Modern AI/ML Methods for Healthcare: Opportunities and Challenges

by

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Modern AI/ML Methods for Healthcare: Opportunities and Challenges

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Abstract. Artificial Intelligence has seen a significant resurgence in the past decade in wide ranging technology and domain areas. Recent progress in digitisation and high influx of biomedical data have led to an unparalleled success of Machine Learning systems in healthcare, which is perceived to be a possible game changer for 'healthcare to all'. This article gives an account of some of the current applications of AI solutions in the medical domains of diagnosis, prognosis and treatment. The article will also illustrate the implications of AI in the fight against the COVID-19 pandemic. Lastly, the article will summarise the challenges AI currently faces in its wide-scale adoption in the healthcare industry and how they can possibly be dealt with to move towards a more intelligent medical future. This may enable moving towards quality healthcare for all. AQ1 AQ2

Keywords: Healthcare · Artificial Intelligence · Machine Learning · Deep Learning · Diagnosis · Prognosis

1 Introduction

At its simplest, Artificial Intelligence (AI) is essentially a branch of computer science that aims to build intelligent machines that can think and learn like humans. Even though the idea of AI has been around for a long time, the term "Artificial Intelligence" was first coined in 1956 at a conference in Dartmouth College [75]. Due to breakthroughs in computational hardware, algorithms, libraries and datasets, AI has seen a significant resurgence in the past decade and has seeped through into various domains. With the digital revolution, the generation of big datasets has been made possible, leading to the significant success of the data-hungry AI techniques of Machine Learning (ML) and Deep Learning (DL).

The healthcare sector, in particular, is responsible for the maintenance and improvement of health for the people through various means like prevention,

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diagnosis, treatment and cure of illness (both mental and physical). But with the industry facing a severe shortage of medical staff [77] to treat an ever growing population, this becomes a very challenging task. The advent of AI into the industry can help physicians, assisting them in difficult areas like diagnosis, prognosis and help them make decisions quickly and efficiently. As various hospital records get digitised, researchers have seen a sharp increase in the amount of viable data that can be used for AI, which has been a severely limiting factor in the past. Due to this high influx of biomedical data, AI in healthcare is currently being dominated by ML and DL. Researchers can now use Machine/Deep learning studies and apply them to existing medical practices to come up with innovative solutions to solve issues faced by the healthcare industry. Multimodal data plays an important role in success of AI in Healthcare. Figure 1 shows how AI utilizes data from different modalities to assist in various sectors of healthcare. This article will look at a few applications of AI techniques in various medical domains like diagnosis, prognosis and treatment. We will also look into how AI has played a pivotal role in the COVID-19 pandemic. Lastly, we will discuss about some of the challenges AI in Healthcare faces and how these challenges can be overcome to move towards a brighter and intelligent medical future.

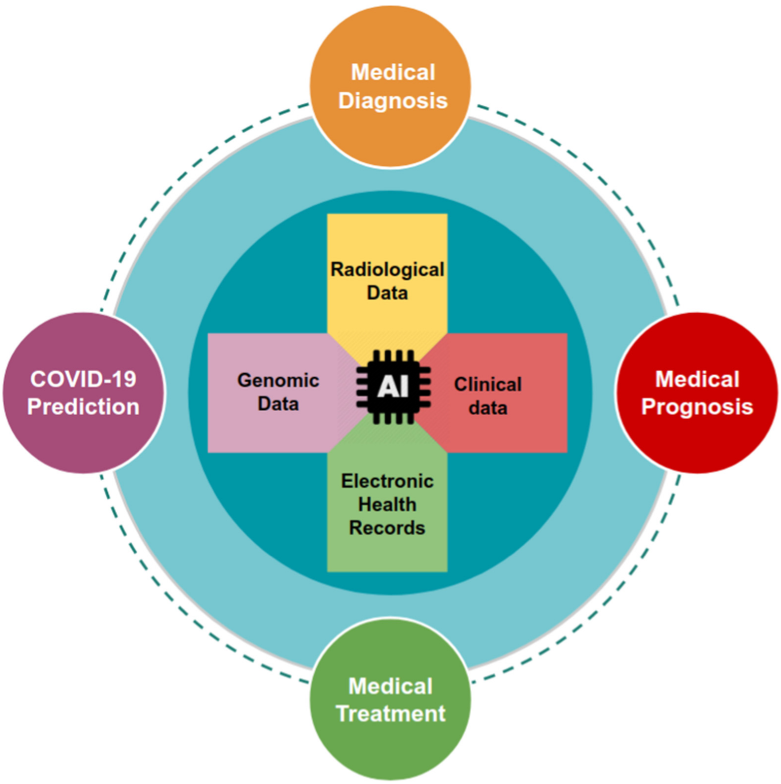

Fig. 1. A schematic of use of multimodal data and AI for different aspects of healthcare problems

2 AI in Medical Diagnosis

One of the essential steps for providing good medical care is to identify the underlying disease. Diagnosis refers to this process of assessing and identifying the underlying condition from the patient's symptoms. Health practitioners may take the help of several methods ranging from patients health history, imaging tests, blood tests etc. to conduct an efficient diagnosis. ML and DL, in particular, have revolutionised the field of Medical Diagnosis and one can argue that the applications of AI in Diagnosis are the most wide-ranging and successful. In the following section, we will summarize the advances of AI in various medical fields (Fg. 2). AQ3

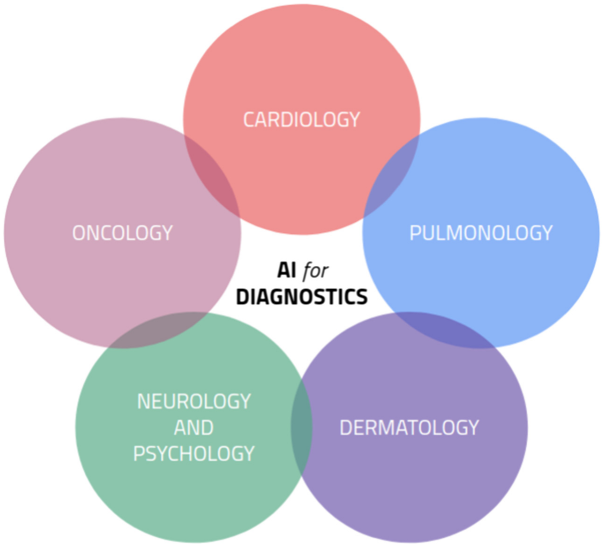

Fig. 2. Five major medical domains where modern AI/ML methods have been used for disease diagnosis

2.1 Cardiology

Cardiology refers to the branch of medicine that involves studying and treating conditions affecting the heart and circulatory system. Cardiovascular diseases (CVDs) are one of the leading causes of global deaths, World Health Organization (WHO) estimates 17.9 million lives are lost annually due to CVDs. Several AI applications have been proposed to help in the early detection of various cardiac diseases through the anomaly detection in cardiac imaging, electrocardiogram (ECG) signals and blood parameters.

Hussain et al. [36] proposed Linear Kernel Support Vector Machine which analysed the heart rate variability signals to detect Congestive Heart Failure with an area under the receiver operating characteristic curve (AUC) of 0.97. Qu et al. [69] proposed ML methods to detect congestive heart failure with an accuracy of 84.0%. Than et al. [93] introduced an ML algorithm MI^3 which used Gradient boosting to generate a score suggesting probability of Myocardial Infarction (MI). MI^3 was trained on a cohort of 3013 patients and used the combination of age, sex and paired high-sensitivity cardiac troponin I concentrations to detect MI. Sharma et al. [80] proposed an ML model which utilised the full length multilead ECG signal to detect MI with an AUC of 0.9945 while Weiss et al. [109] utilised Statistical Relation Learning Algorithms to detect MI from Electronic Health Records. Akella et al. [3] trained a Neural Network on a cohort of 303 patients to detect Coronary Artery Disease (CAD) with an accuracy of 93% using 14 different medical parameters. Wang et al. [104] used Random Forest Classifier to detect CAD with an AUC of 0.948.

2.2 Pulmonology

Pulmonology is the domain of medicine which deals with the treatment of diseases affecting the respiratory system. Respiratory diseases negatively affect a large part of the global population. According to WHO, chronic obstructive pulmonary disease (COPD) is the 3^{rd} leading cause of death, which is attributed to over 3.2 million deaths in the year 2019. Early detection of respiratory diseases is an essential step for efficient medical treatment. AI has shown promise in playing a pivotal role in the diagnosis of respiratory diseases [65,72,85,88].

An interesting application of AI to detect COPD using saliva samples was introduced by Zarrin et al. [115]. The authors used biosensors to detect the dielectric properties of the saliva samples. The eXtreme Gradient Boosting (XGBoost) algorithm based model is then trained upon these properties to detect the presence of COPD with an accuracy of 91.25%. Porieva et al. [68] used a dataset of 296 lung sounds representing 3 classes of normal, bronchitis and COPD. Authors extracted different features from the sound recordings and used a combination of ML models to achieve an overall accuracy of 93% for bronchitis and COPD detection. Recent advances in deep learning and computer vision have lead to an emergence of models which can detect pulmonary fibrosis [24], pulmonary arterial hypertension [89], pneumonia [94] using different chest imaging.

2.3 Dermatology

Dermatology is the branch of medicine involving the study and treatment of skin, hair and nails. Visual inspection is one of the essential steps in diagnosing a dermatological problem. The advancements of computer vision has opened up new horizons for the field of AI in dermatology and have led to some of the recent DL models which can provide a diagnosis which is at par with some of the field's leading experts [31,96]. With the help of AI, mobile devices can provide easy and cheap access to high-quality medical diagnosis to the parts of population who were previously left behind [19,98].

Kim et al. [44] trained a Convolutional neural network (CNN) using clinical images belonging to 90 different patients. The CNN was able to detect Onychomycosis with a positive predictive value/negative predictive value of 73.4%/61.5% which was comparable with the results of 5 dermatologists with positive predictive value/negative predictive value of 69.3%/66.7%. EczemaNet [64] is a CNN trained on clinical images to predict the severity and presence of Atopic Dermatitis with a high accuracy. Gustafson et al. [34] proposed a Natural Language Processing (NLP) based algorithm for Electronic Health Record based phenotyping to identify Atopic Dermatitis in adults. Ros-Net [15] is an Inception-ResNet-v2 trained to detect rosacea with an accuracy of 89.8%. AI based solutions for diagnosis of Psoriasis [99], Onychomycosis [44] are also being proposed. Recent advancements in AI in Dermatology will improve the overall well being of global population.

2.4 Neurology and Psychiatry

Neurology is the science of treating and diagnosing the diseases of the nervous system. Early detection of neurological diseases can help in improvement of provided medical care. AI plays an important role in early detection of neurological disorders [8,27,59,73,78,87,91]. Recent studies have aimed for early detection of neurodegenerative diseases using non-coding RNAs and MicroRNAs [29,50,51,117]. AI solutions for early detection of Alzheimer's disease using Electroencephalography (EEG) [83,97] are also being put forward. Liu et al. [48] proposed a new method which uses speech data to extract spectrogram features to detect Alzheimer's disease. Recent studies have tried to exploit gait for early detection of Parkinson's disease [5,13]. Several DL based solutions have also been proposed which can help in accurate and precise detection of brain hemorrhage in brain CT images [16,40]. Dammu et al. [26] developed an ML model to classify Autism Spectrum Disorder with an accuracy of 73.6% using the resting state functional magnetic resonance imaging (rs-fMRI).

Psychiatry is the branch of medicine associated with the diagnosis, prevention and treatment of mental disorders. Diagnosis of mental illness is an inaccurate and challenging process where a psychiatrist or psychologist tries to evaluate a patients mental health. A large part of the global population does not have access to good psychiatric diagnosis. WHO estimates depression alone affects 5% of the worldwide population, and early detection of depression can make enormous improvements in its medical treatment. AI based depression detection models are being deployed, which use NLP and emotion detection to detect potential patients of depression from their social media feeds [7,28,37,61]. Sato et al. [76] developed ML model to detect people susceptible to major depression using the functional magnetic resonance imaging (fMRI) data. Schizophrenia (SCZ) affects 20 million people worldwide and early detection can help in providing patients with better medical care. ML and DL models are being developed to detect SCZ using the EEG signals [21,116], genomic data [95] and fMRI data [86] for early and accurate detection of SCZ.

2.5 Oncology

Cancer is the second leading cause of death and led to one in six deaths in 2018. Oncology is the branch of medicine associated with the treatment of cancer. AI can play an important role in early and accurate cancer diagnosis. Mobile devices equipped with AI can provide cheap and easy access to remote population [30]. Esteva et al. [31] trained a deep Convolution Neural Network (CNN) on a dataset of 129,450 clinical images to detect skin cancer. The CNN was able to achieve performance on par with 21 board-certified Dermatologists. DL models are being proposed which can detect and classify brain cancer [20,101], breast cancer [43, 100] and renal cancer [90] from radiological and histopathological images. Whole genome sequencing data is also being used to train ML models which can enable early detection of different cancers [22,103].

3 AI in Medical Prognosis

After successful diagnosis of a patient's underlying condition, health professionals move on to determine their prognosis. Medical prognosis refers to the process of predicting or forecasting the expected developments and even the outcome of a medical condition for a given patient. Determining an accurate prognosis can be very difficult due to the various factors involved. Healthcare professionals look at factors like disease progression, patient's current health and patient's medical history to determine a suitable prognosis. Recent developments in ML and DL in the healthcare industry has helped healthcare professionals greatly increase the accuracy and their confidence in their prognosis. In further sub-sections we discuss how AI has helped prognosis prediction in different kinds of studies.

3.1 Cancer Progression Studies

Once a patient is diagnosed with cancer, determining a suitable prognosis is very important as it helps determine the next course of action medically. Cancer is estimated to affect 1 in 10 people on average in the USA [81], making the task of predicting cancer progression very important. Nie et al. [60] developed a 3D deep learning framework to automatically extract features from pre-operative multi-modal images like MRI, fMRI, DTI of high-grade glioma patients (i.e., patients suffering from a type of brain tumors), achieving accuracies as high as 89.9%. CNNs are being used to segment a brain tumor from healthy tissue, once the tumor data is extracted, regression is used to predict the number of days of overall survival [38]. Boeri et al. [17] built an ML model to predict outcomes after surgery for breast cancer patients with an accuracy of 95%. Using various deep learning techniques, survival prediction for Non-small cell lung cancer (NSCLC) is being predicted with good accuracy [47,114]. Tang et al. [92] came up with a novel approach for predicting prognosis of Kidney renal clear cell carcinoma (KIRC). Using lasso regression, a prognosis model on the basis of methylation-driven genes was developed. The survival rates of patients were then predicted using both clinical information and the methylated prognosis model, finally giving a C-index value of 0.838 for the test data. Instead of targeting a specific type of cancer, there has been research using multi-modal data for pan-cancer prognosis. These papers make use of DL techniques on histopathology slides and other clinical information to finally predict single cancer and pancancer overall survival [23,82].

3.2 Mortality Prediction Studies

Mortality prediction refers to the process of predicting the risk of a critically ill patient's mortality or death. Building an accurate mortality predictor using AI can assist physicians perform appropriate clinical interventions for critically ill patients, thus helping them improve the patient's medical care.

Kong et al. [46] were able to use ML to predict the mortality of sepsis patients in the ICU with moderate success. They built four different kinds of machine-learning based classifier models and trained them on the medical information mart for intensive care (MIMIC) III dataset. They found the gradient boosting machine (GBM) performed the best, giving an AUC of 0.845. Using gradient boosting, Parikh et al. [66] were able to predict 6-month mortality for patients with cancer successfully with an AUC of 0.87. Studies of mortality prediction is also being done for different kinds of cancer specifically like advanced hepatocellular carcinoma (HCC) [52] and metastatic colorectal cancer (mCRC) [74].

The need for calculating mortality risk for traumatic patients admitted to the ICU is very high, Servia et al. [79] conducted a series of experiment using the RETRAUCI database which is the national trauma registry of 52 Spanish ICUs from the period of 2015–2019. The 9 different ML models they developed used a set of variables derived from the deviation of both physiological and anatomical parameters to predict the death risk of a given traumatised patient. Elderly trauma patients generally have a very high risk or mortality, Morris et al. [58] present a set of novel outcome scores, quick elderly mortality after trauma (qEMAT) score and a full elderly mortality after trauma (fEMAT) score, for predicting mortality of elderly trauma patients. They achieve an AUC of 0.84 for the qEMAT and 0.86 for fEMAT.

Stillbirth can be defined as death of a fetus after 20 or 28 weeks of pregnancy. It is a devastating outcome which accounts to two-thirds of perinatal mortality or live-born children who are yet to complete 7 days of life [32,57]. Using a combination of features like current pregnancy complications, congenital anomalies, maternal characteristics, and medical history, researchers were able to use regularised logistic regression, decision tree based on classification and regression trees, random forest, extreme gradient boosting, and a multilayer perceptron neural network which could predict the risk of stillbirth with mild success, i.e., the best performing classifier XGBoost was able to predict 45% of stillbirths among all women in the dataset [55].

Mortality prediction studies in the field of cardiology has been very active, as cardiovascular diseases account for a large amount of deaths worldwide. Adler et al. [1] trained a boosted decision tree on a cohort of 5822 hospitalized patients with Heart Failure (HF). Using eight key variables the model was able to give a risk score with an AUC of 0.88. Wang et al. [108] proposed a feature rearrangement based DL system for heart failure mortality prediction, which works well even on imbalanced datasets. The researchers also propose a method called Feature rearrangement based convolutional layer, where they show that the order of the input features is also essential for the convolutional network. Numerous studies on the risk stratification and mortality prediction for COVID-19 patients have been reported in the last one and a half years, which are discussed later.

4 AI in Medical Treatment

In the previous sections we discussed how AI has greatly impacted the way healthcare professionals accurately diagnose and give prognosis to patients. In this section, we will look at how AI techniques like ML and DL have helped improve the quality of the treatment they provide to their patients.

The development of a emergency department (ED) triage systems that are able to differentiate patients according to care they need remains a challenging task. Raita et al. [70] were able to build a deep neural network to predict if patients coming to the ED were critically ill with an AUC of 0.86. As the leading cause of mortality and morbidity, CVDs are very time sensitive in nature, especially if the patient suffering from it is admitted to the ED. Using data from about 17,661 ED patients with suspected CVDs, researchers used a set of ML models like multinomial logistic regression, extreme gradient boosting, random forest and gradient-boosted decision tree to train on 80% of the data, keeping the rest for testing. They achieved AUC of 0.937 for XGBoost, 0.921 for gradient-boosted decision tree, 0.919 for random forest and 0.908 for multinomial logistic regression [39]. Klang et al. [45] developed a novel prediction model to find patients in who require head CT exam during Emergency Department (ED) triage. Using a gradient boosting model with a dataset containing 595,561 ED visits, the model showed an AUC of 0.93, with sensitivity of 88.1% and specificity of 85.7%.

AI in robotics has greatly influenced the healthcare industry, we can see that even though AI controlled robotic systems are used proficiently in healthcare laboratories and for manufacturing healthcare equipment with precision [110], it's adoption into mainstream medical practices like surgery has been scarce. Minimally invasive surgery is a great alternative to open surgery options as it reduces surgical trauma and eases post-surgery rehabilitation, but it comes with its own set of disadvantages as surgeons now need to handle a confined work space, loss of depth perception, and compromised hand-eye coordination. There has been console operated robotic systems, like the da Vinci surgical system which is able to perform minimally invasive surgery by replication the hand movements of a surgeon with high precision [33]. Concentric Tube Robots (CTRs) which are a special class of continuum robots (i.e., a type of robot characterised by infinite degrees of freedom and number of joints [84]) has shown great potential for minimally invasive surgery due to its miniaturization potential and maneuverability [4].

The advent of AI in healthcare has also come as a boon for hospitals themselves. Re-admission in hospitals is generally defined as admitting a patient again within, generally, 30 days of initial admission. Ajay et al. [2] showed the cons of re-admission in hospitals and proposed how it can be prevented using ML techniques. Vivanco et al. [102] used ML techniques to identify patients likely to overstay in hospitals, these patients are partly responsible for high waiting times and bed shortages in the hospital. Using a decision tree classifier, they were able to achieve a F-Measure of 0.826 for patients at a tertiary teaching hospital and an F-Measure of 0.784 at a community hospital. Yala et al. [112] built a classifier to parse classical breast pathology reports automatically by extracting pertinent tumor characteristics into readily available data with an average accuracy of 97% of individual categories.

Hypoxaemia is the condition where there is an abnormally low concentration of oxygen in the blood. Researchers were able to use a ML based system to predict the prevention of hypoxaemia during surgery. They were effectively able to double the rate of prediction of hypoxaemia by anesthesiologists from 15% originally to 30% with the use of their system [53]. Wijnberge et al. [111] used a ML algorithm that predicts hypotension during surgery in combination with personalized treatment. Hatib et al. [35] built a custom ML based algorithm to predict intraoperative hypotension, they were able to achieve a sensitivity of 88% and specificity of 87% 15 min before a hypotensive event with an AUC of 0.95.

5 AI in COVID-19

Coronavirus Disease 2019 (COVID-19) is an infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Virus. The outbreak of COVID-19 originated from Wuhan, China and rapidly spread across the world, bringing the global population to a standstill. Severe cases of COVID-19 can lead to serious respiratory disease and pneumonia, which might even lead to death. By the end of October 2021, WHO has confirmed over 4.9 million deaths due to COVID-19. AI interventions can help in controlling the pandemic. AI models are being used to quickly and accurately identify individuals who are not wearing face masks [12,49]. COVID-19 is an infectious disease that spreads very rapidly and poses immense pressure on the existing health infrastructure of the world. Early prediction of an upcoming surge in the COVID-19 positive cases can help the authorities in taking proactive measures that can save thousands of lives. Researchers have developed AI based models for epidemic waves forecasting [10,67,107]. These models can predict the approximate time and intensity of the forthcoming surge of positive cases. Several prognostic and diagnostic applications of AI for COVID-19 are also being developed, proving the immense significance of AI in this fight.

5.1 AI Based COVID-19 Diagnosis

Early detection of COVID-19 is an essential step to stop the spread of the virus. Several studies tried to use AI based solutions to help in accurate and fast COVID-19 diagnosis. Many studies trained ML models using chest X-rays [11,71,105], while others tried to exploit the chest CT images [14,42] for the early detection of COVID-19. Although radiological imaging based solutions tend to perform well, they are expensive and complex. Some studies proposed using cough or respiratory sound recordings for COVID-19 detection [56,62,63]. Aly et al. [9] used a dataset of 1299 sound samples to train an ML model that detected COVID-19 positive samples with an AUC of 0.96. Zoabi et al. [118] proposed an ML model trained on records of 51,831 individuals. The model could detect COVID-19 positive cases with a high accuracy by just using the symptoms and basic patient information like age and sex.

5.2 AI Based COVID-19 Prognosis

COVID-19 has posed an unprecedented pressure on global health infrastructure due to the enormous inflow of patients demanding medical care. In times of distress, efficient utilisation of critical resources like oxygen and ventilators becomes an important step, which, if not appropriately enacted, can lead to the deaths of many. The efficient prognosis of COVID-19 patients can help in the early identification of high-risk patients. Authorities can then provide preferred medical care to individuals who stand a chance of developing severe complications, which might help in saving thousands of lives. Many AI solutions for early and quick COVID-19 prognosis are being developed. Wang et al. [106] proposed ML models based on clinical and laboratory features to predict mortality of COVID-19 patients with an AUC of 0.83. Bolourani et al. [18] developed an ML model that utilised features like age, respiratory rate, serum lactate to predict respiratory failure with an accuracy of 91.9%. ML models to predict mortality and severity of patients using chest X-rays and CT scans have also been proposed [25,54].

In further sections, we will look at two different COVID-19 risk stratification and mortality prediction studies to get an in-depth understanding of the research in the domain of AI for COVID-19.

5.3 Machine Learning Based Clinical Decision Support System for Early COVID-19 Mortality Prediction

Karthikeyan et al. [41] proposed an ML model to predict COVID-19 patient Mortality. The model uses a combination of five readily available features: neutrophils, lymphocytes, lactate dehydrogenase (LDH), high-sensitivity C-reactive protein (hs-CRP), and age to predict mortality with an accuracy of 96%. Various ML models like Support Vector Machine, XGBoost, random forests, logistic regression, neural network and decision trees were trained and tested to get the best performing model. The neural network performed the best with an ability

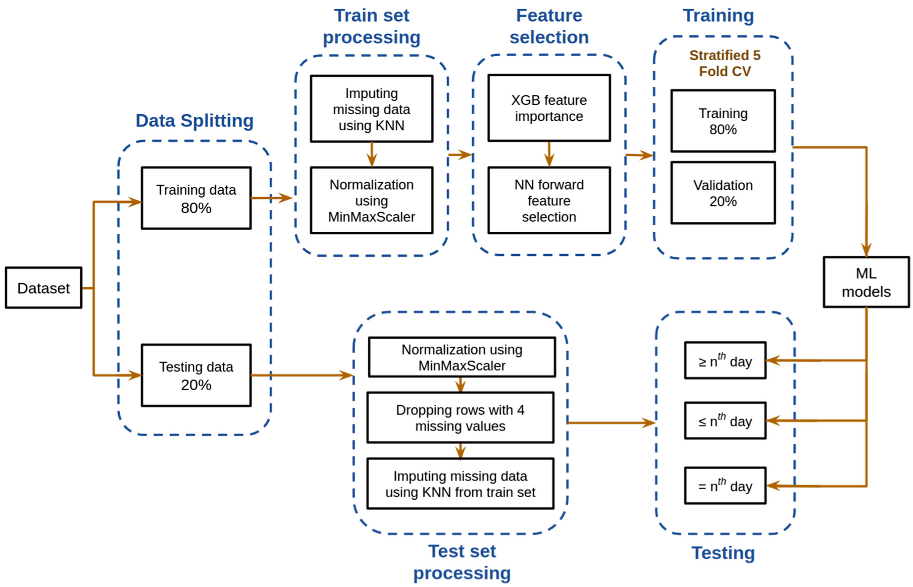

Fig. 3. ML pipeline used by Karthikeyan et al.

to predict mortality with an accuracy of 90% as early as 16 days before the outcome. Figure 3 depicts the ML pipeline used for the study.

For the study, the authors used the publicly available dataset provided by Yan et al. [113]. The dataset is a time-series data of 375 COVID-19 patients from Tongji Hospital in Wuhan, China. It contains the information corresponding to 74 biomarkers and data sample time, admission time, discharge time and outcome. After data cleaning, K-Nearest Neighbour algorithm was used to impute the missing values followed by Min-Max scaling. The pre-processed dataset consisted of 1,766 data points coming from 370 different patients. Since the dataset is time series, a single patient had multiple data points corresponding to different days of hospital stay. To ensure exclusive patients for train and test set, authors divided the dataset such that all the data points corresponding to 80% of the randomly chosen patients were considered for the training set while all the data points of the remaining 20% of the patients were considered for the testing dataset. The test set had a balanced distribution, where 56.3% of data points correspond outcome as 'died' while 43.7% data points had 'survived' as the outcome.

After the data pre-processing and data splitting, XGBoost classifier was used to get the relative feature importances of all the available features. The average importance of features was found by taking the arithmetic mean of feature importance of 100 different runs, where each run takes a random 80% of the training data points. XGBoost feature importance produced the list with the top 4 features being neutrophils (%), lymphocyte (%), LDH and hs-CRP.

Later age is added to the top of the feature importance list owing to its ease of procurement. After determining the feature importances, the number of most important features that need to be used to train the ML models must be determined. A neural network with two hidden layers was trained and validated on the training dataset. The AUC after five-fold cross validation was chosen as the evaluation metric to compare the neural network's performance corresponding to the different number of features. Neural network feature selection suggested the combination of the top 5 features, as these features gave the optimum results. Although the top 6 features gave slightly better results, authors felt the increase in performance was not enough to add another feature to the model. Finally, 5 features of age, neutrophils (%), lymphocyte (%), LDH and hs-CRP were chosen as the optimal set of features and were thus used for further analysis.

The selected combination of features is then used to 6 different ML algorithms, namely Logistic Regression, Random Forests, XGBoost, Support Vector Machine, Decision Trees and Neural Network. Extensive hyper-parameter tuning for the Logistic Regression, Random Forests, XGBoost, Support Vector Machine, and Decision Trees was done using GridCV with stratified five-fold cross validation. Adam optimizer with Binary Cross Entropy loss was used to train the neural network consisting of 2 hidden layers and ReLU activation.

Figure 4 shows comparison of overall test accuracy, F1 score and AUC of different ML algorithms used in the study. The graphs suggest neural network performs the best with an overall accuracy of 96.53% (±0.64%), F1 score of 0.969 (±0.006) and AUC of 0.989 (±0.006). Neural network was hence chosen as the ML model for all the further analysis.

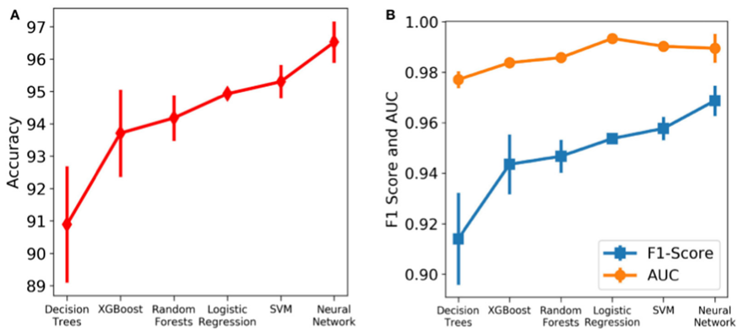

Fig. 4. Comparison of the performance of different ML algorithms. Standard deviation is denoted by the vertical lines.

The authors of the study also tested the model's capacity to predict mortality with respect to number of days to outcome. Figure 5 shows the analysis where model is tested on different datasets varied with respect to different cutoff for days to outcome. For the value of cutoff set as 'n' a new dataset is generated where only the data points which have the number of days to outcome '$\geq$ n' are selected. The Fig. 5 suggests model was able to achieve an accuracy of 90% for cutoff set as 16 days, hence model is able to predict mortality with an accuracy of 90% as early as 16 days in advance to day of outcome.

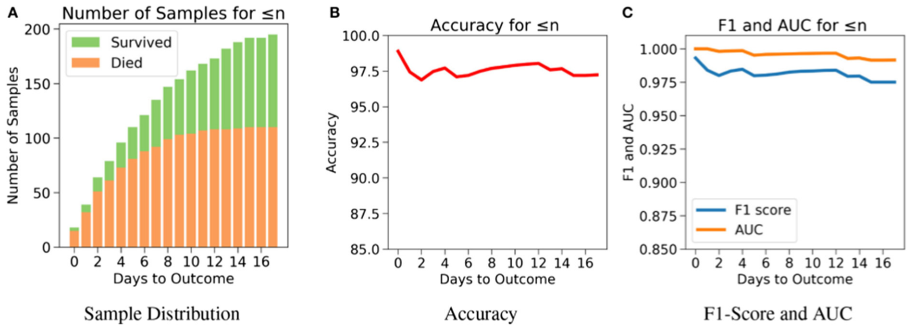

Fig. 5. The performance of neural net on the test data when only data points with days to outcome ≥n are chosen. (A) Class wise distribution of varying dataset. (B) Accuracy of the model with respect to varying dataset. (C) F1-score and AUC of the model with respect to varying dataset.

5.4 COVID-19 Risk Stratification and Mortality Prediction in Hospitalized Indian Patients

Even though studies regarding COVID-19 had been done in the past, analysis of Indian COVID-19 patients was required. Alle et al. [6] conducted a detailed study to understand the COVID-19 disease progression in the Indian cohort. The data for the study was collected from the Max Group of Hospitals, New Delhi, India. The authors developed XGboost based ML model for risk stratification with an F1 score of 0.81, while a logistic regression classifier was used for mortality prediction with an F1 score of 0.71. The study also tried to investigate the differences between disease progression in Wuhan and New Delhi cohorts.

A time-series data of 544 COVID-19 cases was collected by the MAX group of hospitals, New Delhi, between June 3rd and October 23rd, 2020. Patient data was anonymised at the data warehouse of CSIR-IGIB, New Delhi, to ensure patient privacy. The data comprised 357 different biomarkers, including vitals, symptoms, comorbidities, blood biomarkers, and medicines administered. The authors categorised the patients into different risk levels. They created three sets of different labels based on mortality, quaternary stratification and binary stratification. Mortality comprised of outcome labels of died and survived. Quarternary stratification had four outcome labels of home quarantined, hospitalised but not on respiratory support, on respiratory support, died based on patient's severity during the disease. Binary stratification had output labels of mild and severe, where mild risk represented home quarantined or hospitalised patients

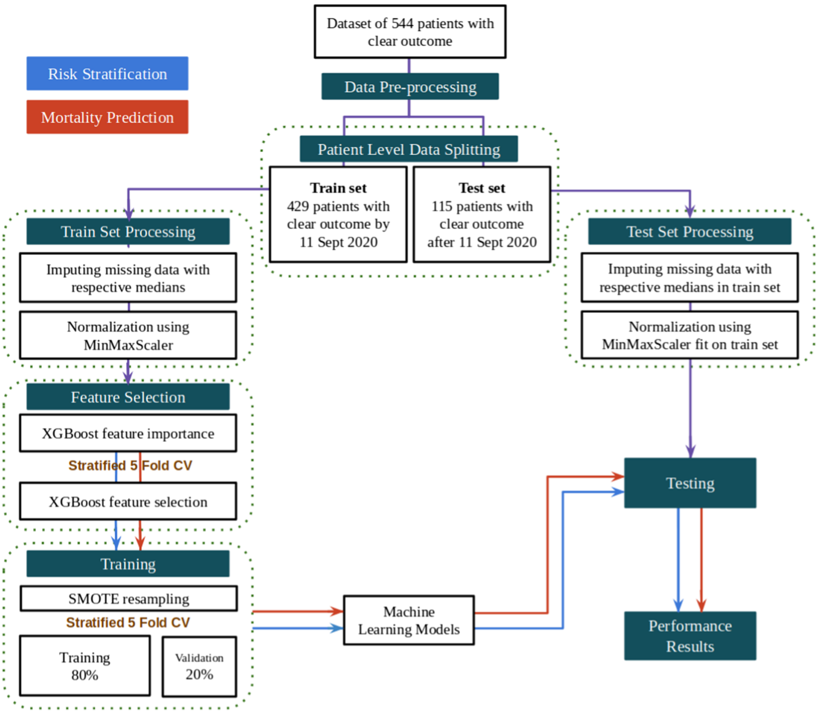

Fig. 6. ML pipeline used by Alle et al.

without respiratory support. The severe risk category comprised patients who were either on respiratory support during their hospital stay or succumbed to the disease.

As the data for the study was a time-series dataset, a single patient had multiple records of data with respect to blood parameters and vitals. For the study, authors considered each blood sample recording as a separate data point. The missing values for a parameter were imputed with the nearest value of the parameter from the patient's past results. All the numerical parameters were scaled within a range of 0–1 using min-max scaler. To ensure patient-level segregation between train and test set, all the 429 patients who had a clear outcome before 11th September 2020 were considered for the training set while the data of other 115 patients was used for the generation of the holdout test set.

Figure 6 depicts the flowchart for ML pipeline. Different sets of features were selected for mortality prediction and risk stratification. These features were then used for training and testing of various ML algorithms. The explanation about feature selection and training is discussed below.

To identify the most important features, the relative importances of all the features were identified using XGBoost algorithm. The number of features to be used for training the ML model was then determined by training XGBoost with different number of features, with features being added in the order of their relative importance. The smallest cluster of features giving the optimal performance was then chosen for model training. To account for high class imbalance of training set, SMOTE algorithm was used for synthetic generation of samples belonging to the minority class. XGBoost, Random Forest, SVM, Logistic Regression based models were then trained for mortality and risk prediction.

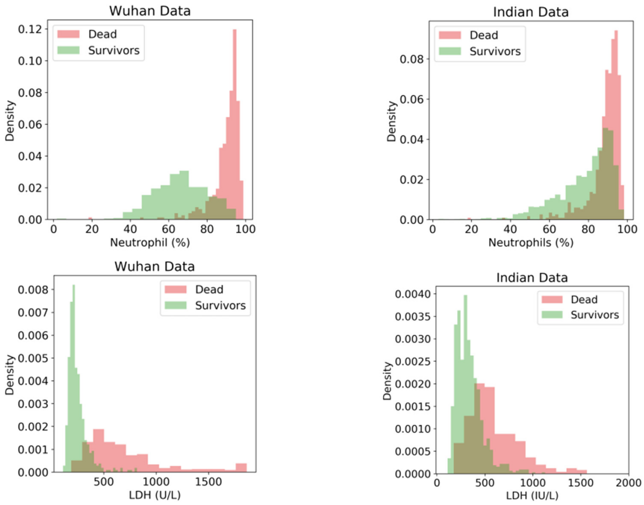

Fig. 7. Density histogram to compare Indian and Wuhan cohort

11 features were selected for the risk stratification task: absolute neutrophil count, LDH, lymphocyte (%), neutrophil (%), record of diabetes comorbidity, ferritin, INR, interleukin-6 (IL-6), oxygen saturation level, absolute eosinophil count and packed cell volume. XGboost algorithm performed best with an F1 score of 0.810 ± 0.01 and AUC of 0.833 ± 0.01. For mortality prediction, a set of 9 features were selected: D-Dimer, Ferritin, Lymphocyte (%), Neutrophil to Lymphocyte ratio (NLR), WBC, Trop I, INR, IL-6 and LDH. Logistic regression performed the best for the task with an AUC and F1 score of 0.927 ± 0.01 and 0.710 ± 0.02.

The authors tried to identify differences between Wuhan and the Indian cohort, for which data provided by Yan et al. was used to understand the disease progression for the Wuhan cohort. Authors plotted density histograms for five different parameters like neutrophil (%), LDH to understand the differences between people who survived and those who did not. From Fig. 7 we can observe that for the Wuhan cohort, the neutrophil (%) and LDH had really high variation between the people who died and those who survived. The Indian cohort did not show such a stark variation.

6 Summary and Outlook

Although AI in Healthcare has shown excellent prospects, it faces many challenges. ML models are data-hungry systems that require enormous amounts of data for training. Healthcare data collection is an arduous task, and often healthcare datasets are inadequate and biased. Data scarcity poses a significant challenge to the success of AI in healthcare. Developing an AI for healthcare solution that generalises well is another challenging task. Often, inadequate and biased training data fails to represent the proper and complete subsample of the data. Healthcare datasets are often plagued with ethnic and racial biases, which pose a severe challenge in the generalizability of the ML and DL models. It is often seen that models trained on the data of the population of one subcontinent fail when tested on data from some other cohort. Under representation of the minority class in the dataset can lead to biased AI models that overfit the majority class. This bias can lead to the seclusion of minorities from the general medical practice. Data privacy is another big hurdle in the success of AI in healthcare. Lack of proper protocols to maintain the anonymity and privacy of intimate health information dissuades patients and hospitals from sharing the data with the researchers. Another big challenge is the lack of interpretability in the developed AI solutions. Most modern ML and DL models are black boxes that take input to produce a quantitative outcome. These black box models fail to explain the reasoning behind the various decisions. This lack of interpretability and generalisability has led to the loss of trust of the medical community in AI. Hesitation from the healthcare industry to deploy and augment AI solutions at the ground level has developed some friction in the growth of AI in healthcare.

Even though many challenges loom ahead of the success of AI in healthcare, we believe in the coming future, AI will play a pivotal role in revolutionising the healthcare industry for good. Cumulative efforts of academia, industry and government authorities might help in the generation of more extensive and unbiased healthcare datasets. Development and training of the AI models which are uninhibited from racial and ethnic biases will play a crucial role in the success of AI in healthcare. Proper protocols and regulations need to be established to dismiss the concerns regarding data privacy and security. Developing trust toward the AI solution is also an essential attribute in the widescale adoption of AI in healthcare. We believe AI would not eliminate the need for human intervention; instead, it will assist radiologists and clinicians in providing more reliable, cheaper and easily accessible medical care to all.

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