Prediction of Coronary Artery Disease using Artificial Intelligence – A Systematic Literature Review

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ABSTRACT

Purpose: *Coronary heart disease and the risk of having a heart attack have both risen in recent years. Angioplasty, lifestyle changes, stent implantation, and medications are only some of the methods used to diagnose and treat various diseases. In this study, we will gather and analyze a variety of health indicators in order to identify heart-related illnesses via Machine Learning and Deep Learning prediction models. The best way to improve treatment and mortality prevention is to identify the relevant critical parameters and use Machine Learning or Deep Learning algorithms to achieve optimum accuracy.*

Design/Methodology/Approach: *Secondary sources were used for this investigation. These included periodicals, papers presented at conferences, online sources, and scholarly books and articles. In order to analyze and present the data gathered from academic journals, websites, and other sources, the SWOT analysis is being used.*

Findings/Results: *Predicting heart problems and their severity with a handful of crucial characteristics can save lives. Machine Learning algorithms such as Linear Regression, Deep Learning algorithms such as Neural Networks, and many others can all be applied to those medical parameters for this goal.*

Originality/Value: *This literature study utilizes secondary data collected from diverse sources. Understanding the many types of coronary artery disease and evaluating the most recent advances in predicting the same using Machine Learning approaches will be facilitated by the learned knowledge. This knowledge will aid in the development of a new model or the enhancement of an existing model for predicting coronary artery disease in an individual. Included are tables detailing the forms of coronary artery disease, a variety of recently published research publications on the topic, and standard datasets.*

Paper Type: *Literature Review*

Keywords: Cardiovascular diseases, Diagnosis of Coronary heart disease, Artificial Intelligence, Machine Learning Algorithm, SWOT Analysis.

1. INTRODUCTION :

Human heart is the principal organ of our body. To put it simply, it controls how much blood is pumped to different parts of our bodies. Discomfort elsewhere in the body can be triggered by cardiac problems. Heart disease is broadly defined as any condition that disrupts the heart's normally efficient operation. Among the leading causes of death in the modern world is heart disease. Unhealthy habits like smoking, drinking alcohol, and eating a lot of fat can raise blood pressure, which can lead to heart disease. The World Health Organization estimates that over 10 million people die annually from cardiovascular disease. The only guaranteed strategy to avoid heart disease is to live a healthy lifestyle and get checked often.

In today's healthcare system, the biggest obstacle is ensuring patients receive the highest quality care and a prompt, correct diagnosis. Although heart disease has emerged as the leading cause of death worldwide in recent years, it is also one of the most treatable conditions. Timely diagnosis is the single most crucial aspect in effective disease management.

Coronary artery disease (CAD) is a leading cause of death from cardiovascular disease in the world. Risk factors for cardiovascular disease include both lifestyle choices and environmental and genetic predispositions. CAD risk factors include diabetes mellitus, high blood pressure (BP), smoking, high cholesterol (lipid), obesity (BMI), homocystinuria, and psychological stress [1]. It is important to compare the associations between major modifiable CAD risk factors such as lipids, systolic blood pressure, diabetes mellitus, and smoking and incident CAD events based on their attributable risk fractions, prognostic performance, and treatment benefits, both in the general population and in subgroups of the population defined by age [2]. The 12-lead electrocardiogram and serum cholesterol screening are two examples of the surprisingly low sensitivity of commonly used diagnostic procedures for CAD. Now the difficulty lies in discovering even better diagnostic biomarkers [3].

Heart disease treatment is not immune to the impending impact of Artificial Intelligence (AI), Machine Learning (ML) and Deep Learning (DL) on virtually every facet of human life. Today's computers can process millions of calculations per second, allowing for more complicated ML systems that bring artificial intelligence one step closer to human intellect.

ML's algorithms and methods can be understood as part of a larger process of knowledge discovery in databases, also known as data mining. The diagnostic and predictive abilities of conventional regression methods can be improved with the use of ML algorithms [4].

Exercise stress tests, chest X-rays, heart scans (CT), cardiac magnetic resonance imaging (MRI), coronary angiograms, and electrocardiograms (ECG) are some of the current procedures used to diagnose the severity of heart disease in individuals. Medical diagnoses are made possible using ML technology's analysis, processing, and interpretation of patient records. Decision trees, support vector machine learning, artificial neural networks, fuzzy neural networks, binary particle swarm optimization, ensemble machine learning, random forest classifier, principal component analysis-based evolution classifier, Bayesian algorithms, neuro fuzzy classifiers, and more have all been used in studies to aid in the diagnosis of heart disease based on clinical data [5].

Using a variety of risk variables and diagnostic biomarkers, this literature review seeks to comprehend the current state of the application of ML algorithms to predict coronary artery disease in an individual, as well as the level of accuracy reached so far with respect to the prediction. To see if the prediction may be made sooner and more accurately through the use of a better prediction model, this work also seeks to identify any gap in the research done so far with respect to the many risk parameters considered for the prediction.

2. OBJECTIVES OF REVIEW PAPER :

(1) Understanding the different types of coronary CAD along with their causes, symptoms, diagnosis methods and treatments.
(2) Understanding the role of ML and DL in the prediction of CAD by studying the architecture of the ML and DL algorithms.
(3) Researching the existing scholarly literature on CAD, ML and DL to understand the current status of the prediction of CAD using ML and DL.
(4) Determining the gap in the research done so far with respect to the prediction of CAD using ML and DL algorithms.
(5) Finalizing the research agendas based on the research gap and deciding the research proposal.
(6) Performing a SWOT analysis of the research proposal.

3. METHODOLOGY :

For this review, we examined through several journal databases, including Elsevier, ScienceDirect, IEEE, Google Scholar, and others, in an effort to find the best articles on using ML and DL to predict cardiovascular diseases and disorders. At the outset, we consolidated all our study materials and analyzed them for commonalities.

Predictions of coronary artery disease are based on an individual's biological and physical characteristics. The selection of features is crucial to developing a more accurate prediction model. The availability of datasets for the chosen characteristics is a significant aspect of the research. Datasets are accessible from a few of the following available sources:

- Kaggle
- GitHub
- UCI Repository

Kaggle

Kaggle lets people interact, find and publish datasets, and use GPU-integrated notebooks to solve data science tasks. This platform's sophisticated tools and resources assist professionals and learners realize their data science goals [6].

Table 1: Sample Kaggle Dataset [7]

	A	B	C	D	E	F	G	H	I	J	K	L	M
1	id	age	gender	height	weight	ap_hi	ap_lo	cholesterc	gluc	smoke	alco	active	cardio
2	0	18393	2	168	62	110	80	1	1	0	0	1	0
3	1	20228	1	156	85	140	90	3	1	0	0	1	1
4	2	18857	1	165	64	130	70	3	1	0	0	0	1
5	3	17623	2	169	82	150	100	1	1	0	0	1	1
6	4	17474	1	156	56	100	60	1	1	0	0	0	0
7	8	21914	1	151	67	120	80	2	2	0	0	0	0
8	9	22113	1	157	93	130	80	3	1	0	0	1	0
9	12	22584	2	178	95	130	90	3	3	0	0	1	1
10	13	17668	1	158	71	110	70	1	1	0	0	1	0

GitHub

GitHub is a code hosting and collaboration platform. It enables remote project collaboration. Repositories, branches, commits, and pull requests are features of GitHub [8].

Table 2: Sample GitHub Dataset [9]

	A	B	C	D	E	F	G	H	I	J	K	L
1	Age	Sex	ChestPain Type	RestingBP	Cholesterol	FastingBS	RestingECG	MaxHR	Exercise Angina	Oldpeak	ST_Slope	HeartDisease
2	40	M	ATA	140	289	0	Normal	172	N	0	Up	0
3	49	F	NAP	160	180	0	Normal	156	N	1	Flat	1
4	37	M	ATA	130	283	0	ST	98	N	0	Up	0
5	48	F	ASY	138	214	0	Normal	108	Y	1.5	Flat	1
6	54	M	NAP	150	195	0	Normal	122	N	0	Up	0
7	39	M	NAP	120	339	0	Normal	170	N	0	Up	0
8	45	F	ATA	130	237	0	Normal	170	N	0	Up	0
9	54	M	ATA	110	208	0	Normal	142	N	0	Up	0
10	37	M	ASY	140	207	0	Normal	130	Y	1.5	Flat	1

UCI Repository

The UCI Machine Learning Repository contains databases, domain theories, and data generators used for empirical machine learning algorithm analysis [10].

Table 3: Sample UCI Repository Dataset [11]

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P
1	id	age	sex	dataset	cp	trestbps	chol	fbs	restecg	thalch	exang	oldpeak	slope	ca	thal	num
2	1	63	Male	Cleveland	typical angina	145	233	TRUE	lv hypertrophy	150	FALSE	2.3	downsloping	0	fixed defect	0
3	2	67	Male	Cleveland	asymptomatic	160	286	FALSE	lv hypertrophy	108	TRUE	1.5	flat	3	normal	2
4	3	67	Male	Cleveland	asymptomatic	120	229	FALSE	lv hypertrophy	129	TRUE	2.6	flat	2	reversable defect	1
5	4	37	Male	Cleveland	non-anginal	130	250	FALSE	normal	187	FALSE	3.5	downsloping	0	normal	0
6	5	41	Female	Cleveland	atypical angina	130	204	FALSE	lv hypertrophy	172	FALSE	1.4	upsloping	0	normal	0
7	6	56	Male	Cleveland	atypical angina	120	236	FALSE	normal	178	FALSE	0.8	upsloping	0	normal	0
8	7	62	Female	Cleveland	asymptomatic	140	268	FALSE	lv hypertrophy	160	FALSE	3.6	downsloping	2	normal	3
9	8	57	Female	Cleveland	asymptomatic	120	354	FALSE	normal	163	TRUE	0.6	upsloping	0	normal	0
10	9	63	Male	Cleveland	asymptomatic	130	254	FALSE	lv hypertrophy	147	FALSE	1.4	flat	1	reversable defect	2

4. CORONARY ARTERY DISEASES AND THEIR TYPES :

Plaque buildup in the arterial walls that carry blood to the heart (called coronary arteries) and other areas of the body leads to coronary artery disease (CAD). Cholesterol, fat and other chemicals are deposited in the artery and form plaque. Due to plaque formation, the interior of the arteries gradually narrows, eventually obstructing blood flow in some cases. This condition is referred to as atherosclerosis. Since chest discomfort is caused by a lack of oxygenated blood reaching the heart muscle, narrowed arteries are a common cause of this symptom [12].

There are 3 types of CAD namely:

- Obstructive Coronary Artery Disease

- Non-Obstructive Coronary Artery Disease
- Spontaneous Coronary Artery Dissection

The following table discusses briefly about the 3 types of CAD [13–22].

Table 4: Types of CAD

	Obstructive CAD	**Non-Obstructive CAD**	**Spontaneous Coronary Artery Dissection**
Description	The gradual narrowing or closure of arteries that provide blood to the heart is termed as obstructive coronary artery disease. Plaque accumulation is responsible for this obstruction. Coronary heart disease (CHD) can refer to more than only clogged arteries in the heart; it can also refer to other forms of heart disease.	Non-obstructive coronary artery disease is less common but equally as deadly as obstructive coronary artery disease. This occurs when the arteries of the heart are squeezed by the surrounding cardiac muscle, or when the arteries are otherwise impaired. Damage to the inner lining of the arteries, incorrect constriction, dysfunction in the tiny branches, and pressure from the overlying heart muscle are only some of the numerous issues that might arise.	The medical term for a tear or separation in the walls of the coronary artery is spontaneous coronary artery dissection (SCAD). To rip in any of the coronary artery's three layers is possible. Within the cracks, blood begins to leak. Because of the pressure of the trapped blood, the artery will expand inward. Because of the bulge, flow of blood to the heart is impeded or slowed. When the flow of blood to the heart is restricted or impeded, cardiac muscle can get damaged or even die.
Causes	Obstructive CAD is caused by atherosclerosis, a slow but steady buildup of fat and cholesterol in the arteries in the form of plaques.	Non-obstructive CAD is caused by hyperactive constriction of the heart's arteries, but its root cause is unknown. It is a common congenital anatomic variety for the heart to be compressed by the muscle above it.	The root cause of SCAD is unknown. It frequently strikes young, healthy, physically-active people who lack the usual risk factors for cardiovascular disease. A higher risk period for SCAD occurs during menstruation or after menopause. These risk variables show that changes in female hormones may have a role. Strength training and carrying heavy objects are major risk factors for causing arterial tears in males. Coronary artery dissections can be brought on by trauma or medical procedures such as cardiac catheterizations.
Risk Factors	1. Hypertension 2. Hyperlipidemia (High cholesterol) 3. Diabetes 4. Usage of Tobacco 5. Family history 6. Age (men above 45 years women above 55 years) 7.Obesity 8.Lack of exercise	1. Hypertension 2. Diabetes 3. High cholesterol 4. Smoking 5. Excess weight 6. Metabolic syndrome 7. Autoimmune disease, including vasculitis.	1. Disorders of the connective tissue, such as Marfan syndrome 2. Blood pressure that is dangerously high 3. Fibromuscular dysplasia (FMD) 4. Hypothyroidism 5. Inflammatory disorders include multiple sclerosis

	9.Unhealthy eating habits 10.Obstructive sleep apnea 11.Emotional stress 12.Excessive alcohol consumption 13.History of preeclampsia during pregnancy	8. Eating a diet high in salt, saturated fat, and processed foods 9.Rheumatologic disorders, such as lupus or rheumatoid arthritis 10. Sedentary lifestyle	(MS), lupus, and sarcoidosis 6. Childbirth 7. Hormone therapy 8. Illegal drug use
Symptoms	The symptoms vary depending on the type of illness a person has, the person's age, gender, and other factors. The disease also shares numerous symptoms with other disorders. 1.Angina (Chest pain) - Stable angina, Unstable angina, Heart attack 2.Irregular heartbeat (arrhythmia) 3.Heart failure 4.Sudden cardiac death 5. Arm, neck, jaw, and/or back pain 6.Breathing difficulty 7.Nausea/vomiting 8.Sweating 9.Fatigue 10.Unexplained nervousness or anxiety 11.Weakness 12.Heart palpitations	1.Chest pain (also called angina) 2. Arm, neck, jaw, and/or back pain 3.Difficulty in breathing 4.Fatigue 5.Light-headedness 6.Heart Palpitations 7.Sleep issues, including insomnia	1.Sudden cardiac arrest 2.Unstable angina 3. Fainting or dizziness (syncope) 4.Symptoms of hyperhidrosis, or excessive sweating, include feeling cold and wet all the time. 5. Arrhythmia or other heart rhythm disturbances 6. A quick heartbeat or a sensation of fluttering in the chest. 7. Neck, back, and muscle pain 8. Indigestion, nausea, and vomiting 9. Difficulties in breathing 10.Extreme fatigue
Types	1.Stable ischemic heart disease - the chronic form. 2. A cardiac arrest brought on suddenly, also known as acute coronary syndrome.	1.Endothelial dysfunction 2.Coronary vasospasm (Prinzmetal's angina) 3.Microvascular dysfunction 4.Myocardial bridging (MB)	1. Spontaneous coronary artery dissection
Diagnosis	A battery of diagnostic procedures is carried out to check for arterial narrowing or blockage. 1.Coronary angiogram or angiography 2.Fractional flow reserve (FFR) 3.Intravascular ultrasound (IVUS) 4.Optical coherence tomography (OCT) 5.Vascular function testing - Endothelial function testing, Index of microcirculatory resistance Other evaluation tests include 1.Physical Examination 2.Blood tests 3.Electrocardiogram (ECG) 4.Stress echocardiogram (echo) 5.Myocardial perfusion (nuclear) scan 6.Cardiac MRI 7.CT coronary angiogram	Diagnosis is aided by a combination of risk factor analysis, family history, and a thorough physical examination. Some more types of specialized tests are: 1.Electrocardiogram 2.Stress test 3.Echocardiogram (echo) 4.CT coronary angiogram 5.Cardiac MRI 6.Heart rhythm monitor 7.Positron emission tomography (PET) scan	Certain specialized exams can aid in the diagnosis of SCAD, including the ones listed below. 1. Enzyme marker test 2. Electrocardiogram (ECG or EKG) 3. Cardiac catheterization - intravascular ultrasound (IVUS), optical coherence tomography screening (OCT) 4. CT coronary angiogram

Treatment	Depending on the extent of the artery blockage, four different therapy options exist for Obstructive CAD: 1.Lifestyle changes - Quit smoking and tobacco products - Diet low in sodium and saturated fat - Regular Exercise - Reduce Alcohol consumption 2.Risk Factor Management - Diabetes - High Blood Pressure - High Cholesterol - High Triglycerides - Obesity / Over weight 3.Medication - Reduce Blood Pressure - Reduce Cholesterol - Manage Stable angina - Reduce risk of blood clots 4.Procedure or surgery - Percutaneous coronary intervention (PCI) - coronary angioplasty or balloon angioplasty - Coronary artery bypass grafting (CABG) - Enhanced external counter pulsation	Depending on the patient's condition, the following treatments may be used for this type: 1.Lifestyle Changes - Balanced heart-healthy diet - Regular Exercise - Maintaining healthy weight - Reducing Alcohol consumption - Stress Management - Quit smoking - Getting sufficient sleep 2.Medication - Aspirin - Blood Thinning drugs - Reduce Blood Pressure - Reduce Cholesterol - Nitrates to open blood vessels - Reduce risk of blood clots - Angiotensin-converting-enzyme (ACE) inhibitors. 3.Surgery - Myocardial bridging can be treated surgically if drugs prove ineffective. Unroofing is a specialized procedure in which the cardiac muscle covering an artery is surgically removed.	Categories of treatment include: 1. Medication - Reduce Blood Pressure - Reduce Cholesterol - Reduce risk of blood clots - Aspirin - Blood Thinning drugs - Reduce chest pain 2. Procedure or surgery - Coronary angioplasty, cardiac catheterization, placement of stent - Coronary artery bypass grafting (CABG) - Left ventricular assist device / cardioverter defibrillator which is implantable (ICD) - Transplantation of Heart (extremely rare)

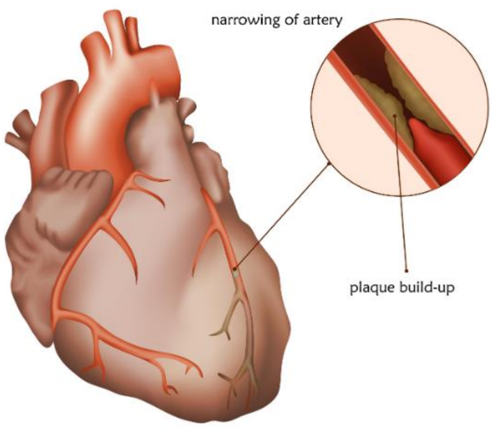

Fig 1: Obstructive CAD [23]

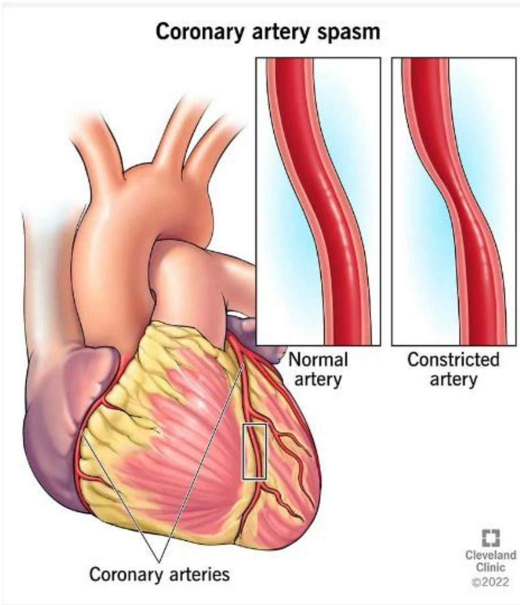

Fig 2: Non – Obstructive CAD (Coronary Vasospasm) [24]

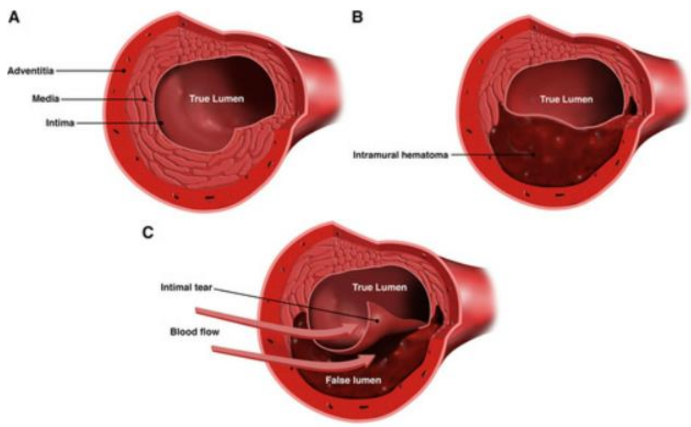

Fig 3: Spontaneous CAD [25]

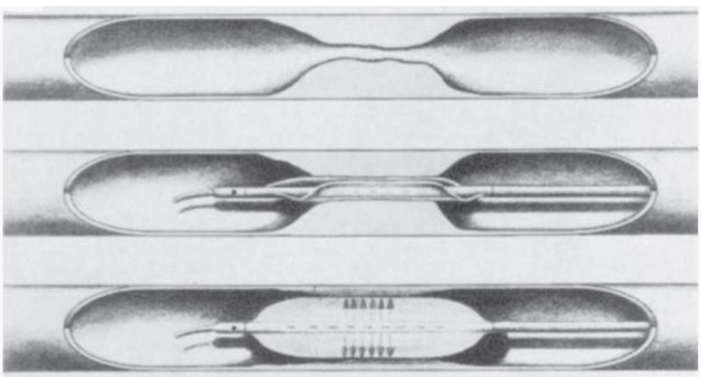

Fig 4: Percutaneous Coronary Angiography to treat stenosis of the coronary artery [26]

Electrocardiogram (ECG or EKG)

Electrocardiograms (ECGs) are among the simplest and quickest cardiac evaluation examinations. An electrocardiogram (ECG) monitors the electrical signals of the heart. It is a standard and painless diagnostic used to swiftly detect and monitor cardiac abnormalities.

But ECG has its own limits. It does not detect underlying heart issues in patients with no symptoms. It is not always helpful for correct diagnosis. More tests are required to identify significant heart conditions that are unnoticed by a normal ECG curve. An ECG cannot detect SCAD and other heart-related conditions [27].

Therefore, more sophisticated diagnostic methods, including as MRI and angioplasty, are necessary.

MRI (Magnetic Resonance Imaging)

MRI or Magnetic Resonance Imaging is a non-invasive imaging technique that creates anatomical images in 3D. There is no danger of getting radiation exposure. In case of certain disorders, when compared to other imaging methods, heart MR scans are the gold standard. This feature makes MRI an essential diagnostic and evaluative tool for the early detection and evaluation of some cardiac disorders, particularly those that involve the heart muscle.

Cardiovascular structural abnormalities (e.g., congenital heart defects), malignancies, functional irregularities (e.g., valve failure), and illness related to CAD and cardiomyopathy (disease which affects the muscles of the heart) have been successfully diagnosed with MRI.

Certain percutaneous methods, such as catheter-based ablation techniques to treat abnormal cardiac rhythms, such as atrial fibrillation, can utilize MRI. MRI has the potential to drastically cut down on processing times while simultaneously increasing accuracy. Other imaging techniques may miss anomalies that are obscured by bone, but MRI can detect them [28].

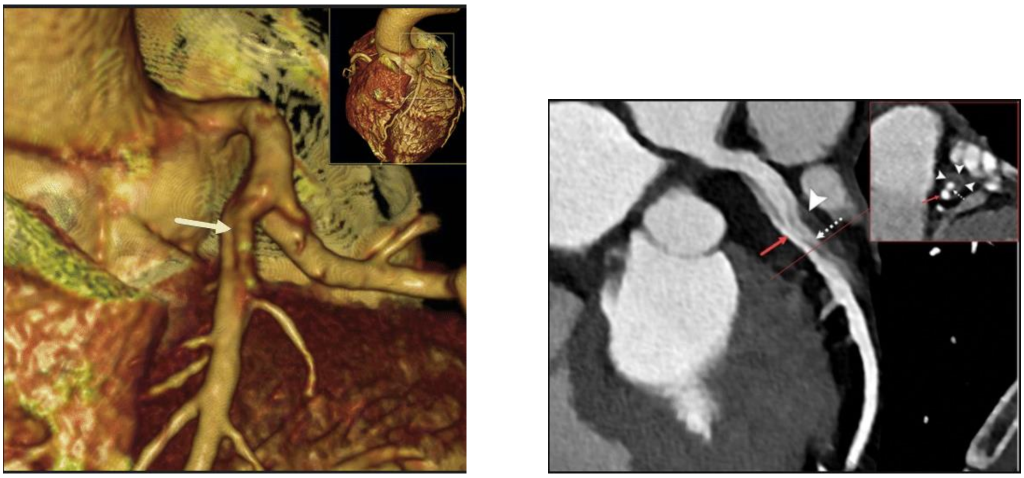

Fig 5: MRI images of SCAD [29]

Angiography and Angioplasty

A coronary angiogram is a test that employs x-rays and a contrast dye to visualize the blood's movement through the coronary arteries and diagnose CAD. Angiograms are performed to examine the condition of blood arteries and the blood flow through them. Angina, blood clots, peripheral artery disease, and atherosclerosis are just some of the vascular issues it can assist identify or explore.

It is possible that coronary angiography provides more accurate anatomical detail than other imaging techniques, especially in the case of smaller blood arteries. The necessity for surgery may be avoided if angiograms are favorable. When surgery is still a must, at least it can be done precisely [30].

Angioplasty is a procedure that clears out plaque from an artery so that it has more space. Angioplasty, which can be done with a balloon, is a procedure that opens arteries to make it easier for blood to flow through them. Angioplasty can help ease the pain and shortness of breath that come from blocked arteries. Angioplasty is also utilized during a heart attack to rapidly unblock a blocked artery and lessen the severity of cardiac damage [31].

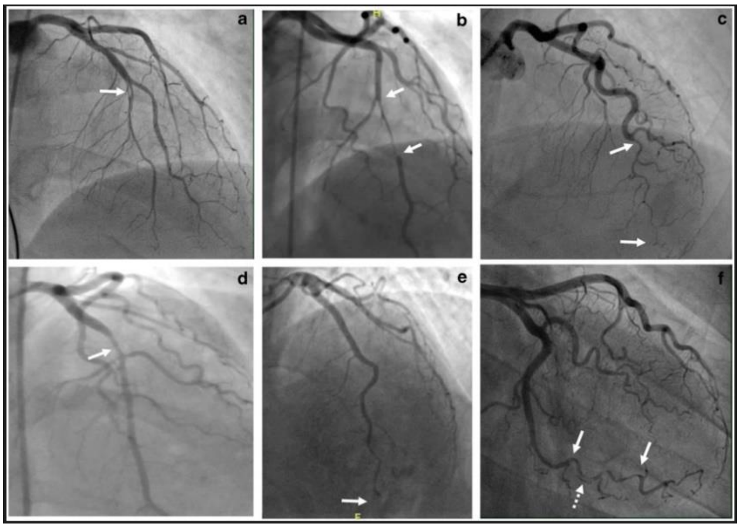

Fig 6: Angiographic MRI image of SCAD [32]

5. ARCHITECTURE OF ARTIFICIAL INTELLIGENCE - ML AND DL :

Artificial intelligence (AI) is the study of how computers can act like humans in terms of intelligence and thought processes. AI, in its broadest meaning, is the branch of engineering concerned with creating machines that can perceive, recognize, decide, classify, detect, and estimate. That is, AI paves the way for machines to act in ways reminiscent of those of humans [33].
Many sectors of industry and academia have benefited from the proliferation of ML and DL owing to the exponential growth of compute power and data storage capacity.
Cardiovascular doctors are interested in ML and DL because of the possibilities they present for enhancing illness diagnosis, research, and patient care.

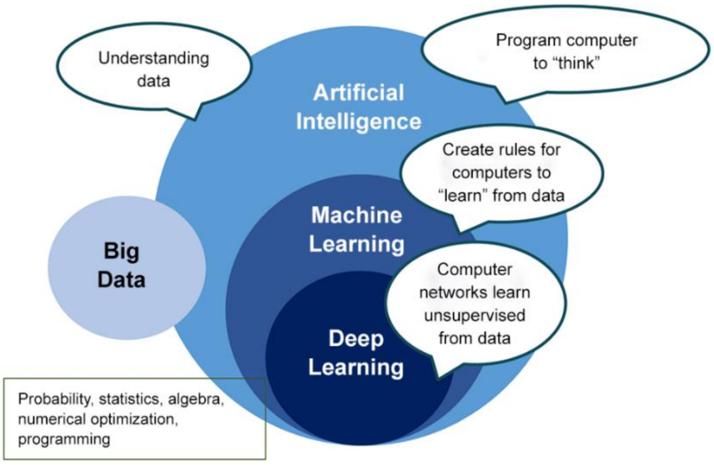

Fig 7: Interaction between AI, ML and DL [33]

Machine Learning (ML)

In order to better analyze a vast amount of training data, machine learning applies statistical analytic methods. To do this, models for autonomous predictions are built, and the analysis algorithm's performance is enhanced by the incorporation of previous data. In machine learning, a model or algorithm is developed by first extracting relevant features from training data, which are then utilized as test data. The method is then used to create a prediction about the thing in question.

Machine learning can be categorized into four distinct types: reactive, limited-memory, theory-of-mind, and self-awareness [33].

Reactive: Reactive machines are programmed to react rather than think and cannot learn from the past to guide their actions in the present. They can, however, recognize data formats, make educated guesses, and select the best available option.
Limited-memory: Limited-memory machines have storage space and can learn from past experiences and retain that information. In order to improve their predictions, these machines can learn from their experiences and adapt in real time, unlike reactive machines.
Theory-of-mind: Machines with a theory of mind can learn from human interactions and modify their own actions accordingly.
Self-awareness: In the future, when self-aware machines have been developed, they will be sentient and able to think for themselves.

There are a few different methods of machine learning, including ***supervised learning, unsupervised learning, and reinforcement learning***.
Data are tagged before training begins in ***supervised learning***. This is a time-consuming and difficult job that demands a lot of information.
For the purpose of ***unsupervised learning***, an algorithm is applied to data that has not been labelled.
To create labels that optimally organize the data, a machine in ***reinforced learning*** learns through experimentation how to interact with its environment, making it comparatively more powerful.

Below are the four stages that make up machine learning:
1. Features are extracted
2. The appropriate machine learning technique is chosen
3. The data model is trained and its efficacy evaluated.
4. Making predictions with the trained model.

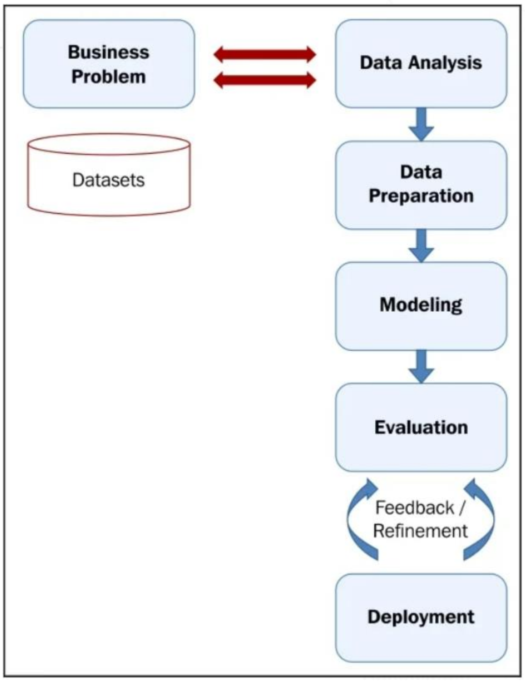

Fig. 8: Architecture of Machine Learning [34]

Deep Learning (DL)

As a branch of machine learning, deep learning entails teaching a computer system new skill through the use of complex algorithms and other computational models. In machine learning, "deep learning" refers to a class of algorithms where each "layer" represents a different "degree of abstraction." There are multiple hidden layers, as well as input and output layers. Voice synthesis, handwriting identification, image analysis, predictive analytics, object recognition, and decision making are just few of the many applications [34].

Generative models, **Discriminative models**, and **Hybrid models** are the three basic categories into which deep learning can be placed [34].

Generative Model: Unsupervised learning makes use of Generative models. Deep Belief Network (DBN), Deep Boltzmann Machines (DBM), Deep auto-encoders are few examples of this type.

Discriminative Model: Models that can tell the difference between two classes are called discriminative models, and they are frequently used in supervised learning. It utilizes Deep Stacking Networks (DSN) and Convolutional Neural Networks (CNNs).

Hybrid Model: Hybrid models combine the best features of both discriminative and generative models. One example of hybrid model is the deep neural network (DNN).

The term "Deep Learning" refers to a set of learning methods that utilize artificial neural networks with many layers to acquire hierarchical representations in deep architectures. Structures for Deep Learning use several layers of computation. When one layer receives data from another, it can use that data to trigger a chain reaction that is not linear. The functionality of Deep Learning is replicated from the mechanics of human brain and neurons for processing of inputs [34].

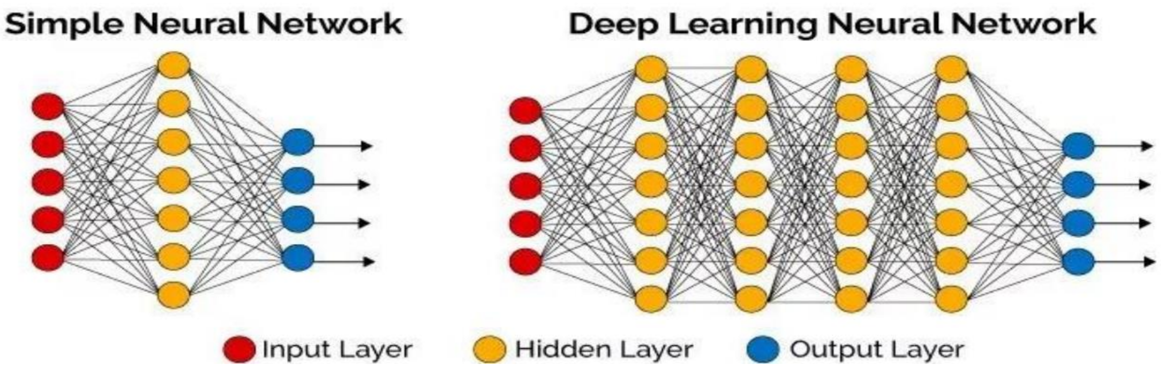

Fig 9: Deep Learning Architecture [34]

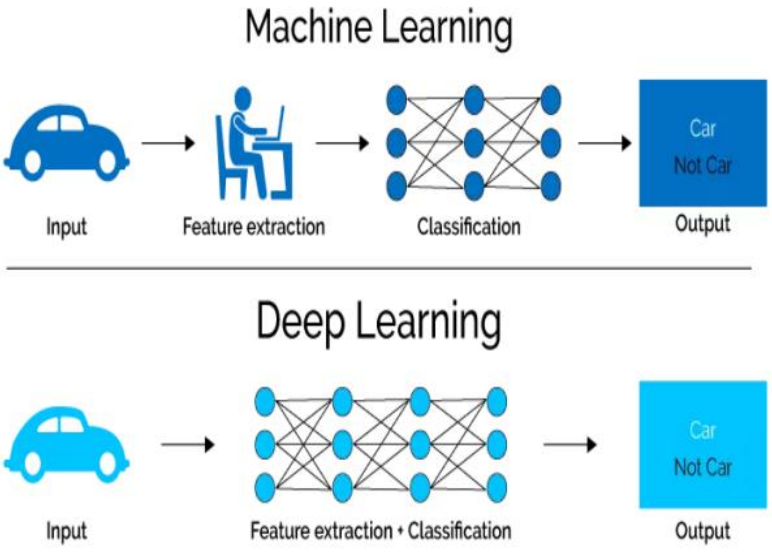

Fig 10: Comparison between ML and DL [34]

AI's potential to improve healthcare's efficiency while cutting costs makes it a key component of the industry's long-term plan for growth. Many nations have established or are establishing AI plans and policies to push forward AI-related study, innovation, and implementation. New AI functions offer novel solutions for healthcare, and the evolution of healthcare requires AI skills to reach a new level. Demand and advancements in both AI and healthcare will drive their respective industries forward in the near future, improving the health and well-being of those who most need it [35].

6. REVIEW OF RELATED WORKS :

Following is a quick summary of the literature review conducted on the study effort described in the published literature on the proposed topic.

Table 5: Scholarly Literature on Cardio Vascular Diseases (CVD) published in 2022

S. No.	Area & Focus of the Research	Outcome of the Research	Reference
1	Identification of cardiovascular disease-related mortality risk factors.	The study uses factors including lifestyle, metabolism, socio-demographic, economic, and health system to explain death due to cardiovascular diseases.	Sahin, B et al., (2022). [36]
2	Flavonols' Impact on the Cardiovascular System	This review shows that flavonol supplements and natural sources, notably quercetin can help in cardiovascular disease prevention and management.	Kozłowska, A et al., (2022). [37]
3	Epicardial Adipose Tissue (EAT) and the role it plays in the development of cardiovascular diseases	EAT loses its preventive qualities due to cardiovascular risk factors and becomes pro-inflammatory, increasing cardiovascular disease. Lifestyle changes and anti-inflammatory medicines can improve EAT function.	Konwerski, M et al., (2022). [38]
4	Oxidative stress and its association with cardiovascular diseases	Excessive oxidative stress in the body can cause cardiovascular diseases. Several oxidative stress biomarkers can diagnose cardiovascular diseases, however more research is needed.	Panda, P et al., (2022). [39]
5	Nanomaterials in cardiovascular imaging, diagnosis, and treatment	Nanotechnology and Nanomedicine can identify and cure heart issues. Institutional and industrial interests, lack of infrastructure, and skills limit nanomedicine in cardiovascular disorders.	Chopra, H et al., (2022). [40]
6	Gender-specific strategies in cardiovascular disease	CVD kills one-third of women. Women have been wrongly thought "protected" against CVD, leading to a lack of preventative and inadequate treatment strategies. Men and women need sex-specific CV treatment techniques.	Abrignani, M. G et al., (2022). [41]
7	Curcumin and the effect of the usage in Cardiovascular diseases and Oxidative Stress	It is hypothesized that various plant-derived chemicals activate distinct cellular pathways and may therefore operate additively or synergistically to reduce the risk of cardiovascular diseases.	Cox, F. F et al., (2022). [42]
8	Mitochondrial DNA (mtDNA) mutations and cardiovascular diseases	Mutations in mitochondrial DNA could be genotyped as a strong family screening tool for cardiovascular disease. A unified method for understanding mtDNA variability and heteroplasmy is necessary for its widespread implementation in clinical practice.	Dabravolski, S. A et al., (2022). [43]
9	CARD9 Adapter Protein and its Role in cardiovascular disease	CARD9 signaling involves cardiac injury and remodeling through pro-inflammatory effects. Inhibiting CARD9	Zhang, H et al., (2022). [44]

		for its anti-inflammatory effects is a viable technique for treating CVDs.	
10	Cardiovascular complications of Corona Virus (COVID-19).	Most COVID-19 cardiovascular symptoms may be 'collateral damage,' but they increase morbidity and mortality. Myocardial damage diagnosis and therapy are critical.	Pillai, A et al., (2022). [45]

Table 6: Scholarly Literature on Diagnosis of Coronary Heart Disease (CHD) published between 2000 - 2022

S. No.	Area & Focus of the Research	Outcome of the Research	Reference
1	Relationship between CHD and mental disorders	CHD is a substantial contributor to extra morbidity and mortality among people with mental illnesses. Death rates are different for people with mental disorders because of how they act and live, as well as because of biological factors that are common to both mental disorders and cardiometabolic diseases.	De Hert, M et al., (2022). [46]
2	Acoustic waveforms for wrist pulse diagnosis of stable CHD	The third- and fourth-layer pulse waveforms on the left Cun pulse can identify stable coronary heart disease patients from healthy people.	Cui, J et al., (2022). [47]
3	CHD prediction using multitask progressive time-series networks	To forecast coronary vascular occlusion, a mixed reinforcement multitask progressive time-series network is presented. The model incorporates DRL pre-training, soft parameter sharing, hard parameter sharing, progressive time-series networks, and other modules to produce accurate predictions.	Li, W et al., (2022). [48]
4	Clinical Status of CHD Patients Following COVID-19	Stressors, systemic infection, and inflammation put COVID-19 patients at risk of instability. COVID-19 patients require cardiological attention, long-term observation, and rapid diagnostic procedures to prevent early and late cardiovascular problems.	Khidoyatova, M. R et al., (2022). [49]
5	AK098656: a novel coronary heart disease patient biomarker	A novel VSMC-dominant lncRNA, AK098656, can accelerate the breakdown of contractile proteins, boost VSMC synthesis, and cause artery constriction and hypertension. According to the study, AK098656 modulates coronary heart disease.	Wang, X et al., (2022). [50]
6	Risk of Cardiovascular Diseases in Women	Women and men appear to have the same cardiovascular disease risk factors, but the lack of women in major research means we know less about their impact. Smoking, hyperlipidemia, hypertension, and diabetes are CHD risk factors in women and should be treated aggressively.	Edmund, E et al., (2000). [51]
7	Identification of CHD in patients based on lipid – lowering drug therapy	Low HDL and high triglycerides (especially with an LDL/HDL ratio >5) are CHD risk factors. Statins are the treatment of choice for most patients with hyperlipidaemia who require pharmacological therapy, based on evidence	Isles, C. G et al., (2000). [52]

		from recent preventive studies and because they are the most potent lipid-lowering medicines available.	
8	Genetic risk score for CHD and its primary preventative screening potential	The genetic score created and validated in the study illustrates the potential for genomic screening in early life to support conventional risk prediction.	Inouye, M et al., (2018). [53]
9	Integrated genetic and epigenetic prediction of CHD	Systemic CHD risk factors are hereditary and environmental. Integration of genetic, epigenetic and phenotype data from the Framingham Heart Study to predict the occurrence of CHD.	Dogan, M. V et al., (2018). [54]
10	Triglyceride glucose index – A marker for predicting subclinical CHD	Triglyceride glucose index (TyG) is an independent measure of CHD in asymptomatic people without typical CVRFs.	Park, G. M et al., (2020). [55]

Table 7: Scholarly Literature on AI published between 2018 - 2020

S. No.	Area & Focus of the Research	Outcome of the Research	Reference
1	Causability and explainability of AI	This article introduces the concept of causability, which differs from explainability in that it is a person's trait.	Holzinger, A et al., (2019). [56]
2	Broad Overview of AI in Medicine	The primary objective should be to create a careful balance between AI, automation and primary care doctors' strengths and judgement. This is important because AI replacing humans in medicine could reduce its benefits.	Malik, P et al., (2019). [57]
3	Application of AI for COVID – 19 pandemic	AI helps treat and monitor COVID-19 patients. It can follow COVID-19 at medical, molecular, and epidemiological scales. Analyzing accessible data helps with virus research. AI can aid in treatment, preventive, medication, and vaccine development.	Vaishya, R et al., (2020). [58]
4	Implementation of AI in Medicine	This study talks about latest scientific research on the advantages, future prospects, and risks of using AI in clinical practice for doctors, medical systems, clinical training, and medical ethics.	Briganti, G et al., (2020). [59]
5	Usage of AI in automation of agriculture	Automation in farming has increased soil yield and fertility. The research presents an IOT-based system for flower and leaf identification and irrigation in botanical farms.	Doshi, A et al., (2019). [60]
6	Implementation factors involved in application of AI in Healthcare	AI is not likely to make a big difference in how much medical treatment and diagnosis cost. Healthcare institutions, government, and regulatory organizations must build procedures to monitor significant issues, react responsibly, and limit harmful impacts.	Davenport, T et al., (2019). [61]

7	Challenges and Chances of AI in Dentistry	The information offered by most dental AI applications today will only partially inform clinical decision-making. Future dentists must be digitally literate in order to use clinical AI solutions.	Schwendicke, F. A et al., (2020). [62]
8	AI in Cardiology	Cardiologists make patient care decisions based on data, and they have more quantitative data than many other specialities. AI will improve medical care since doctors can evaluate more data in-depth.	Johnson, K. W et al., (2018). [63]
9	Challenges in Translation of AI to clinical practice	The primary concerns and limits of AI in healthcare, in addition to the actions that need to be taken to get these new ideas from the lab into actual clinical outcomes.	Kelly, C. J et al., (2019). [64]
10	AI and Sustainable Development Goals	Fast AI development needs regulatory knowledge and control for sustainable growth. Lack of transparency, safety, and ethics could occur.	Vinuesa, R et al., (2020). [65]

Table 8: Scholarly Literature on Machine Learning Algorithm published between 2019 - 2022

S. No.	Area & Focus of the Research	Outcome of the Research	Reference
1	Real-World applications of Machine Learning Algorithms	The paper describes machine learning algorithms that can boost an application's intelligence and capabilities. It also identifies problems and research directions.	Sarker, I. H (2021). [66]
2	Explainable Machine Learning in Cardiology	This study discusses explainable machine learning in cardiology. Interpretability vs explainability and global vs local explanations are discussed. Explainability approaches have several limitations. At the end of the study, a general rule of thumb for employing explicated black-box models is provided.	Petch, J et al., (2021). [67]
3	Prediction and Classification of CVD using ML and DL Techniques	This survey paper compares how CVDs are grouped and how they are predicted. Data Mining methods, ML and DL prediction models for CVD are all discussed.	Swathy, M et al., (2022). [68]
4	Narrative Review of AI in Cardiology	The report reviews recent breakthroughs in practically all fields of cardiology and suggests AI will play a significant role.	Koulaouzidis, G et al., (2022). [69]
5	AI opportunities in cardio-oncology	The paper discusses machine learning in cardio-oncology and the related factors to be considered. It also examines the relevance of wearables and AI in predicting heart dysfunction and atrial fibrillation (AF).	Ruddy, K. J et al., (2022). [70]
6	Prediction of ICU Admission and Mortality in COVID – 19 using ML Algorithms	This study evaluates 18 machine learning methods for predicting COVID-19 ICU admission and mortality. Ensemble-based models predict 5-day ICU admission and 28-day death from COVID-19 better than other models.	Subudhi, S et al., (2021). [71]
7	Prediction of CVD using ML Algorithms with Relief and LASSO	The research provides a model to predict cardiac disease using many approaches. Relief and LASSO pick suitable features. By combining classic classifiers with bagging and boosting, new hybrid classifiers are created. The report	Ghosh, P et al., (2021). [72]

	Feature Selection Techniques	concludes that utilizing Relief feature selection approaches provided the most accurate model.	
8	Prediction of CVD using Machine Learning Classification	A machine-learning-based cardiac disease detection system has been developed. Relief, MRMR, LASSO, LLBFS, and FCMIM are used to tackle feature selection problems. System uses LOSO cross-validation to choose hyperparameters.	Saboor, A et al., (2020). [73]
9	Prediction of Stress and Anxiety using ML Algorithms	5 machine learning algorithms determined anxiety, sadness, and stress severity levels. Important variables for Anxiety, Depression, and Stress were 'scared without good reason,' 'Life was meaningless,' and 'Difficult to relax.'	Priya, A et al., (2020). [74]
10	Clinical Applications of ML Algorithms	ML algorithms in the clinic can increase knowledge and care if we dedicate enough resources to revealing the black box for doctors and patients.	Watson, D. S et al., (2019). [75]

Table 9: Scholarly Literature on SWOT Analysis published between 2018 - 2021

S. No.	Area & Focus of the Research	Outcome of the Research	Reference
1	Prediction of Parkinson's Disease using ANN Algorithm	This research presents a back propagation artificial neural network system to help clinicians diagnose Parkinson's Disease. The neural network system design improves robustness. Network recognition reached 100%.	Sadek, R. M et al., (2019). [76]
2	Prediction of Diabetes using ANN Algorithm	In this paper, the proposed neural network model tries to minimize error. After training the ANN model, the average neural network error function was 0.01 and the accuracy of predicting diabetes was 87.3%.	El_Jerjawi, N. S et al., (2018). [77]
3	Clinical Disease Prediction using Random Forest Classifier	The dataset is used to find a diabetic, coronary heart disease, and cancer diagnosis model. The preprocessed dataset is classified, and Bayesian and random forest models are created. Finally, model accuracy and efficiency calculations are used to analyze. Random forest model outperforms Naïve Bayes classifier for three diseases.	Jackins, V et al., (2021). [78]
4	Prediction of Heart Disease using Random Forest Algorithm	Analyzing 303 samples and 14 attributes. Random forest classifies and processes datasets. Dataset accuracy, sensitivity, and specificity are represented as percentages. Predicting cardiac disease was 86.9% accurate with 90.6% sensitivity and 82.7% specificity. According to receiver operating characteristics, random forest predicts heart disease with 93.3% accuracy.	Pal, M et al., (2021). [79]
5	Particle Swarm Optimization for Disease Detection	PSO is used to tackle real-world nonlinear complicated optimization issues. Researchers have offered PSO versions for	Pervaiz, S et al., (2021). [80]

		medical disease diagnosis in health care. The study outlines many medical disorders used in PSO techniques for medical disease identification in healthcare.	
6	Heart Disease Prediction using Particle Swarm Algorithm	Particle Swarm Optimization (PSO) merged with Lion Algorithm (LA) update algorithm, a hybrid of LA and PSO algorithm, is introduced in this research. Accurate prediction is this paper's main goal. Finally, the proposed work is compared to existing methods and shown to be more efficient in certain performance criteria.	Cherian, R. P et al., (2020). [81]
7	Prediction of COVID-19 pandemic based on time series data using SVM	The study uses Support Vector Machine Algorithm to predict COVID-19's global population's registered, deceased, deaths, and mortality rate. The author found that COVID-19 mortality increases with confirmed cases. The study proposes stopping people from travelling to reduce COVID-19 transmission.	Singh, V et al., (2020). [82]
8	Human- and ML- based Embryo Assessment – SWOT Analysis	Evaluations of embryos by humans and by machine learning are SWOT-analyzed in the paper. ML-based systems have many advantages and drawbacks. Combined research and development on new technologies creates technology-push (ML models) to meet demand-pull for medical systems that work well and are clear.	Tran, H. P et al., (2020). [83]
9	SWOT Analysis of AI in Radiology	AI techniques are used in radiology for image-based evaluation, CAD tools, radiologic imaging segmentation and registration, medical image classification, and lesion detection and classification. Traditional imaging jobs that take a lot of time and require a lot of human input can be done with less human help with ML approaches.	Noguerol, T. M et al., (2019). [84]
10	Clinical Decision Support system using SPM for CVD	The research provides a cardiovascular disease prediction clinical decision support system using better sequential pattern mining and association rules. The dataset was analyzed using Improved SPM (Two Phase) and association rules, which outperformed previous classifiers. The SPM with ARM algorithm predicts disease with the highest accuracy (92.01%).	Harini, C et al., (2021). [85]

Table 10: Scholarly Literature on Prediction of different types of CAD using ML and DL published between 2020 –2022

S. No.	Type of CAD	Parameters Used	Dataset Information	Simulation Model	Algorithm Used	Reference
1	Obstructive CAD	Coronary artery calcium - CAC	REFINE-Reykjavik study results	gologit2 command in stata	Ordinal Logistic Regression	Gudmundsson, E. F et

		Carotid Plaque Total Carotid Plaque Area – TPA	(948 individuals)			al., (2022). [86]
2	1.Obstructive CAD 2.Acute Myocardial Infraction (AMI)	Plasma Lipoprotein(a) – Lp(a)	Singapore Coronary Artery Disease Genetics Study (SCADGENS) (2025 individuals)	STATA Version 16	1. Kruskal-Wallis test 2. chi-square test 3.Linear Regression analysis	Loh, W. J et al., (2022). [87]
3	1.Obstructive CAD 2.Myocardial Infraction (MI)	Soluble urokinase plasminogen activator receptor - Plasma suPAR	Cohort of unselected consecutive patients undergoing coronary angiography at a single regional Danish hospital (1635 patients)	IBM SPSS Software version 25	1.Chi-square test 2.Multivariate Cox analysis	Hodges, G et al., (2020). [88]
4	1.Low-grade inflammation (LGI) 2.Endothelial dysfunction (ED) leading to depression	Plasma biomarkers of LGI 1.serum amyloid A (SAA) 2.high sensitivity CRP 3.IL-8 4.TNF-a 5.IL-6 6.sICAM-1 Plasma biomarkers of ED 1.sVCAM-1 2.vWF 3.sE-selectin 4.sICAM-1	The Maastricht Study (3451 participants)	1.IBM SPSS Statistics version 25.0 2.Mplus8	1.Cox proportional hazard regression analyses 2.Multinomial logistic regression analyses	Janssen, E. P et al., (2021). [89]
5	Mortality in Burn Patients due to Endothelial Dysfunction	1. Tissue Factor Pathway Inhibitor (TFPI) 2. Plasma levels of Syndecan-1 (SDC-1)	Cohort of Burn patients who were enrolled and were treated at a regional burn center (158 patients)	1.SAS version 9.4 2.GraphPad Prism version 8 for Windows	Receiver operating characteristic (ROC) curve	Keyloun, J. W et al., (2021). [90]
6	1.Coronary Artery Obstruction	1.Age 2.NSTEMI(non-ST-elevation	Yokohama City University - IHD Registry (UMIN0000418	JMP® Pro 15 (SAS Institute	Multivariate Logistic Regression Analysis	Gohbara, M et al., (2022). [91]

	2.Coronary Artery Spasm	myocardial infarction) 3.DM(Diabetes mellitus) 4.BNP(Brain natriuretic peptide) 5.N/L ratio(Neutrophil-to-lymphocyte ratio) 6.HDL-C(high-density lipoprotein cholesterol)	36) (753 patients)	Inc., Cary, NC, USA)		
7	Vasospastic Angina using 1.optical coherence tomography (OCT) 2.computational fluid dynamics (CFD)	1.Shear stress from OCT images 2.Shoreline Development index	Wakayama Medical University (17 patients)	JMP pro version 14 for Mac (SAS institute, Cary, NC, USA)	Linear Regression analysis	Tanaka, A et al., (2021). [92]
8	Assessment of myocardial bridging	Standard 2-D echocardiography, stress-echocardiography test (SE) using treadmill exercise, and in-depth functional assessment of MB through coronary angiogram were performed. 1.Conventional-FFR 2.Diastolic-FFR	60 symptomatic patients	IBM SPSS Statistics for Windows, version 26.0 (IBM Corporation, Armonk,NY)	1.Univariate binary logistic regression analyses 2.Multivariate regression model 3.Receiver operating characteristics curves	Aleksandric, S. B et al., (2021). [93]
9	Ischemia related to Myocardial Bridging	Dynamic CT myocardial perfusion imaging (CT-MPI) and Coronary CT angiography (CCTA) were performed.	498 symptomatic patients	MedCalc version 19.2 (MedCalc Software bvba)	Receiver operating characteristics curves	Zhang, J et al., (2021). [94]

		1.Change in CT-FFR across myocardial bridging in different cardiac phases				
10	Prediction of mortality in patients with Spontaneous Coronary Artery Dissection (SCAD) using various Machine Learning (ML) and Deep Learning (DL) prediction models	1.36 Baseline Characteristics 2.7 Vital Signs 3.13 Lab Values	Mount Sinai Health System EHR (375 SCAD patients)	Caret, Scikit-learn and Keras sofware (R and Python, respectively)	Comparison study of the following ML and DL algorithms: 1.Deep learning 2.AdaBoost 3.Support vector machine 4.K-nearest neighbors 5.Extreme Gradient Boosting 6.Decision tree 7.Logistic regression 8.Random forest	Krittanawong, C et al., (2021). [95]

Gudmundsson, E. F et al., [86] have identified that significantly better prediction of major adverse cardiovascular events is seen along with carotid plaque and coronary artery calcium (CAC) in comparison to more conventional risk variables. Total carotid plaque area outperformed risk scores and well-established risk variables in predicting incident CAD.

Loh, W. J et al., [87] have explored the hypothesis that Lp(a) predicts CAD in a South East Asian population. They have also looked into whether or not Lp(a) is a predictor of acute myocardial infarction (AMI) and severity of coronary artery stenosis among individuals with existing CAD. Among a South East Asian population that is overwhelmingly male, they found that a higher plasma Lp(a) concentration was a predictor of coronary heart disease and acute myocardial infarction.

Hodges, G et al., [88] discuss that patients with suspected or confirmed CAD had a higher risk of death or MI if their suPAR is high; however, the existence or severity of CAD is not connected with suPAR in this cohort. Also, suPAR represents end organ damage rather than the severity of atherosclerosis, which is likely why this is the case.

Janssen, E. P et al., [89] have researched to identify if incident depression was linked to LGI and ED. Mediating the link between ED and new-onset depression is LGI. ED could tell the difference between the result groups that had just experienced a single episode of depression and the groups that had experienced chronic depression. Results from this study point to a significant role of the cardiovascular system in both the development and maintenance of depressed symptoms.

Keyloun, J. W et al., [90] have aimed to determine whether tissue factor pathway inhibitor (TFPI) and syndecan-1 (SDC-1) plasma levels upon admission may be used as parameters to predict 30-day mortality in patients with burn injuries. In fatally burned patients, endotheliopathy biomarkers SDC-1 and TFPI are elevated. Decision-Making in the clinic, such as the selection of resuscitative or transfusion items, can benefit from an accurate assessment of the extent to which endothelium damage has occurred in a patient.

Gohbara, M et al., [91] have researched to determine whether coronary artery (CA) obstruction or spasm is the underlying cause of acute coronary syndrome (ACS) and have developed a risk scoring model for the same. The probability of obstructive CA-induced ACS without p-STE may be determined using a straightforward 6-variable risk scoring model. If the overall score is less than 20, it is reasonable to believe that the ACS was caused by a CA spasm, and a spasm provocation test may be necessary.

Tanaka, A et al., [92] have investigated how the intricacy of the coronary lumen correlates with refractory symptoms in vasospastic angina patients (VSA). Due to the increased medial thickness of the coronary artery, which results in lumen complexity and increases shear stress, patients with VSA may develop refractory symptoms. OCT pictures and the shoreline development index can be used to calculate shear stress, which can be used as a marker for irritability of the medial layer of coronary arteries in future medication efficacy studies.

Aleksandric, S. B et al., [93] have used myocardial ischemia induced by exercise as a reference point, and compared the efficacy and diagnostic value of d-FFR (diastolic-fractional flow reserve) during provocation by dobutamine to that of conventional-FFR during provocation by adenosine. Diastolic-FFR during stimulation with dobutamine is more indicative of the functional relevance of myocardial bridging in relation to myocardial ischemia induced by stress than conventional-FFR.

Zhang, J et al., [94] have utilized dynamic CT-MPI (CT myocardial perfusion imaging) as a reference standard, and analyzed the accuracy with which CT-FFR (CT fractional flow reserve) diagnoses ischemia due to myocardial bridging. The most important finding of this study was that the difference in systolic CT-FFR had the highest sensitivity and Negative Predictive Value of all indicators for detecting myocardial bridging-related ischemia, while the disparity in diastolic CT-FFR had the highest specificity.

Krittanawong, C et al., [95] discuss that acute coronary syndrome (ACS) caused by spontaneous coronary artery dissection (SCAD) is a diverse illness with a low death rate. This study compares the accuracy of classical logistic regression, ML modelling, and custom-built DL models in predicting death in patients with SCAD using data from a large city's electronic health record (EHR) system. A high c-reactive protein, hypertension, atrial fibrillation, and steroid use were all found to be significant predictors of SCAD mortality in the study. Further, DL models were more effective than regression and ML models.

7. CURRENT STATUS & NEW RELATED ISSUES :

Artificial intelligence (AI) based prediction models have rapidly expanded in the medical profession. The use of these AI-based prediction model tools and software in the treatment of cardiovascular patients is a challenge for cardiovascular researchers and healthcare professionals to comprehend both the potential and the potential boundaries of AI-based predictions.

The following key points need to be addressed while using AI based prediction for cardiovascular diseases [96]:

- Although there are many prediction models already, only a few of them are really used. A new complex model's value over an already-existing simpler model is not assured.
- To recognize and address cultural and technical hurdles, it is crucial to understand where a model fits into the therapeutic process.
- For model calibration, representative data at the development stage is crucial. Predictive performance measurements may be skewed if those with unusual presentations or missing data are excluded.
- The outcome status should be accurately verified. Predictions and estimates of predictive performance may be biased by inaccurate verification.
- Rigorous both internal and external validation processes must be used to test the effectiveness of AI prediction models.
- To measure the effectiveness of prediction, several different statistics are available. Clinical effects of utilizing the AI prediction model are not described by traditional performance statistics.
- It might be useful to determine which features are most important for making predictions using an explainable AI methodology. It is uncommonly warranted to draw conclusions about causality and effect just from the outcomes of prediction modelling.

For reliable ML-based prediction models of CAD, it is important to have the following features [97]:

- Stronger findings, such as death, the CAC score, or coronary artery stenosis

- Validations in the lab or in the hospital
- Adapting to a multiethnic group while using untested AI
- The fusion of traditional, lab-based, image-based, and medication-based biomarkers

Krittanawong, C et al., [98] have published an article to evaluate and appraise the general predictive performance of ML algorithms in cardiovascular disorders. A total of 344 studies have been evaluated by them. The following are the key outcomes of the evaluation:

- Multiple predictive criteria were used to develop traditional ways of making predictions as the Framingham risk score, SCORE, PCE model, and QRISK. These risk scores include few predictors and neglect key variables. To accurately anticipate CAD, stronger prediction tools are needed.
- Accuracy in predicting cardiovascular disease using ML algorithms is high (AUC 0.8-0.9 s).
- In terms of AUC, custom-built CAD prediction algorithms performed better than boosting techniques. Custom-built algorithms must be transparent and repeated in numerous experiments using the same group of independent variables before being used in clinical practice.
- In contrast to traditional risk scores, most ML models included laboratory data and a shared group of quantitatively different demographic factors (such as age, smoking status, sex). Although each of those factors has not been well verified in clinical investigations, in some cases they may offer predictive value. Studies directly contrasting ML algorithms with conventional risk models are required.
- The research problem and the dataset's structure should be taken into consideration while choosing an ML algorithm.

According to the study, out of the 103 cohorts examined, 12 cohorts analyzed cardiac arrhythmias, 45 cohorts investigated CAD, 34 cohorts studied stroke, and 12 cohorts assessed heart failure.

8. DESIRED STATUS & IMPROVEMENTS REQUIRED :

One of the difficult issues facing medical science in the current decade is the diagnosis of cardiac disease. Every doctor now faces a very challenging task when attempting to anticipate the disease because of the numerous ambiguities and risk factors. If the heart attack can be detected sooner, the patient's life can be spared by appropriate medicine, and the damage to the heart can also be reduced significantly.

Over the years, numerous investigations on the cardiovascular prediction system have been conducted by various authors employing a variety of ML and DL algorithms. With the help of datasets, various algorithms, experimental findings, and ongoing work to improve the system, they have attempted to develop effective approaches and accuracy in detecting heart illnesses.

Traditionally, AI or ML models are defined as "black boxes" in which the input data sequences that lead to specific outputs are unknown. In a classification task, the algorithm may be able to achieve ideal performance, yet it may be impossible for humans to understand the underlying intrinsic factors. Complex and non-linear models, which are well-suited to advanced risk prediction, are especially responsible for the black-box behavior of AI algorithms [99].

Explainable AI (XAI) is a set of techniques for understanding the logic behind these intricate models. XAI can shed light on novel elements of a dataset and a disease by showing the forecasting value of input variables including risk variables, characteristics, and protein expression levels. In contrast, basic models like principal component analysis (PCA), Cox regression model and logistic regression model provide clear indications of a feature's worth via its model parameters [99].

A lot of research has been conducted utilizing different ML and DL algorithms to predict CAD in general. There is very little research on how to anticipate a specific kind of CAD, such as SCAD, myocardial bridging, or coronary vasospasm. It is possible to conduct more study on the prediction of a particular form of CAD or on the prediction utilizing a particular biomarker with increased prediction accuracy.

9. RESEARCH GAP :

From the available literature and research, it is clear that many people have looked into the topic of predicting CAD using several biomarkers and machine learning and deep learning algorithms. So far, "Black box" ML algorithms have dominated the studies' utilization in this area. Research into the application of Explainable AI Algorithms to CAD prediction is essential for the development of better, more approachable models upon which to base critical decisions. In the completed review study, the following gaps in research were identified:

- **Research Gap 1:** Usage of Explainable AI in prediction of CAD.
- **Research Gap 2:** Usage of unique biomarkers for prediction of specific type of CAD like SCAD or Coronary Vasospasm.
- **Research Gap 3:** Usage of DL algorithms like Yolo algorithm or ResNet algorithm for prediction of CAD.
- **Research Gap 4:** Exploration of availability of datasets for prediction of specific type of CAD.
- **Research Gap 5:** Possibility of designing a new algorithm for prediction of any specific type of CAD based on unique biomarkers.

10. RESEARCH AGENDA BASED ON RESEARCH GAP :

Based on the Research gaps identified the following are the key points of the Research Agenda.

- Identifying the different Explainable AI methods and exploring the architecture and usage of the algorithms.
- Identification of distinctive biological parameters which can help in better prediction of CAD has to be done.
- It is necessary to investigate the potential of DL algorithms like Yolo and ResNet for CAD prediction.
- It is necessary to verify the data set accessibility for distinct biomarkers.
- Analyzing the viability of developing a new, more accurate CAD prediction model for predicting a less common type of CAD.

11. ANALYSIS OF RESEARCH AGENDAS :

1) Support Vector Machine (SVM), Artificial Neural Network (ANN), AdaBoost, and Random Forest are only few of the ML and DL algorithms that have been studied extensively for their potential to forecast CAD. Algorithms from the realm of Explainable AI, such as LRP (Layer-wise Relevance Propagation), DTD (Deep Taylor Decomposition), have the potential to aid with CAD prediction. There has to be a comprehensive investigation into the potential of Explainable AI systems for CAD prediction.

2) Significant work has been done utilizing AI to predict whether a person has CAD based on their physical and biological characteristics. There has not been a substantial amount of research on the ability to predict a particular kind of CAD or the ability to predict mortality based on particular health conditions and biomarkers. Coronary vasospasm and SCAD are not as common as other kinds of CAD, hence there has been less work done on developing prediction models for these. Research has to be done in this regard.

3) There has been an extensive usage of DL algorithms like Deep Neural Networks (DNN), Artificial Neural Networks (ANN) to build prediction models for CAD. Understanding the scope of algorithms like Yolo and ResNet has to be done and the capabilities of these algorithms to build prediction models with improved accuracy has to be done.

4) The development of more accurate prediction models relies on the discovery of novel biomarkers for a variety of uncommon forms of CAD. Exploring the availability of dataset repository for such requirements plays a key role in the research undertaken.

5) Research requires investigating the feasibility of developing a novel model that can forecast a less common form of CAD utilizing an under-explored algorithm such as the Explainable AI algorithm. It is necessary to evaluate the algorithm's effectiveness in terms of its predictive abilities.

12. FINAL RESEARCH PROPOSAL :

By focusing on rare forms of the illness, such as SCAD, Coronary Vasospasm, and Myocardial Bridging, the research aims to develop a more accurate prediction model. Yolo, ResNet, and the Explainable AI mindset are just a few of the underutilized algorithms that will be the focus of the research.

SWOT ANALYSIS :

SWOT stands for strengths, weaknesses, opportunities, and threats. The SWOT analysis highlights the significance of any system's potential strengths. Throughout the deployment of an innovative digital healthcare system, weaknesses and threats should be addressed [100].

Since the introduction of AI methods in medical field, there has been a notable qualitative and quantitative advancement in the comprehension of medical images and the interpretation of huge data for imaging analysis. There is a wide variety of established clinical uses for AI methods in the healthcare industry today [101].

Here we conduct a SWOT analysis to weigh the pros and cons of the study objectives.

Table 11: The SWOT Analysis

Strengths	Weaknesses
• AI can enable early diagnosis and improved treatment options. • The interpretation of the results becomes easier. • Explainable AI gives ways to penetrate AI black-box models and use AI to achieve two goals: accurate predictions and explanations. • Using a prediction model that is easy to understand can help patients accept the results. • AI can classify images and lesions. Advanced picture segmentation tools are available which can extract more data from the image.	• AI techniques cannot perform subjective associations like a cardiologist's intellect. • Availability and accessibility of huge amount of dataset based on the specific requirement is a challenge. • Patient engagement is crucial. Patients must know how data, evidence, and analytics affect their treatment and be involved in healthcare decision making. • DL algorithms lack transparency and interpretability though they have more prediction accuracy. • Involves an extensive process of developing technology • AI-based health care solutions are expensive. • Lack of skilled labor, significant initial investment are major challenges.
Opportunities	**Threats**
• There are a great number of unexplored therapy avenues in which additional research could be conducted. • The implementation of AI technologies can result in a reduction in treatment costs and an improvement in patient care. • Continuous use of newly acquired data pertinent to diagnosis and treatment. • AI focuses on refining existing ML algorithms and developing new ones to offer more accurate diagnosis without human input. • Availability of many free and open-source AI frameworks help construct stronger prediction models.	• Reality is complex, incomprehensible. Big data analytics is biased since it relies on data and algorithms. • Data and algorithms have limitations and biases that stem from human cognitive limitations and prejudices. • Incomplete, erroneous, and missing data distort analytics. • There aren't enough accountability and frameworks for regulating the process.

13. SUGGESTIONS :

AI has not lived up to its potential, notably in cardiology, despite tremendous efforts and enthusiasm. However, only a small percentage of AI project results have actually made through into the cardiac clinical guidelines that doctors use every day. It is a huge challenge for medical professionals to apply the results of clinical studies conducted using machine learning to actual patient treatment. Carefully crafted instruments, such as maybe interactive dashboards, should be developed to appropriately explain output of AI risk models during patient visits.

14. LIMITATIONS OF THE PROPOSAL :

The prediction of coronary artery disease is the primary focus of this research, and its scope is constrained by the characteristics of the cohort that is being studied. In the scope of this research, other cardiovascular diseases, and disorders, such as heart failure, stroke, aortic diseases, and peripheral artery diseases, will not be examined.

15. CONCLUSION :

The article gives a brief review of the utilization of AI in the prediction of CAD. Symptoms, diagnosis, and treatment options for coronary artery disease (CAD) and its many subtypes have been covered. Recent academic works have been briefly cited to illustrate the development and current stage of using ML and DL algorithms. The gaps in the research done so far have been listed along with reference to the lack of sufficient study on usage of Explainable AI in the prediction of CAD. A SWOT analysis of the planned study and the research proposal based on the research gaps have been discussed. According to the results of the literature review, more research is needed to develop a more open and patient-friendly prediction model.

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