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Analysis of Multi-modal Data Through Deep Learning Techniques to Diagnose CVDs: A Review

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Abstracts: In cardiology, there has been a surge in artificial intelligence (AI), machine learning, and deep learning techniques. Artificial intelligence (AI) and electronic health records have the potential to advance our knowledge of disease states and enable personalized cardiac care in the era of modern medicine. With its latest data fusion techniques of non-imaging and imaging data (including cardiac magnetic resonance imaging, echocardiography, and cardiac computed tomography), the field of cardiac medicine is evolving, leading the revolution in precision cardiology. Although these data were previously used in isolation, new developments in deep learning (DL) and machine learning (ML) allow these data sources to be integrated to generate multimodal insights. There is growing interest in the application of data fusion, which uses ML and DL techniques to integrate data from multiple modalities into cardiac care. We review the most advanced research in this paper, emphasizing how the new methods of data fusion are delivering clinical and scientific insights uniquely to the field of cardiovascular medicine. Although multi-modal deep learning yields more reliable estimations than multi-modal machine learning and unimodal techniques, it suffers from limitations related to scalability and the time-consuming nature of concatenating information.

Keywords: Multimodal ML (MML), Multimodal Deep Learning (MDL), Cardiac Magnetic Resonance Imaging (CMR), Coronary Artery Disease (CAD), Myocardial Infarction (MI), Ischemic Heart Disease (IHD), Logistic Regression (LR), Convolutional Neural Networks (CNNs).

1. INTRODUCTION

The heart and its blood vessels make up the cardiac system in our body [1]. This system can have many different issues, some of which include abnormalities of the arterial and venous system, heart valves, and endocarditis [2]. Cardiovascular diseases (CVDs), encompass four conditions: aortic atherosclerosis, peripheral artery disease (PAD), cerebrovascular disease, and coronary artery disease (CAD) [3-5]. Reduced heart perfusion in CAD leads to ischemia [6], which may progress to myocardial infarction (MI) [7, 8]. One-third and half of all cases of cardiovascular diseases are caused ischemia [9]. The condition known as cerebrovascular disease is linked to transient ischemic attacks (TIAs) and strokes [10]-[12]. A condition known as peripheral arterial disease (PAD) primarily affects the limbs and can cause claudication. The condition linked to abdominal and thoracic aneurysms is atherosclerotic cardiovascular condition [13, 14].

A major cause of death and loss of health worldwide is cardiovascular disease [15, 16]. Approximately 17.8 million deaths worldwide in 2017 were attributed to CVDs, meaning that 330 million years of life were lost and an additional 35.6 million years lived with disability [15, 17]. However, in 2019, the data from the Global Burden of Disease study estimated 523 million cases of cardiovascular diseases (CVDs) [15]. By 2030, sociodemographic changes, such as population aging and the rising prevalence of risk factors (such as obesity, hypertension, and diabetes), are expected to raise this number to 23.6 million deaths [18]. Three-quarters of deaths from CVDs occur in low-middle-income countries (LMICs), according to the WHO [19]. The ischemic heart disease and ischemic stroke are the primary causes of 85% of deaths from CVDs and one-third of these deaths happen too soon in individuals under the age of 70 [20, 21]. Ischemic heart disease was ranked at the top among all CVDs as the leading cause of mortality causing 9.4 million deaths [15, 22].

Early on in their development, CVDs have mild symptoms that gradually worsen [23-25]. When beginning CVD, most people experience symptoms like fatigue, breathlessness, swelling in the ankles, fluid retention, and other symptoms [26]. The best methods for identifying CVDs are blood tests, electrocardiography (ECG) signals, and medical imaging [27]. A wide range of imaging technologies, including computed tomography (CT), multiple types of magnetic resonance imaging (MRI), echocardiography (Echo), and X-rays, are used in cardiac assessment [28]. However, the patient's medical history, family history, risk factors, lifestyle, and physical examination are also the main components of the diagnosis [29].

We can coordinate the findings from multiple modalities and forecast the presence of disease based on procedures and results [30]. Data that spans several contexts and types (such as genetics, text, or imaging) is referred to as multimodal data [31]. The basic goal of multimodal data fusion techniques is to merge data with values from various scales and distributions into a global feature space, or database, where the data can be more consistent [30, 31]. This uniformity can be used to improve performance on tasks like classification and prediction [32]. It is possible to predict the prognosis of cardiovascular disease, enhance the identification of required therapies, and forecast treatment response by combining various data types [33]. It is hoped that by using multiple types of data, more accurate models can be constructed than if only unimodal data is used [31-34]. Although a single modality has been the focus of the majority of artificial intelligence research in the cardiac care industry, as the field develops, more efforts are being made to use multiple modalities for diagnosing CVDs [35].

Multimodal machine learning (MML) techniques have been analyzed in previous reviews and used in the diagnosis of various cardiovascular diseases in the last few years [36-39]. However, there is a gap in the analysis and implementation of multimodal deep learning (DL) in the diagnosis of cardiovascular diseases: heart disease, ischemic heart disease, atrial fibrillation, stroke, coronary artery disease, and myocardial infarction [40-61]. The articles mentioned in this review have utilized deep learning algorithms for the training of one modality and then fused two or more different modalities for classification using an ML model [40-61]. MDL offers benefits over MML for data fusion. Multimodal deep learning enables the direct application of deep learning algorithms to classification tasks by integrating data from multiple modalities at an early stage of the process [62]. In particular, a systematic review of the literature has been conducted from the following perspectives:

RQ1: What is the current state of the art for predicting CVDs using multimodal data, and what are the literature and technological gaps in the prediction of heart diseases?

RQ2: Which multimodal ML frameworks are currently in use, and why there is a need for applying deep learning algorithms to analyze multi-modal datasets?

RQ3: How multimodal ML is different from multimodal DL?

1.1. Types of Data Modalities for Diagnosing CVDs

The different types of data modalities that can contribute to the diagnosis of cardiovascular diseases (CVDs) are given below:

1.1.1. Clinical Data

A fundamental component of most health and medical research is clinical data [63]. Clinical data is gathered as part of official clinical trial programs or in the course of continuing patient care. The data that is collected includes biometric and demographic profiles, prescription medication details, diagnoses, treatment modalities, laboratory results, statistics on physiological monitoring, hospitalization records, and patient insurance information.

For example, blood tests offer data on blood sugar levels, triglycerides, cholesterol levels (LDL, HDL, and total cholesterol), and inflammation markers like C-reactive protein (CRP). When assessing the risk of atherosclerosis and other cardiovascular diseases, these markers are essential [64].

1.1.2. Electrocardiograms

The electrical activity of the heart is measured indirectly by an ECG, also known as an EKG. To create a 12-lead ECG, electrodes containing a conductive medium are applied to each extremity and multiple locations on the chest wall [65, 66]. This allows for a recording of the electrical currents within the heart. Every particular portion of an electrode offers a trace, or lead. By using 12 leads, a more comprehensive image of the electrical activity in the heart can be obtained from 12 distinct perspectives [66]. Its application is essential for the assessment and treatment of a variety of cardiovascular conditions, such as arrhythmias, atrial fibrillation, ischemic heart disease, and pericardial and myocardial disease [67].

1.1.3. Imaging Modalities

The most common imaging modalities that are used in cardiology are echocardiography, CT angiography, and cardiac MRI. Sound waves are used in cardiac ultrasound, also known as echocardiography (Echo), a non-invasive technique for imaging heart tissue [68]. Echo evaluates the heart's pumping cavities, analyses blood flow through them, and assesses the structure of the heart to assist doctors in identifying different kinds of CVDs [68-70]. The other non-invasive imaging method that can be used to identify a range of CVDs is computed tomography (CT) [71]. Specifically, cardiac CT offers an anatomical assessment of the heart, with a focus on coronary artery disease [72]. Non-contrast CT and contrast-enhanced coronary CT angiography (CTA) are used in this imaging modality [73]. One of the main drawbacks of cardiac CT imaging is radiation exposure [72, 73]. The degree of myocardial infarction/fibrosis and cardiac chamber volume/function can both be quantitatively assessed using CMR imaging [74, 75]. For the diagnosis of various CVDs, such as ischemic heart disease [76], myocarditis [77], and atrial fibrillation [78], it is a modality that is advised by guidelines. This aids in the early diagnosis and accurate phenotyping of the various CVDs, both of which are critical for prompt and customized patient treatment [79].

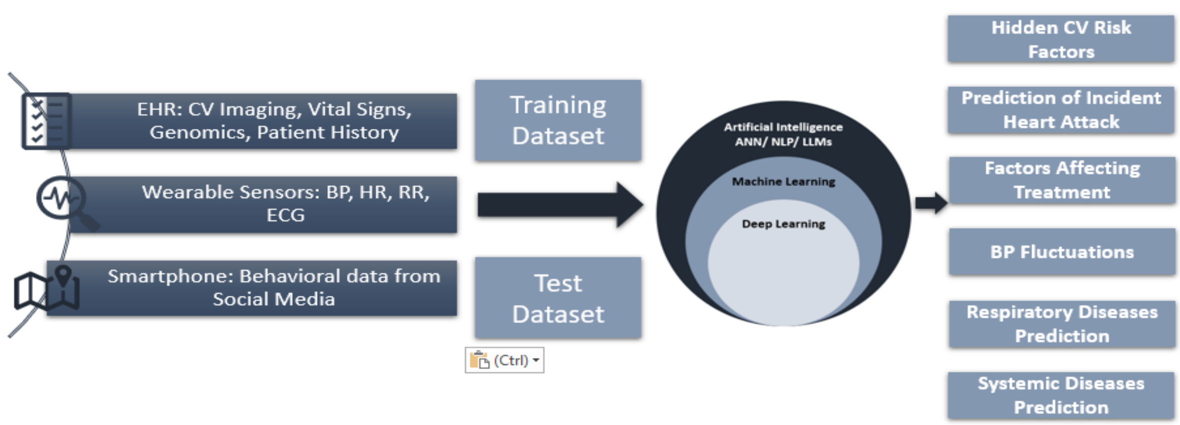


Figure 1: An improved cardiac healthcare approach using wearable sensors, EHRs, and social media data to improve predictive analytics with machine learning and deep learning models

2. LITERATURE REVIEW

Javeed et al. stated that there have been several uses of machine learning, data mining techniques, and various modalities of data in the past [80]. They conducted a review of automated diagnosis for the prediction of heart disease using a variety of modalities, including images, ECG, and clinical data separately. A great number of articles were analyzed utilizing different data types and each mode of data was individually discussed. Additionally, the limitations of the earlier approaches were presented in this paper along with a critical evaluation of them. The paper concludes by outlining some potential paths for future research in the area of automated cardiac disease detection using a variety of data modalities and machine learning.

Moshawrab et al. analyzed the use of MML in cardiac care. They found out that MML facilitates the amalgamation of various models in the pursuit of a solitary, all-encompassing resolution to a multifaceted issue [81]. The technical aspects of multimodal machine learning were covered in this review. Furthermore, this article delved deeply into the application of multimodal machine learning in the identification and prognosis of CVDs, emphasizing the outcomes achieved thus far and potential avenues for further advancement in this domain. The article has analyzed multimodal ML and data fusion categories in a well-structured manner but the articles relevant to cardiovascular diseases have been discussed less. Only a general overview of multimodal ML in cardiac care has been provided.

Ahsan & Siddique used a qualitative approach to identify the problems related to unbalanced data in cardiac diseases' predictions to give a more comprehensive picture of the body of existing literature [82]. They examined 49 pieces of cited literature with consideration given to the following aspects: type of cardiac disease, algorithm applied, current applications, and solutions. Their analysis showed that the existing methods struggle with several unresolved issues when handling unbalanced data, which ultimately limits their usefulness and functionality. This review highlights the imbalanced datasets problem in multi-modal ML. However, the imbalanced dataset problem has been properly analyzed but the use of deep learning algorithms in multi-modality has not been discussed.

Milosevic et al. summarized the last five years' worth of research on AI applications for multi-modal imaging in cardiology [83]. They found out that there have been many encouraging developments in the registration, segmentation, and fusion of various MR imaging modalities with CT scans but there are still numerous issues that need to be resolved. Papers on modalities like echocardiography, X-ray, and non-imaging modalities are rare. The paper presents an extensive review but only the imaging modalities have been discussed.

Amal et al. reviewed the latest research in multi-modal cardiac care emphasizing how the newest methods for data fusion are delivering clinical and scientific insights unique to the field of cardiac care [84]. They concluded that clinicians and researchers alike will be able to diagnose and treat cardiovascular diseases (CVD) more accurately, precisely, and quickly with the help of these new data fusion capabilities. Although these data were previously used in isolation, new developments in deep learning (DL) and machine learning (ML) allow these data sources to be integrated to generate multimodal insights. This review study was found to be the most updated in terms of multimodality in cardiac care but the number of cited research articles is less. Moreover, the study focuses on multimodal machine learning techniques and has not discussed multi-modal deep learning.

Stahlschmidt et al. discovered that deep fusion strategies frequently perform better than shallow and unimodal methods. They analyzed that multimodal deep learning approaches offer the chance to train comprehensive models that can understand the intricate regulatory dynamics underlying different diseases, as these data sets become more widely available. Similarly, using transfer learning could help datasets from various modalities overcome sample size constraints. The review provides a detailed analysis of MDL techniques for versatile biomedical data [85]. It was considered for analyzing MDL techniques in diagnosing and predicting cardiovascular diseases. Summaira et al. provided a comprehensive review of recent developments in multimodality and a thorough examination of baseline techniques from the past and present. A detailed taxonomy that goes into greater detail about the different multimodal deep-learning applications was suggested. These applications' datasets and architectures, as well as the metrics used to assess them, were also covered [86].

Prior research on automated techniques for CVDs primarily focused on one particular kind of data modality. Additionally, a few survey articles with varying foci have been published on multimodality for cardiovascular diseases highlighting the use of MML algorithms [80-86]. All those research articles have been analyzed in this study which have employed machine learning algorithms for classification or regression and used deep learning algorithms for unimodal data training for each data type separately [87-108]. The various MDL fusion techniques for heterogeneous data have not been reviewed. This is covered in the current review, where we highlight the use of the most advanced MDL fusion techniques which have been utilized in other fields like pulmonology [62] but still not in cardiology. Furthermore, we provide a taxonomy that describes subcategories that are helpful for practitioners and researchers looking to improve or apply existing methods in addition to outlining the conventional classification of early, intermediate, and late fusion.

3. METHODOLOGY

The overall methodology that was used for this systematic literature review is given as:

3.1. Articles Collection

Several protocols adhered to guarantee an excellent review of the literature on multimodal data analysis through multi-modal deep learning for CVD diagnosis. In January 2024, a thorough search of peer-reviewed literature was carried out (reports, editorials, posters, dissertations, and short papers were not included). Preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines were considered. All articles were extracted containing terms: CVDs, stroke, ischemic heart disease, atrial fibrillation, multi-modal deep learning, coronary artery disease, multi-modal machine learning, myocardial infarction, and multimodality from PubMed, Google Scholar, Cochrane, CINAHIL, MDPI, Elsevier, and IEEE-Xplore. 403 peer-reviewed publications were found through the search process. The specific criteria defined in the search strategy were used to choose the literature for this study: only heart disease (HD), Ischemic Heart Disease (IHD), atrial fibrillation, stroke, aortic atherosclerosis, and coronary artery disease (CAD) were targeted, and the articles published after 2014 were included only.

3.2. Search Strategy

During the selection process, the overall validity of the literature review is assessed, so defining precise inclusion and exclusion criteria is crucial [109]. We used six quality standards given below, which were influenced by relevant literature [110]. Studies focusing on multimodal data analysis using deep learning were therefore qualified for inclusion. The papers were first evaluated based on their titles and then abstracts and then on the basis of their complete texts using the defined criteria of the selection process. The overall strategy is depicted in Figure 2. The quality standards that were considered for the inclusion of research articles are given below:

1. Articles published within the last ten years were included
2. The studies that investigated the use of MML and MDL for the prediction or diagnosis of CVDs
3. Research articles that used multi-modal data such as clinical features, images, and ECG, for analysis
4. Studies that clearly explained the architecture, data preprocessing, feature extraction, and fusion techniques of the deep learning and machine learning models used
5. Studies that mentioned the measurable outcomes related to accuracy, sensitivity, specificity, and AUC or ROC.

6. Only peer-reviewed journals and conferences were included to ensure credibility and quality

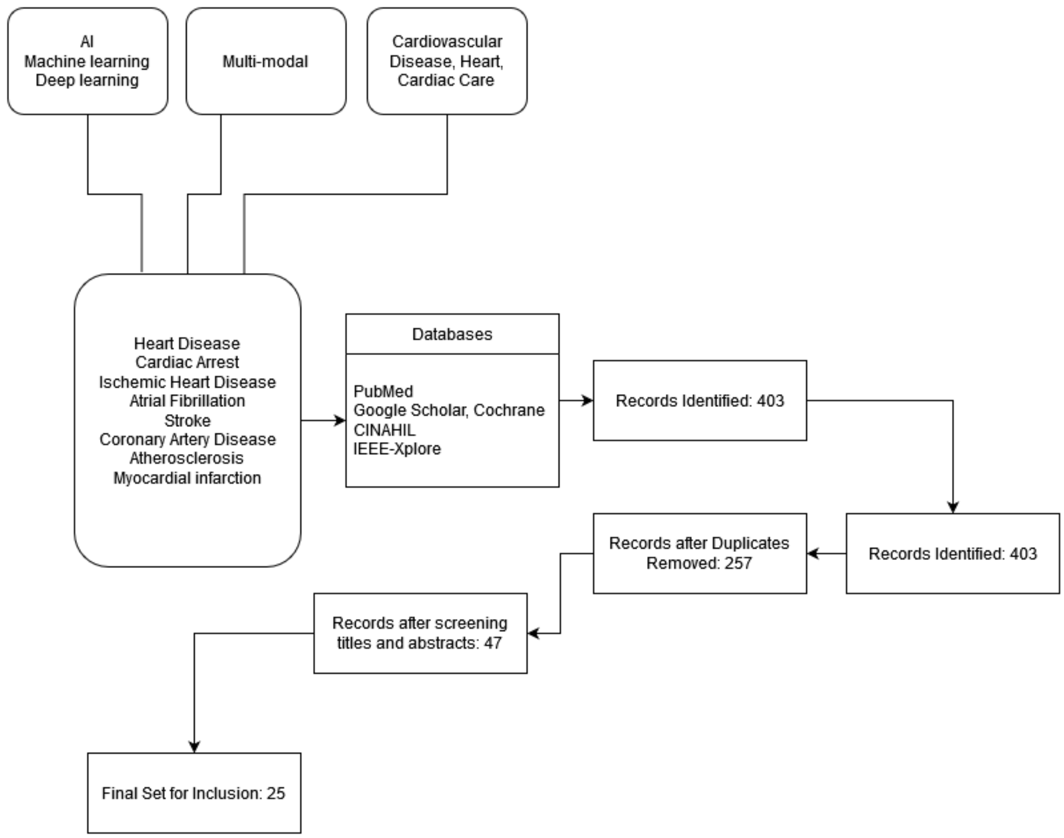


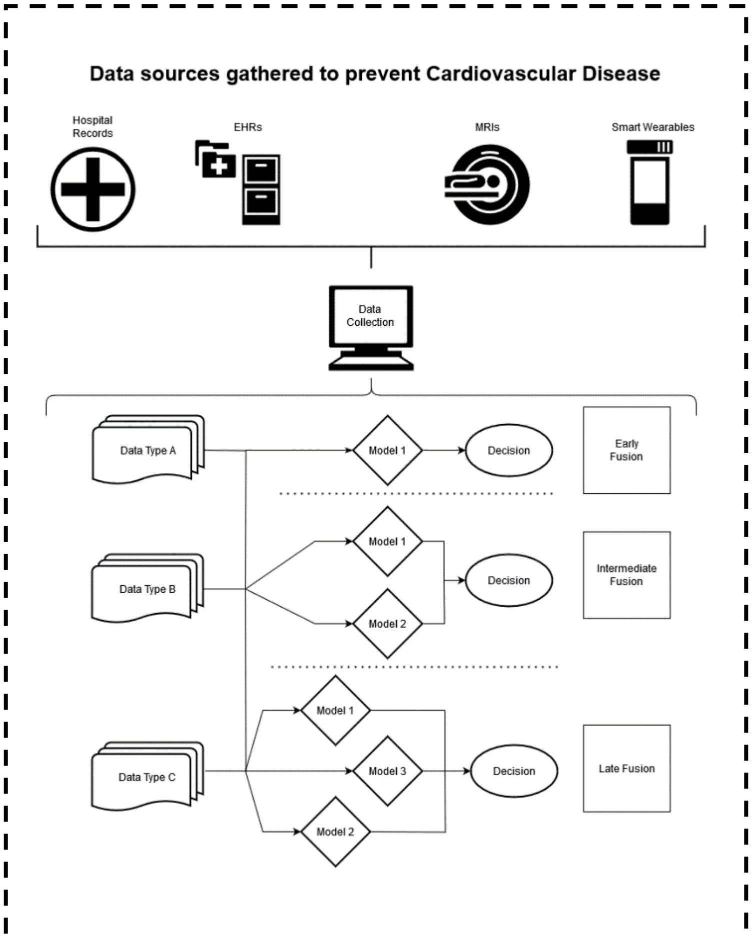
Figure 2: Reviewing Literature and Filtering Stages

4. RESEARCH FINDINGS

The findings of this systematic review are given below:

4.1. Data Fusion

"The process of combining data to refine state estimates and predictions" is the precise definition of data fusion [111]. Fusion is primarily carried out at three levels: early fusion, late fusion, and joint fusion. It can occur at various points during a modeling process. Data fusion is the discipline that covers the process of combining data from various sources using machine learning or deep learning algorithms. To process more than one kind of data, the "data fusion" technique is essential [111]. The authors of [112] provide evidence in favor of this definition by stating that a process involving the association, correlating, or fusion of data from one or more sources to produce enriched information is referred to as data fusion. There are three distinct approaches to implementing data fusion which go by different names depending on the research area and domain of application. There is no agreement on the best way to combine disparate data in data fusion given in the literature [111-113]. The different types of data fusion in cardiology are given in Figure 3.



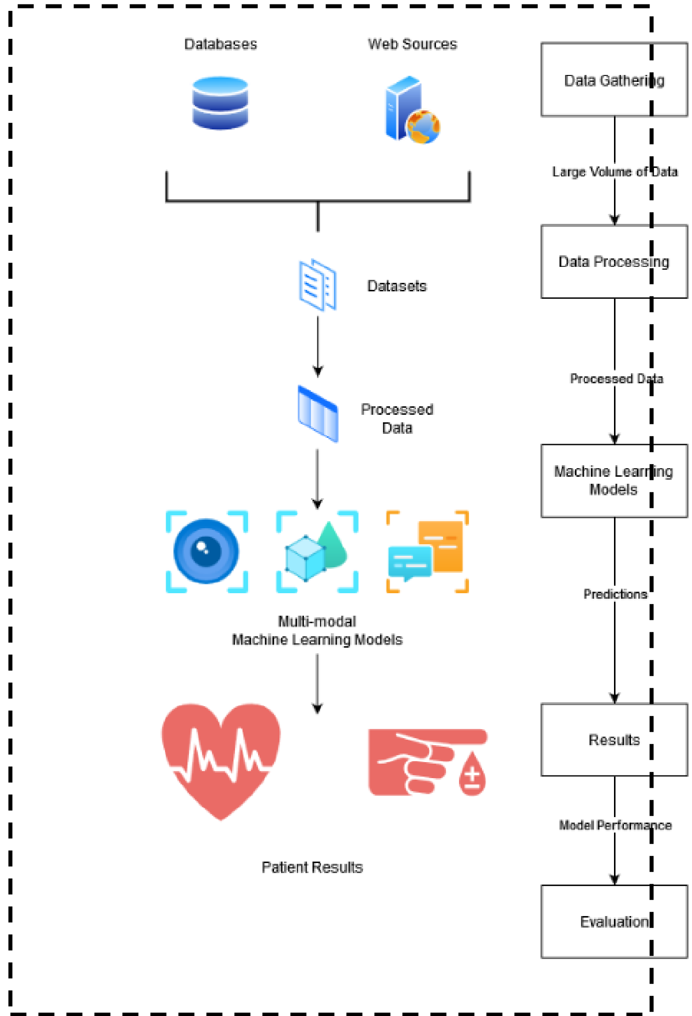


Figure 3: Stages of Data Fusion for diagnosing cardiovascular diseases using multi-modal datasets

Figure 4: Current Multimodal ML approaches which are being used in cardiology

Early Fusion is the type of data fusion that is the most basic, combining several data sources into a single feature vector before a single machine learning algorithm uses it. It is also referred to as low-level fusion. As such, it can be called a multiple-data input and single-algorithm output [114]. One problem with early fusion is that when the data are highly dissimilar, it is unclear how to combine the data from various modalities. Ali et al. suggested data normalization as a potential solution to this problem. The different data values and distributions can be scaled or normalized between 1 and 0 with different normalization techniques, allowing for the combining of data. Additionally, by lowering the noise, this strategy may enhance model predictions [115].

When all data sources have the same format, intermediate fusion occurs in the interim period between an ML architecture's input and output. This is also known as feature-stage fusion. Features are combined in this phase to carry out different tasks like feature selection, decision-making, or data-driven prediction [114]. For instance, mean muscle radiodensity and the VAT/SAT ratio were first extracted and then merged with clinical data in Zambrano Chaves et al.'s construction of the segmentation plus clinical fusion algorithm [89]. Late Fusion is the process of combining conclusions from several machine learning algorithms that were trained on various sets of data. This is also called decision-level fusion. Additionally, different classifiers' decisions are combined according to different rules [4]. For example, the EHR data and biomarkers data fusion model by Zhao et al is an example of late fusion [106].

Early fusion, can transform all data from various modalities into a single representation that can be classified using reliable classical models like Support Vector Machine or Random Forest, is the most popular type of fusion [87, 88]. Nonetheless, a late fusion approach is more convenient to use when the input modalities are highly uncorrelated and have widely differing dimensionality and sampling rates as shown in all the relevant papers [89-108]. Furthermore, because late fusion's performance is so problem-specific, there is no concrete proof that it is superior to early fusion. However, both early and late fusion provide the greatest flexibility in terms of the number of deep learning and machine learning models that can be used to analyze the data [87-108]. All the articles that have been mentioned in Table I have utilized the intermediate or late fusion approach. In most cases, each modality's data has been trained first using a neural network, and then each modality's data is classified using a machine learning algorithm [87-108].

Table I: The summarized literature review for the diagnosis of cardiovascular diseases using a multi-modal machine learning approach

Author, Year	Target Variable	Input Features	Models	Dataset	Outcome	Output	Results
Tiwari - 2022	Heart Disease	14 Clinical features	MML	Heart Disease University of California Irvine dataset-303 records	Early Prediction of Heart Disease	Binary	Acc.: 87.91
García-Ordás et al. - 2023	Heart Disease	11 Clinical features Demographics	MLP and CNN-SAE	Cleveland, Hungarian, Switzerland, Long Beach, stalog-918 samples	Risk of Heart Disease	Binary	Acc.: 90.88
Zambrano Chaves et al. - 2023	Ischemic Heart Disease	Abdominopelvic CT Images Clinical features	XGBoost	OL3I dataset	1-prediction 5-year prediction	Binary	AUROC: 0.86 AUCPR: 0.76
You et al. - 2023	Ischemic Heart Disease	Exercise ECG Clinical Risk Factors	LSTM - LR	UK Biobank – 58,892	12- year prediction	Binary	Acc.: 73.68
Liaqat et al. - 2020	Atrial Fibrillation	ECG Data Clinical features	MML-LSTM	MIT-BIH Atrial Fibrillation Dataset	Detection of AF	Binary	Acc.: 98
Atta-Fosu et al. - 2021	Atrial Fibrillation	Cardiac CT scans Clinical data	XGBoost	Pre-catheter ablation CT scans-68 Patients with AF recurrence within the first year of ablation: 37 Patients without AF recurrence: 31	AF Recurrence or No Recurrence	Binary	AUC: 0.78
Tang et al. - 2022	Atrial Fibrillation	Intracardiac atrial signals 12-leads ECG Clinical features	MML-CatBoost	Patients who underwent catheter ablation - 156	AF Recurrence or No Recurrence	Binary	Acc.: 85.9
Zhou et al. - 2023	Cardiovascular mortality	12-leads ECG – 250 features EHR data – 93 features	MML-XGBoost	Total subjects with heart failure: 2,868 New onset AF (Atrial Fibrillation): 1,150 New onset stroke/TIA (Transient Ischemic Attack): 668	AF and Stroke	Multi-class	Acc.: 89
Rawshani et al. - 2024	Atrial Fibrillation	12-leads ECG Demographics – Age, sex HRV	MML-AlexNet	PTB-XL, CPSC Extra, Georgia – 35,634	Prediction	Binary	AUROC: 0.92
Kim et al. - 2020	Atrial Fibrillation	3D Images of Left Atrium-CT 3D Images of LA-Echo Patient Demographics	MML-CNN	Catholic Medical Center, South Korea - 527	Recurrence of AF after PVI	Binary	AUC: 0.61
Li et al. - 2021	Cardiovascular disease	ECG data PCG data	MML-LSTM	PhysioNet/CinC Challenge 2016 - 405	Presence of CVD	Binary	AUROC: 0.93
Brugnara et al. - 2020	Acute ischemic stroke	Clinical data CT Images-Native	MML-GB	Germany dataset - 246	Accurate Prediction of mRS-90	Multi-class	Acc.: 80

		CT, CT angio, CT Perfusion Endovascular treatment data					
Zihni et al. - 2020	Stroke	Clinical data TOF – MRA	MML, CNN	1000Plus study - 316	Outcome Prediction	Binary	AUC: 0.75
Yu et al. - 2020	Stroke	facial motion Speech data	MML-ResNet	Stroke dataset - 376	Prediction	Binary	Acc.: 79.27
Billot et al. - 2022	Stroke	Neuroimaging data Demographics Behavioral data	MML-RF	Treatment Response Data - 55	Post Stroke language Rehablitation	Binary	F1: 0.87
Cai et al. - 2022	Stroke	One-minute facial video data Audio data	MML-CNN	Eddy Scurlock Stroke Center at Texas Hospital	Prediction	Binary	Acc.: 73.7
Agrawal et al. - 2021	Coronary Artery Disease	Survey data Biomarkers data Clinical Diagnoses Anthropometric measure	$ML4H_{EN-COX}$	UK Biobank - 13782	10-year risk score for CAD.	Regression	C: 0.796
Bagheri et al. - 2020	Atherosclerotic Cardiovascular condition	Demographics Historical data Laboratory data	MI-LSTM	UMC Utrecht - 5603	Prediction	Binary	AUC: 0.84
Puyol-Antón et al. - 2022	Symptomatic Heart Failure	CMR data 2D-Echo data	MML - SVM	UK Biobank – 700 EchoNet-Dynamic – 10, 030 Gut and ST Thomas NHS Foundation – CRT- 100 GSTFT – Echo - 12	Cardiac Resynchronization therapy Response Prediction	Binary	Acc.: 77.38
Zhang et al. - 2020	Coronary Artery Disease	Echocardiography Phonocardiography Biomarker levels Holter monitoring	SVM	CAD Patients – 32 Normal - 30	Prediction	Binary	Acc.: 96.67
Yoon & Kang - 2023	Cardiovascular Disease	12-lead ECG data	Res-Net-50 and LR	Chapman University Shaoxing People's Hospital	Prediction	Binary	Acc.: 93.97
Xiao et al. - 2023	Myocardial Infarction	12-lead ECG data Demographics	Multi-modal ML-CNN	PTB-XL – 21,837	Prediction	Binary	Acc.: 87.4
Sievering et al. - 2023	Myocardial Infarction	Invasive Coronary Angiography Images Clinical data	Multi-modal ML-ANN	Switzerland - 445	Prediction	Binary	Acc.: 81.12

4.2. Multi-modal ML Vs. Multi-modal DL

The development of algorithms and models that can comprehend and learn from vast and multiple modalities of data, such as text, image data, audio, and video, is the aim of multimodal machine learning as depicted in Figure 4. Research on MML is booming, and it has the potential to revolutionize many different fields specifically biomedical science. To create effective that can utilize versatile instances from numerous modalities and produce more reliable and accurate predictions in the real world, it is imperative to comprehend the technical aspects of MML. As a result, whether a dataset is multimodal or unimodal in architecture, multimodal datasets define the data itself. And, these datasets are independent of the nature of the algorithms used to analyze the data. However, an early fusion approach that is a form of MML and MDL is thought to involve combining multimodal datasets. It helps in unifying their representation into a single vector, and then analyzing them using an ML model or a DL model.

MML has been used extensively for examining and deciphering complex cardiac data that came from various modalities and sources [87-108]. To improve the viability and usability of MML in cardiac care, researchers have overcome the particular difficulties that came with working with diverse datasets [89-108]. However, there were many challenges in unifying and standardizing different data sources and creating connections between them. Combining heterogeneous data that only slightly overlap or do not share any common characteristics has been challenging. Furthermore, there were differences in the amount of pre-processing steps required for data from various sources, particularly when it came to noise reduction and managing missing values [87-108]. This obstacle is evident in the fact that till now, the majority of multimodal representations were just unimodal representations concatenated together [87-108]. To guarantee accuracy and dependability, preprocessing and normalization of data was done [87-108]. In addition, the process of fusion was difficult whether it was used on the data itself [87-91] or on several pre-trained models to identify a single result [92-108].

MDL offers benefits over MML for data fusion. The traditional version of deep neural networks (DNNs) is fully connected neural networks (FCNNs). These DNNs use multiple hidden layers of nonlinear computational operations to map input x to label y through [85]. By identifying straightforward relationships between underlying disentangled data, these algorithms seek to discover highest representations of the input data that enhance the predictions of a final classifier model or algorithm [85, 86]. The deeper layers or hidden layers combine earlier layers' simple abstractions of the data to create more abstract representations that are explanatory for the learning task. Most importantly, nonlinear relationships between different modalities and cross-modality relationships can be modeled by multimodal DL [86]. Table II compares the MML with the MDL technique.

Table II: Difference between multi-modal ML and multi-modal DL

Aspect	Multi-modal Machine Learning	Multi-modal Deep Learning
Definition	involves merging data from several modalities to enhance prediction accuracy or decision-making.	enhances prediction or classification tasks by automatically learning representations of data from multi-modalities using layered neural networks.
Data Fusion Strategy	**Early Fusion:** Merges data before algorithm application **Late Fusion:** combines features at the output level **Hybrid Fusion:** Combination of both early and late fusion	**Feature-level fusion:** Before feeding features into a deep learning model, features extracted from various modalities are combined **Decision-level Fusion:** Outputs from models trained on various modalities are integrated. **Intermediate fusion:** Integrates decisions or features at deep neural network layers that are hidden
Algorithms	ML algorithms integrated with neural networks	Integrated deep neural networks
Challenges	Manual Feature Selection	Automated Feature Extraction
Advantages	Less Computational Power	Enhanced Accuracy and precision

MLD techniques have been widely used to combine biomedical applications for drug repurposing, cancer patient clustering, and disease-gene pair prediction. A multimodal Deep Boltzmann Machine (DBM) was used by Suk et al. based on positron emission tomography (PET) scans and magnetic resonance imaging (MRI). Their model outperformed SVM and LDA [116]. In order to aid in pan-cancer classification, Zhang et al. presented a thorough Variational Autoencoder (VAE) framework that included learning a task-specific unified representation from data of two modalities i.e., DNA methylation and gene expression [117]. This architecture continuously outperformed a support vector machine.

Malik & Anees proposed four novel convolutional neural network (CNN) models. These CNNs were trained on different image-level representations for the classification of nine different chest diseases. Additionally, the suggested CNN made use of several novel techniques, including multiple-way data generation (MWDG), dropout, batch normalization layers (BANL), max-pooling layer, and rank-based average pooling (RBAP). The sounds of coughing were converted into a visual representation using the scalogram method. The Synthetic Minority Over Sampling Technique (SMOTE) approach was used to calibrate the Chest X-Ray (CXR) and Computer Tomography (CT) scans, along with the cough sound images (CSI) of nine distinct chest disorders, before starting to train the developed model. The suggested model was trained and evaluated using data from 24 publicly available chest illness cases datasets of CXR, CT scan, and CSI [62]. No such research has been conducted for the diagnosis of CVDs using a multimodal DL approach especially using multi-modal images (CMR, CCT, and ECHO) and ECG signals. Figure 5 gives the multimodal DL approach that can be utilized in cardiac care.

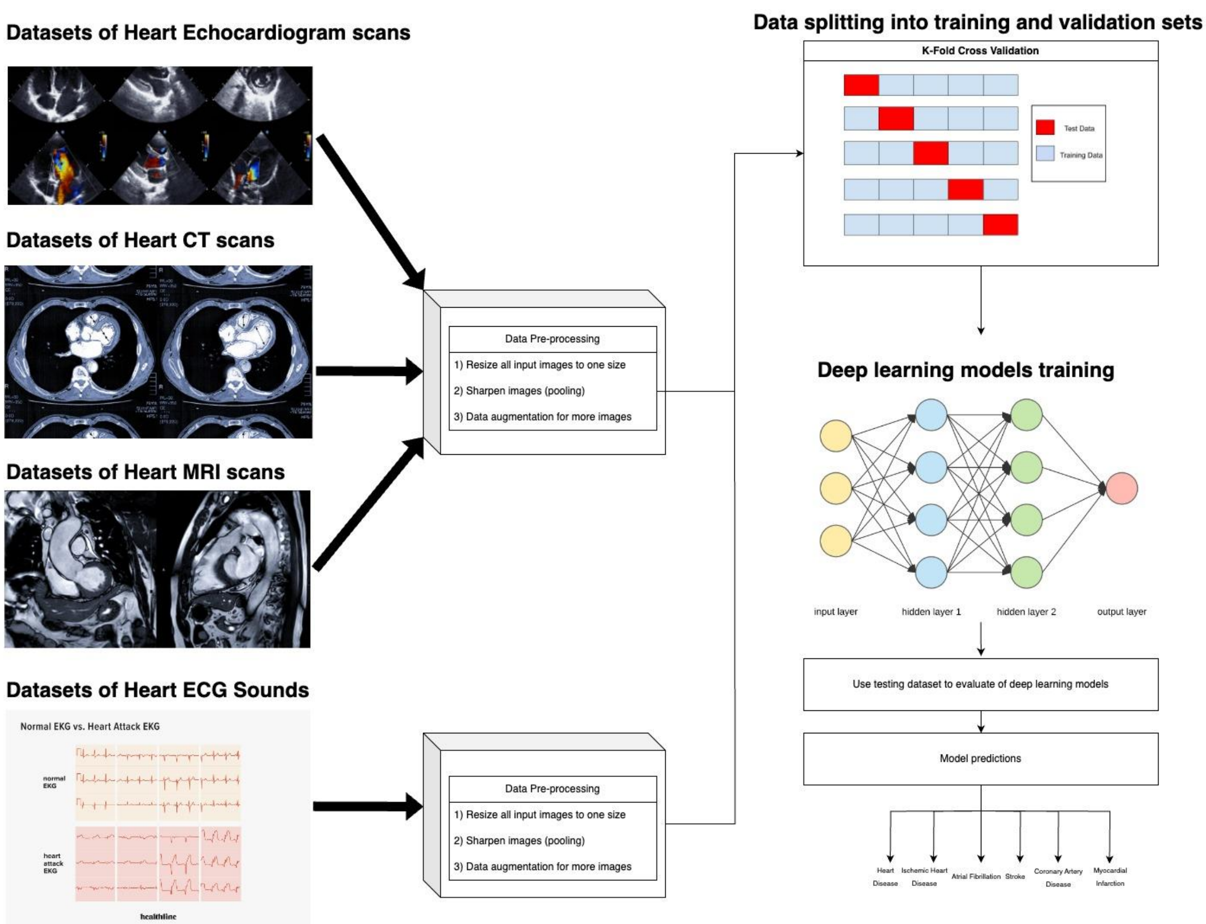


Figure 5: Entire process for analyzing heart diseases: from gathering multimodal cardiac data to preprocessing, validation, and training multi-modal deep learning models

5. CHALLENGES AND LIMITATIONS

It is difficult to combine data from various sources that have different intrinsic distributions and the data having varying degrees of structure. In a way that is not possible for a single modality like ECG alone, data fusion techniques seek to combine several data observations from CMR, CCT, and clinical data into a coherent and varied depiction to diagnose a CVD. But fusion itself faces difficulties from high dimensionality, missing or sparse data, and noisy and irrelevant images that could impact model performance. Further difficulties arise from the possibility that such a combination of data may call for more complex data (containing images, videos, and text) normalization procedures (which include correcting errors and variations ingrained in data from various sources) and more advanced models rather than pre-trained models [87-108], which may be computationally costly to train. Model "explainability" suffers as a result of this fusion of data and level of complexity. For instance, the sonographer's skill level has a significant impact on the quality of the ECHO data. As a result of its high reliance on a human skill, data fidelity from ECHO can differ greatly, which could have an impact on model's performance [118]. However, this problem highlights the potential of multimodal data fusion, which can augment variable data by integrating knowledge from various sources.

Usually, to understand what additional performance data fusion produces, MML and DL models are compared to models with fewer data modalities. Evaluation metrics include measurements of accuracy, specificity, sensitivity, calibration, AUC, AUCPR, and positive and negative predictive values. These metrics are generally the same across ML and DL domains. The goal of the study and the dataset are the primary determinants of the evaluation metric to choose. For instance, to classify the probability of myocardial infarction as the reason behind chest pain, healthcare practitioners must grasp both model calibration and AUC. Model calibration is the degree to which the risk predicted by a model corresponds to the total risk that is observed in the particular population that is being studied. Additionally, practitioners can assess the likelihood that both positive and negative results are true using precision-recall metrics like the AUCPR [87-108]. The degree of balance in the datasets used for model testing and training is another crucial factor. For example, in many patient populations under study, the percentage of patients with a given disease is substantially lower than that of patients without it. In this case, evaluating a model's performance using alternative metrics like the F1 score, which combines precision and recall through their harmonic mean is more equitable than evaluating each metric separately [87-108].

Multimodal approaches often perform better than unimodal ones, as demonstrated by DL-based fusion strategies. Moreover, multimodal DL techniques are frequently found to perform noticeably better than multimodal ML techniques. Even though the literature is probably biased toward positive outcomes, it is now evident that DL-based fusion consistently produces the anticipated gains. The same difficulties that MML in cardiac care faces generally i.e., data volume, quality, and interpretability are also faced by multimodal DL approaches. However, fusion strategies are required to address multimodal-specific challenges like missing entire modalities. Various methods have been suggested, including multimodal dropout, generative models, and multitask learning. In addition to incorporating strategies to improve clinical relevance during the learning process, techniques should show resilience in handling a variety of missing modalities patterns. Furthermore, fusion strategies must take these combinations of modalities into account as more heterogeneous data become available. For this challenge, heterogeneous fusion and late fusion are especially well-suited.

6. DISCUSSION AND FUTURE WORK

Using a variety of data sets that might not all follow the same structure, format, or type and that are usually compatible with traditional ML algorithms is known as MML. The MDL is for the use of deep learning algorithms for training multimodal data. These methods accommodate variations in data characteristics and improve learning by enabling models to be trained across multiple modalities. Multimodal ML and Multimodal DL could be used to train models on a sizable distributed dataset of patient data from various clinics or hospitals in the field of disease diagnosis. This approach makes it possible to combine knowledge and information to solve challenging issues. More comprehensive and varied datasets can be used to create models that are more reliable and accurate [119]. However, there are various perspectives on how MDL can be applied for disease prediction, particularly cardiovascular diseases, and these are covered in detail in this section.

There are plenty of opportunities for additional research in multimodal data fusion, even with all of the advancements in the field. However, data fusion for medical imaging is still difficult. To enable fusion to be implemented more quickly and easily, more effective algorithms might be required before clinical applications can be realized [120]. Representation learning in the analysis of images, which enables automated image segmentation and speeds up the creation of fusion images, is partially to blame for this improvement. Real-time predictions are critical in use cases where decisions need to be made more quickly, and faster model predictions will be necessary to make this possible [121]. The creation of innovative, user-friendly frameworks to help researchers comprehend the information gained or lost from various data modalities should be one of the next areas of study. Although multimodal data fusion can yield better performing models, this is not always the case [122]. Therefore, a more solid framework for assessing the effectiveness of different data modalities will benefit researchers.

Furthermore, putting data integrity first from a data-centric standpoint can enhance model projections, helping researchers to fully utilize AI in the healthcare industry. Especially cardiac medicine. Although standards and regulations for reporting data quality have received less attention up to this point, new reporting standards and guidelines must be operationalized. There are several reasons why enhancing data quality is just as vital as developing new technologies, but the two most crucial ones are reproducibility and generalizability in research. When developing data fusion algorithms, it is important to take into account not only the quality of the data but also its relativity to the model and an effective comparison to standardized guidelines, as these factors can have a significant impact on model adoption. Finally, to further validate the usefulness of fusion modeling, prospective studies comparing variations in care resulting from multimodal fusion modeling to traditional modeling or current regulatory guidelines should be the main focus of future research directions.

CONCLUSION

In conclusion, Multimodal DL is a novel approach that permits the concurrent use of several DL models and data types in the development of intricate diagnostic models encompassing MDL and MML. By addressing the issue of data heterogeneity, multimodal DL has the potential to greatly increase the accuracy and efficacy of computer-aided diagnostic (CAD) applications, particularly in cardiology, where it is becoming a crucial component of routine patient care. Specifically, the technical aspects of MDL, like workflows and data fusion, were discussed, and the distinctions from other technologies, like Ensemble Learning, were emphasized. A summary of the current use of multimodal machine learning in the diagnosis and prognosis of cardiovascular disease was also given, emphasizing the promising outcomes to date and the potential for improvement utilizing MDL in the diagnosis of cardiovascular diseases. As with any rapidly developing technology, there are still issues that need to be resolved, including patient privacy, bias, and the interpretability of results. But these challenges can likely be overcome with more study and innovation, and multimodal machine learning will keep being crucial to the creation of AI applications across a range of industries, most notably healthcare.

Author Contributions

Writing original draft: A.S.; writing review and editing: A.S., A.A., M.U., and A.T.; conceptualization: A.S. and A.T.; formal analysis: N.D.; investigation: S.S.; methodology: A.S., M.U., and A.A.; supervision: N.D., A.T., and S.S.; visualization: M.U. After reading the published version of the manuscript, all authors have given their approval.

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Declaration of Competing Interest

The authors declare no conflict of interest.

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