensemble Methods. Ensemble methods are a category of learning algorithms that build a set of classifiers and then classify new data points via (maximally) weighted voting. The ensemble method is mainly based on Bayesian averaging, yet its newer algorithms include bagging, stacking, and boosting [34, 35]. The ensemble method uses the prediction capacities of several poor learning techniques for a given dataset and achieves better prediction results by combining their outputs. The idea behind the ensemble method is interesting since the ultimate output is based on

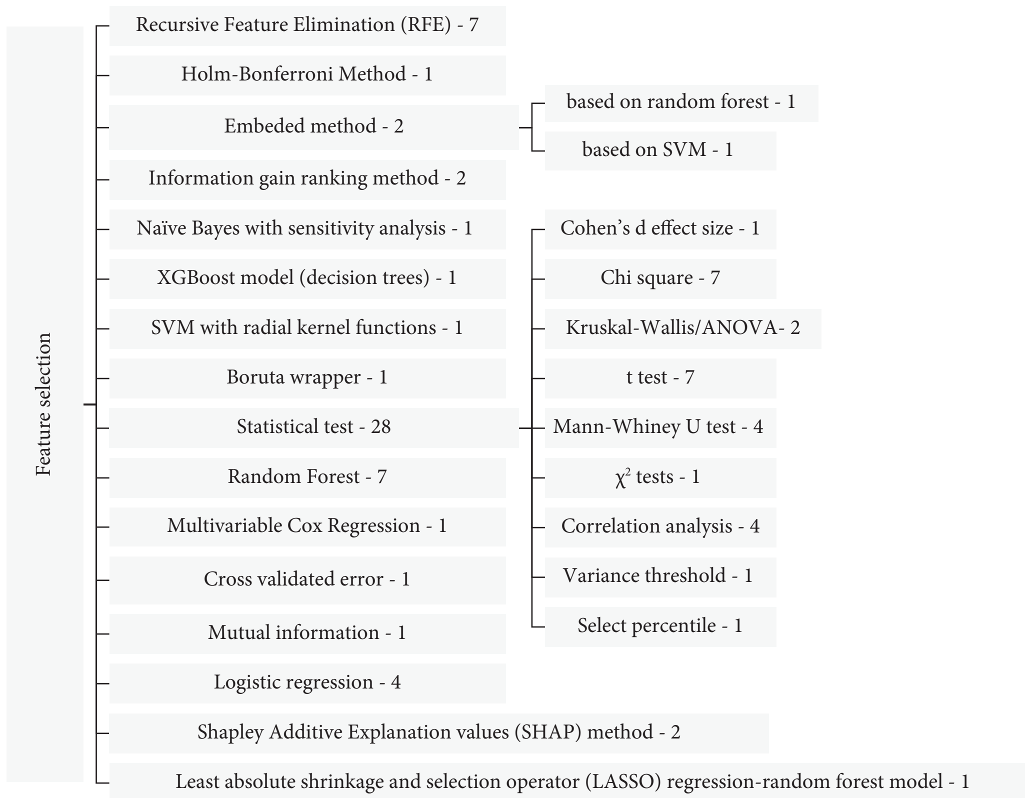

Figure 6: Feature selection methods and algorithms in CAD diagnosis using ML.

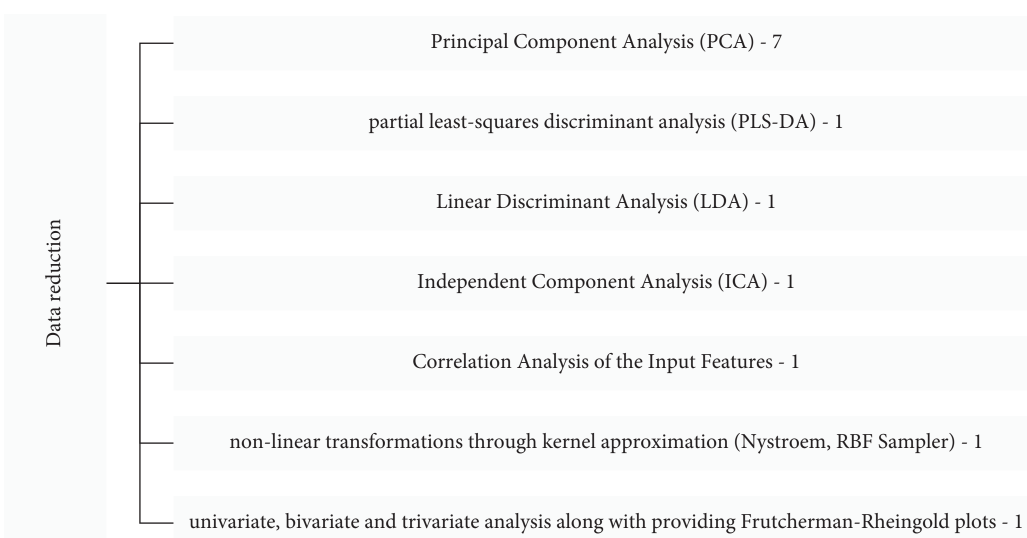

Figure 7: Data reduction techniques in studies that used ML in the diagnosis of CAD.

a combination of various outputs that lead to more accurate results. This method helps moderate the problem of finding global minimums for a given input function against individuals and isolates techniques and algorithms since one of the problems of classification techniques is finding the global minimums of the function. Although sufficient train data is available in many cases, these techniques need countless computational sources to determine global minimums. The ensemble method obviates this problem by averaging or combining the local optimum solutions of several poor learning techniques for a given input function [36, 37]. Many studies have employed different ensemble methods of various machine learning algorithms for CAD estimation and diagnosis. Table 4 represents the extent to which various ensemble methods of ML algorithms have been used.

Table 3: TML method and algorithm in studies that used ML in the diagnosis of CAD.

TML methods	Type of TML algorithms	Number of frequency
FCM	ReAFCM	3
KNN	KNN	1
Regression	Elastic net Cox regression Regularized LR PCR (principal component regression) L1-regression adjusted Logistic regression	7
Decision tree	QUEST CART	3
Bayesian network	Hill climbing Naïve Bayes	3
SVM	SVM NuSVM + GA (genetic algorithm) SVM + BS	9
Dimension reduction	Nan	1

Table 4: Different ensemble algorithms applied in CAD diagnosis.

Ensemble algorithms	Number of uses in CAD diagnosis
Bagging	4
Stacking	1
Boosting	15
Other	1

4.4.3. Neural Network and Deep Learning. Neural networks (NNs) are among the principal methods used for analyzing medical data. Inspired by brain function, these networks have achieved extraordinary results in diagnosing and classifying diseases. NNs, also known as fully connected neural networks, have a long history. Articles use these networks under the name "Multilayer Perceptron (MLP)." MLP possesses a topology that often exploits the gradient decent methodology and yields excellent results in discovering the patterns of nonlinear models in healthcare data [38].

Concerning the large datasets of some studies, NNs were no longer responsive to the volume of computations, and deep networks were required. CNNs were among the most conventional types of these networks and were part of deep learning concepts. CNNs are a subclass of NNs and possess a minimal convolution layer. Feature selection is performed automatically, not manually, in CNNs [34, 39]. Table 5 displays the extent to which various NNs have been employed.

Table 6 presents all studies using ML methods for CAD diagnosis and classification. The first column of this table provides the first author and the year and country of publication. The other columns give information about the research purpose, data type, data size, dataset, cross-validation technique, type of ML methods, type of ML algorithms, and data preprocessing methods.

Table 5: Different types of NN algorithms applied in CAD diagnosis.

Method	Number of uses in CAD diagnosis
MLP	8
CNN	15
RCNN	1

To answer the fifth research question and examine the effectiveness of the ML methods in analyzing CAD data, we attempted to visualize their degree of utilization and diagnostic performance on a map by probing all evaluation metrics for 54 papers in the research population. The ML models and techniques applied in these studies have been classified in Figure 8 hierarchically. According to this chart (drawn using Microsoft Visio 2021), the ML methods have been classified into three general groups: traditional learning, ensemble models, and deep learning. The diagnostic CAD models that are based on various ML algorithms have been demonstrated in the next layers. Hence, SVM and regression, with 9 and 7 models, are the most intensively used models in the traditional learning group. With 15 models, Boost allocates the maximum number of models to itself in the ensemble models group. Likewise, the highest frequency in the neural networks and deep learning group belongs to multilayer perceptron (MLP) with 8 models.

In this chart, the datasets on which learning models have been implemented and the model assessment results have been presented in rectangular boxes. The assessment indices, being the ACC and AUC metrics in many studies, have been mentioned with an accuracy of two decimal places in the chart. Since many studies have employed the AUC criterion in their articles, we showed the respective AUC index for a better comparison of the results if a paper had reported the ACC and AUC of its proposed model. Empty and colored boxes display ACC and AUC values, respectively. The three yellow boxes show different assessment criteria, such as PPV, C-index, and c-statistics. The maximum AUC value equals 0.997 and is associated with the stacking technique applied to the Z-Alizadeh Sani Dataset. Similarly, the maximum ACC value equals 1.0 and is related to the CART and MLP models implemented on the Z-Alizadeh Sani dataset.

Numerous studies have employed the demographic, clinical, and laboratory data of hospitalized CDA patients. Some studies have implemented their models based on the available data in hospital systems (EMR/HER/Registries) or the present datasets for this disease. All in all, the Z-Alizadeh dataset was applied more than other datasets, and the results of implementing various models on this dataset were more accurate.

This study employed a comparative graphic chart to compare the extent to which various algorithms of ML methods were used. The chart in Figure 9 which was drawn in VOS viewer version 1.6.17, illustrates the relationships between different methods and their algorithms in analyzing CAD features. These methods are depicted as nodes, and the intermethod comparison in every study is shown by edges. Thus, if a study has compared several methods, they fall into

Table 6: Studies that classified and diagnosed CAD diseases using machine learning algorithms.

Authors, years, and country	Aim of study	Data and features	Sample size	ML method and algorithms	Performance	Validation technique	Detail
Abdar et al. 2019, Poland [40]	Accurate diagnosis	Alizadeh dataset: demographic; symptom, examination, ECG, laboratory, and echo	303	C-SVC, NU SVC, and linear SVM	F_1 score = 91.51 ACC (accuracy) = 93.08	10-fold	One hot encoding, genetic algorithm, and genetic optimizer
Al-Zaiti et al. USA, 2020 [19]	Prediction of ACS	ECG features	1244	LR, GBM, and ANN	Sen (sensitivity): 52% compared to commercial interpretation soft Sen: 37% compared to experienced clinicias	10-fold	Fusion model Limited-memory BFGS
Al'Aref et al. USA, 2020 [41]	Prediction of obstructive CAD	CT angiography data from CONFIRM registry	82 lesions (containing 124 cls)	Ensemble ML (XGBoost)	Spe (specificity) = 89.3% for	10-fold	Model type hyperparameters Cohort study
Al'Aref et al. USA, 2019 [42]	In-hospital mortality prediction	Demographic and diseases and physical indicators	79,804	AdaBoost (adaptive boosting), XGBoost (extreme gradient boosting), RF (random forest), LR	AUC (area under cure) = 0.927	5-fold	Predictive model 1-hot-encoding
Amarbayasgalan et al. 2019, S. Korea [32]	CHD risk prediction	Demographic and diseases and physical indicators History of medical cardiac procedure	25,990	NB, KNN, DT, RF, SVM, and PCA-DNN	ACC: 86.33% Pre (precision): 91.37% Rec (recall): 82.9%	10-fold	The DAE-general is used for data grouping and selection of the CHD risk prediction model Deep autoencoder
Ayatollahi et al. 2019, Iran [43]	Predicting	Local dataset including demographic and life style features	1324	ANN and SVM	SVM ACC > NN ACC SVM Sen: 92.32%	10-fold	Predicting model
Baskaran USA 2020 [17]	Prediction	Demographic, risk factors, and medication use angina characteristics	1,028	XGBoost	AUC = 0.705 Sen = 89.2%	5-fold	Cohort study
Beunza et al. Spain 2019 [44]	Prediction	Demographic, life style, and laboratory features	4240	SVM	AUC = 75%	NM (not mention)	DT, RF, SVM, and ANN
Borracci et al. Argentina 2021 [45]	Acute coronary events score discrimination	40 demographic and laboratory features	1255	NN algorithms	NN ACC: 97.1%	NM	Two-hidden layer MLP Radial basis function network
Bouzid et al. 2021, USA [27]	Diagnosis of ACS at the emergency department	ECG	73	LR	Classified 10 to 29% cases correctly	NM	RF used to ECG feature selection, NN, FSS (feature subset selection), LR, and PCA
Candemir et al. 2020 USA [46]	Detection of CAD	CCTA (coronary computed tomographic angiography)	493	3D-CNN (3D convolutional neural network)	ACC = 90.9% Sen = 68.9% Spe = 93.6%	5-fold	Proposed CNN model was applied as main detection model

Table 6: Continued.

Authors, years, and country	Aim of study	Data and features	Sample size	ML method and algorithms	Performance	Validation technique	Detail
Huang et al. 2017, China [20]	Prediction of ACS	Demographic and clinical and laboratory features from EMR (electronic medical records) (268 feature)	2930	Boosted	ACC = 89.5% Sen = 89.8% Spe = 88.9%	5-fold	Boosted resampling classification. Rf, AdaBoost, smote, and SVM
Dogan et al. 2018, USA [47]	Predicting the risk for five-year incident coronary heart disease	Demographics and conventional coronary heart disease (CHD) risk factors	1704	Ensemble RF	Sen = 70% Spe = 74%	NM	Prediction model-based DNA
Gola et al. 2020, Germany [48]	Predicting CAD	Six imputed data Feature not specified	15,510	NB and SVM	AUC = 0.92	10-fold	Quality control of data. Regression, RF, GB, and SVM
Forssen et al. 2017, UK [30]	Prediction of CAD	Metabolomic data	1474	PCA	AUC: 0.767%	50-fold	PCA, LR, and RF
Ghiasi et al. 2020, Canada [49]	Diagnosis of CAD	Z-Alizadeh Sani dataset	303	DT (CART)	ACC = 100%, Sen = 100%, Spe = 100%	10-fold	SMO (sequential minimal optimization), NB (Naïve Bayes), ANN C4.5, J48, bagging, CART
D'Ascenzo et al. 2021, Italy [50]	Prediction of adverse events following an ACS	25 clinical features (demographic, health history, and procedure features)	19,826	Proposed praise model	AUC = 0.74–0.93	NM	AdaBoost, NB, and KNN
Davari Dolatabadi et al. 2017, Iran [28]	Automated diagnoses of CAD	ECG recordings of 80 human subjects	86	SVM	ACC = 99.2% Sen = 98.43%, spe = 100%	NM	PCA was used to data reduction
Du et al. 2020, China [51]	Prediction of CHD	Demographic, health history, and procedure features	42,676 patients	Ensemble XGBoost	AUC = 0.94	NM	XGBoost, KNN, RF, LR, and SVM, DT
Gupta et al. 2019, Canada [16]	Estimating risk of CAD	Z-Alizadeh Sani (demographic, health history, and medical procedure features)	303	BN (Bayesian network)	AUC = (0.93 + 0.04)	10-fold	LR, SVM, and ANN Graphical reasoning introduces
Goldman et al. 2021, Israel [52]	Prediction of coronary heart disease risk	Demographic, health history, and medical procedure features	3066	ANN	ANN_{AUC} > FRS (framingham risk score) AUC	5-fold	Proposed ANN model has high accuracy in screening CHD
Golpour et al. 2020, Iran [53]	Prediction to necessity for coronary angiography	Demographic, life style feature, and clinical data	1187	NB	NB AUC = 0.74%	NM	LR, NB, and SVM

Table 6: Continued.

Authors, years, and country	Aim of study	Data and features	Sample size	ML method and algorithms	Performance	Validation technique	Detail
Hu et al. 2019, China [54]	Prediction of ACS	Clinical dataset from EHR	2930	Ensemble	AUC = 0.715	5-fold	SVM, LR, cart, bagging, and AdaBoost (ensemble approach)
Kim and Kang 2017, S. Korea [18]	CHD risk prediction	Korean dataset (demographic and clinical data)	4146	NN	PPV = 67.5 NPV = 89.0 ACC = 87.63	NM	LR, NN, FRS, and NN_FCA
Kayvanpour et al. Germany, 2021 [55]	Diagnosis of ACS	Demographic and clinical data	134	Developed NN	ACC: 0.96 (95% ci 0.96–0.97) Sen: 0.95% Spe: 0.96%	10-fold	KNN, NB, RF, DT, and SVM
Jung et al. 2021, S. Korea [33]	Prognosis, and diagnosis of CAD	Demographic and laboratory features	2055	PCLR	AUC = 0.70	5-fold	Statistical analysis PCA
Zhou et al. 2019 China [56]	Identification of CHD	Demographic, laboratory, and medical feature	1072	SVM	AUC = 0.963 and 0.990	NM	SVM
Zhou et al. 2020 China [57]	Prediction of CAD	Demographic, laboratory, and medical features	6722	RF	AUC = 0.816	5-fold	Statistic technique
Joloudari et al. 2020, Iran [58]	CAD diagnosis	Z-Alizadeh Sani dataset	303	DT (decision tree)	AUC = 91.47	10-fold	RTS (random tree), SVM, and DT
Huang et al. 2021, China [59]	CAD detection	Demographic and laboratory features	209	MLPNN	ACC: 89.5% Sen: 89.8% Spe: 88.9%	NM	11 diagnostic models Statistical analysis PCA
Krittanawong et al. 2021, USA [60]	Predict mortality in patients with spontaneous CAD	Demographic, laboratory, and medical features	30,425	RF	AUC = 0.95	10-fold	LR, SVM, RF, KNN (K-nearest neighbors), and AdaBoost
Zreik et al. 2018, Netherlands [61]	Detection of coronary artery plaque and stenosis	CCTA	163	RCNN	AUC = 0.80	4-fold	Classification
Liu et al. 2021, China [62]	Prediction of mortality in CAD	24 features (demographic and medical features)	2037	LR model	Spe = 0.69 ACC = 0.93	5-fold	LR, RF, and SVM
Soflaei et al. 2021, Iran [63]	Prediction of CAD by dietary features	34 dietary features	716	DT	ACC = 82.94%	10-fold	QUEST, C5.0, and C & R tree
Steele et al. 2018, UK [64]	Predicting mortality in CAD (Prognosis)	586 features from HER (demographic, laboratory, and medical features)	80,000	Cox regression	AUC = 0.80	10-fold	RF and DT (C4.5)
Li et al. 2021, China [65]	Prediction of CAD	Demographic, laboratory, and medical features	5819	Ensemble	AUC = 0.75%		BN, RL, GDBoost, RT, and DL (deep learning)
Md Idris et al. 2020, Indonesia [66]	Risk prediction in CAD	Demographic, laboratory, medical features, and health history	49,406	DT	AUC > 90%	10-fold	LR, NN, kNN, DT, NB, SVM, and DL Chi-squared test for FS (feature selection)

Table 6: Continued.

Authors, years, and country	Aim of study	Data and features	Sample size	ML method and algorithms	Performance	Validation technique	Detail
Motwani et al. 2017, USA [67]	Prediction of mortality in CAD	Clinical feature and CCTA	10030	Boosted ensemble algorithm	Sen = 90% Spe = 90%	10-fold	DT, boosted ensemble algorithm
Noh et al. 2019, S. Korea [68]	Prediction of ACS	20 features (demographics and laboratory)	9539	SVM	AUC = 0.860	5-fold	SVMs and LDA (linear discriminant analysis)
Orlenko et al. 2020, Finland [69]	Predicting of coronary artery disease	Demographics and laboratory	925	DT	AUC = 0.77 ACC = 0.77	10-fold	LR, TPOT (tree-based pipeline optimization tool), RF, and BNB (Bernoulli Naïve Bayes)
Pattarabanjird et al. 2020, USA [31]	Prediction of CAD severity	Demographics and laboratory	481	NN (ID3 rs11574)	AUC = 72% to 84%	NM	CRF and ID3
Pieszko 2019, Poland [70]	Mortality prediction in ACS	Hematological markers	5053	Gradient-boosted tree	AUC = 0.9		Cox regression model
Polero 2019, Argentina [71]	Risk prediction of ACS	Demographics and history of cardiovascular disease	161	RF	AUC = 0.89 Sen = 0.8552 Spe = 0.8588	10-fold	NN RF
Naushad et al. 2018, India [72]	Risk prediction of CAD	Demographic and genetic characteristics	648	EMLA (ensemble machine learning algorithm)	Acc = 89.3	NM	*t* test and Fisher
Zhang et al. 2020, China [73]	Detection of CAD	Holter monitoring, echocardiography (ECHO), and biomarker levels (BIO)	62	Holter model	Sen = 96.67% Spe = 96.67% ACC = 96.64%	5-fold	Random forest and SVM BIO examination reach best result
Ricciardi et al. 2020, Italy [74]	Prediction of CAD	22 features (laboratory and medical history)	10,265	LDA and PCA	ACC = 84.5 and 86.0 Spe > 97% Sen > 66%	10-fold	PCA and LDA for feature extraction PostgreSQL, a DBMS
Roy et al. 2020, India [75]	Predicting risk of CAD	Histories of diabetic features (7 risk factors)	296	J48, CRDT, SVM, (SMO), Naive Bayes	Different result was calculated	10-fold	The chi-squared test has been used by the researchers to find feature relevancy
Sherazi et al. 2020, S. Korea [76]	Mortality prediction ACS	65 features (demographic and medical history)	10,813	GBM (gradient boosting machine)	ACC = 94.7%	4-fold	GBM (gradient boosting machine), GLM (generalized linear model), RF, and DNN (deep neural network) *T*-test and chi-square test for categorical variables
Velusamy and Ramasamy 2021, India [77]	Diagnosis and prediction of CAD	Z-Alizadeh Sani dataset	216	WAVEn	Sen = 98.97% Spe = 100% ACC = 96.3%	10-fold	RF, KNN, and SVM Ensemble (AVEn, MVEn, and WAVEn)

TABLE 6: Continued.

Authors, years, and country	Aim of study	Data and features	Sample size	ML method and algorithms	Performance	Validation technique	Detail
Tayefi et al. 2017, Iran [78]	Predictive model for CHD	12 feature (age, sex, FBG, TG, hs-CRP, TC, HDL, LDL, SBP, and DBP)	2346	CART	Sen = 96% Spe = 87% ACC = 94%	NM	Statistical tests include: chi-square, one-way ANOVA, and Kruskal–Wallis
Tama et al. 2020, S. Korea [79]	Detection CHD	5 dataset (Z-Alizadeh Sani, Statlog, Cleveland, and Hungarian)	303	Two-tier ensemble (GBM, XGBoost, and RF)	Proposed AUC > other ensemble and individual models	10-fold	Random forest (RF) and gradient boosting Correlation-based feature
Wu et al. 2021, China [80]	Prediction of in-hospital cardiac arrest in patients with ACS	Demographic and medical history	166	XGBoost	AUC = 0.958 ACC = 88.9% Sen = 73%	NM	XGBoost, C4.5, RF, LR, SVM, BP NN, NB, KNN. *t*-tests, Wilcoxon rank-sum tests, and χ^2 tests
Iong and Chen 2021, Taiwan [81]	Early prediction of CAD	7 features (demographic and medical history)	NM	SVM with pooling layer	SVM	NM	SVN NB
Chen et al. 2020, China [82]	Detection of CAD	1163 variables (morphological)		Polynomial SVM with grid search optimization	ACC = 100%	10-fold	LR, DT, LDA, KNN, ANN, and SVM

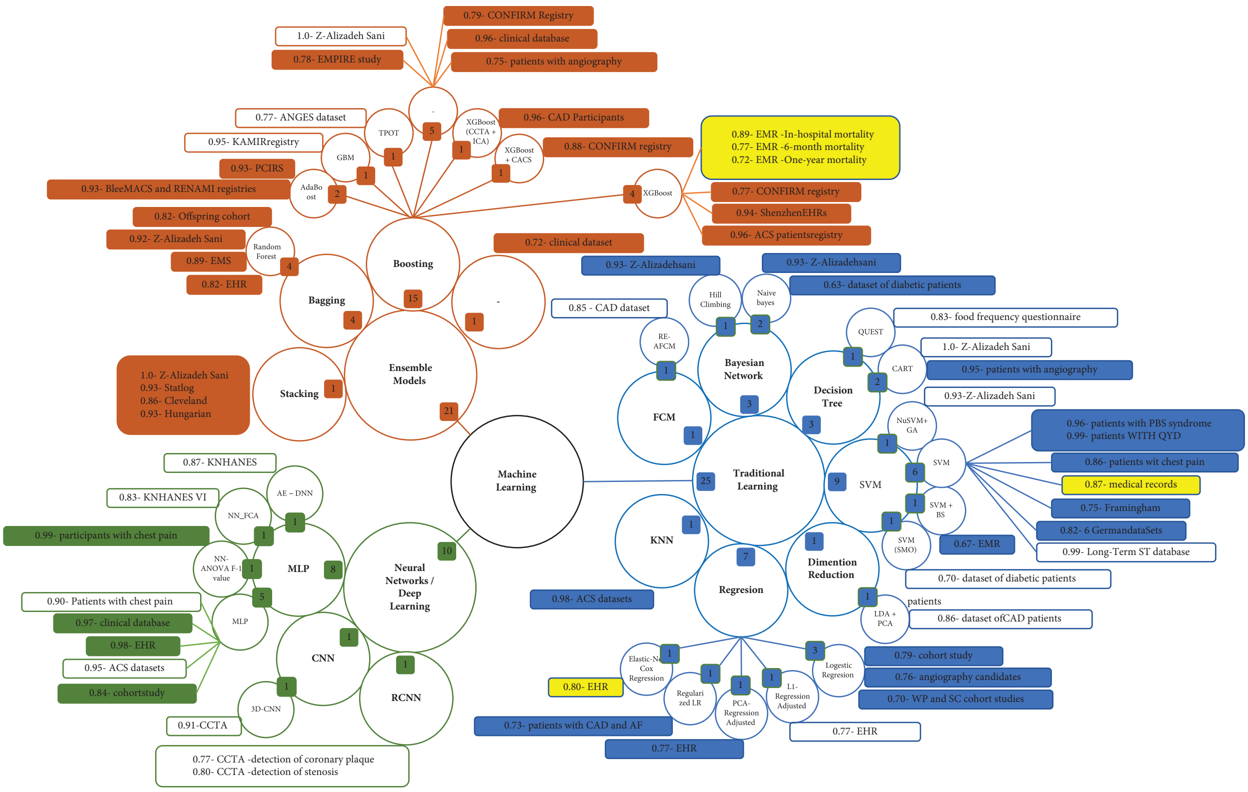

Figure 8: Types of ML methods plus algorithms of the subset of these methods along with the number of their use.

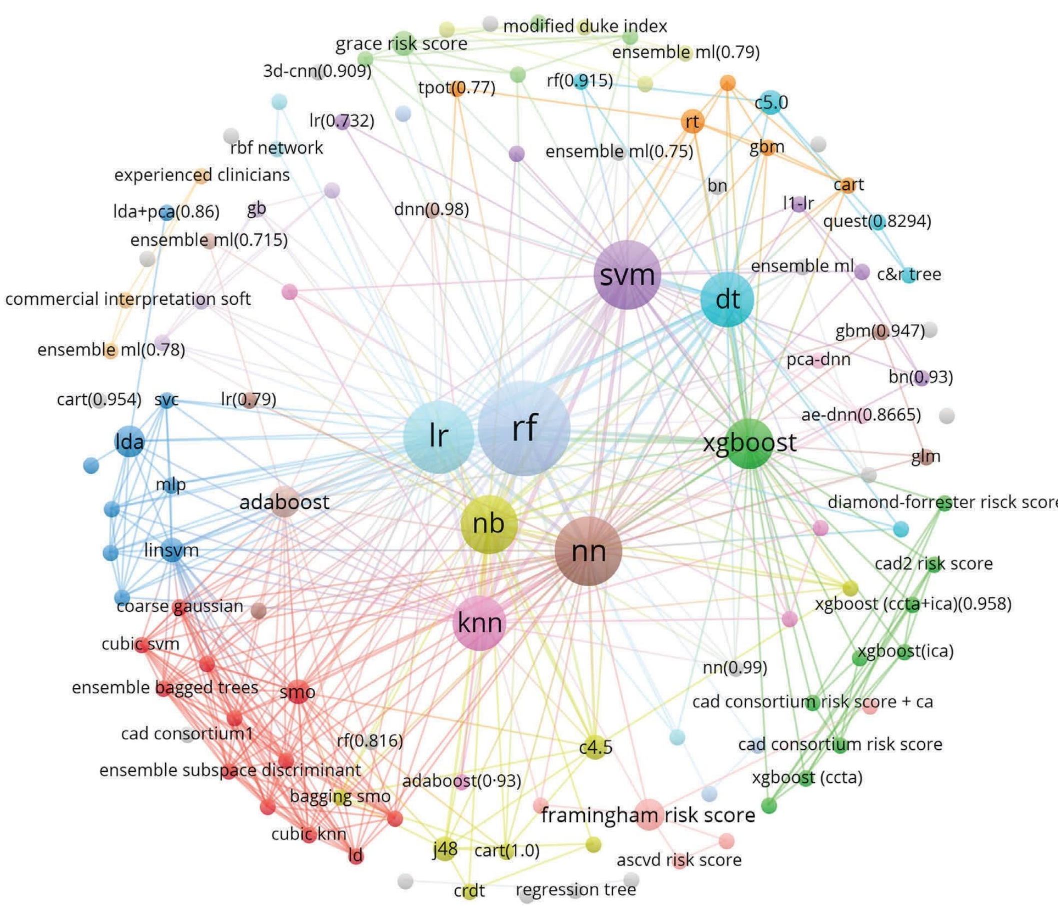

Figure 9: The relationship between different types of ML methods in diagnosing CAD.

a group (every group is shown with the same color). Every study using an ML methodology with higher AUC or ACC indices is displayed in parentheses. Besides, this network shows which methods have had the highest implementation frequency and which methods have outperformed others. A glance at the graphic chart reveals that the random forest (RF), linear regression (LR), neural networks (NNs), support vector machine (SVM), K-nearest neighbor network (KNN), Naïve Bayesian (NB), decision tree (DT), and XGBoost were used in many studies for evaluation and comparison with other methods.

5. Discussion and Further Recommendations

With recent advancements, the use of ML-based diagnostic methods in the healthcare domain has attracted the attention of researchers and specialists in various areas. These methods have been intensively employed for CAD detection and classification during the past five years. The present study synthesized 54 studies addressing the use of ML in analyzing CAD data and delineated its examination and comparison results in tables and figures. If studies employed clinical, laboratory, and ECG data, their intention behind using these data for CAD detection was to present a model for screening out the unnecessary use of invasive and costly tests, such as CCVT, echocardiography, and angiography. However, if they used clinical visual data, such as Echo, for CAD diagnosis, they aimed to present a framework for automatic detection or offer consultation for thorough decisions. To answer the sixth research question, we can refer to many challenges and provide future studies with recommendations by meticulously examining studies and their barriers and problems.

With the uptrend of intelligent models based on ML methods and new DL algorithms in early CAD detection and the presentation of correct clinical decisions, we believe there are some problems to be considered in future studies. These gaps include as follows:

(i) *Data Preprocessing.*

According to the texts, the performance of ML models does not solely lie in the topology and structure of networks; rather, a significant step toward the efficiency of learning models and their convergence is data preparation and preprocessing. Some studies have neglected data preprocessing, e.g., data normalization, standardization, segmentation, feature engineering, and data categorization. It is suggested that the preprocessing and feature selection operations be performed according to the data type for better results for the model.

(ii) *Sufficient Data.*

A significant factor in the success of ML methods is the use of voluminous datasets. Concerning DL methods, larger datasets play a determinant role in the pattern recognition of cardiac diseases. If these methods apply insufficient data, the likelihood of overfitting increases, and the validation of ML models is tainted. Hence, we cannot rely on them as tools for solving clinical diagnostic challenges.

(iii) *Escape Overfitting Technique.*

The investigation of the studies on CAD detection with various ML methods revealed that a large number of these studies had not tackled overfitting concepts and had not presented techniques for escaping this serious challenge of ML methods. However, overfitting arises in some ML methods, and preventive approaches should be adopted for the implementation of these models. In this respect, this review suggests employing more voluminous datasets and the dropout technique in the DL domain.

(iv) *Comparing Different ML Techniques or CNN Pretrained Network.*

Various ML algorithms and DL networks manifest varying performances in the pattern recognition and detection of CAD. Hence, future studies are proposed to employ several algorithms and select one as the most efficient. Likewise, concerning CNNs, we suggest comparing the performance of various types of pretrained networks and optimizing the hyperparameters of the most efficient network selected to enhance its efficiency.

(v) *Free Platform.*

Several studies have only implemented models within the research and development confines. However, models based on DL networks and CNN algorithms are implementable in mobile, tablet, and PDA equipment. Thus, we recommend using CNN networks, especially lightweight networks, for CAD data analysis in portable equipment that enables the point-of-care testing of this ML-based software and is accessed by clinical specialists inclusively.

6. Conclusion

With the development of AI methods, such as ML and DL, the models based on these methods will soon be an inseparable part of diagnostic equipment in the field of coronary artery disease. The employment of these tools paves the way for providing clinical specialists with specialized consultations in the CAD detection area. As instruments in clinical specialists' hands, these models as screening software modules prevent risky and invasive diagnostic tests and take the high financial burden of CAD detection and other coronary artery diseases from the shoulders of clinical care systems. Even DL-based systems can be used to design mobile applications for patients in the future. Furthermore, their equipment can enhance the quality of life of CAD patients by promptly notifying Alert and Alarm tools.

After reviewing many methods in the field of CAD diagnosis using machine learning, it is suggested to use a combination of images and other metadata in future studies for a faster and more accurate diagnosis of this disease and other heart diseases. It is also suggested that the edges of new technology such as pretrained networks should be studied in future research. Of course, in the countries that use active and robust EHR, the data of its repositories can be used in the timely diagnosis of heart diseases using machine learning algorithms.

Data Availability

No data were used to support this study.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Acknowledgments

We thank the Department of Artificial Intelligence of the Smart University of Medical Sciences, for providing an appropriate condition to apply this study.

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