Clinical Decision Making and Outcome Prediction for COVID-19 Patients Using Machine Learning

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Abstract. In this paper, we present the application of a Machine Learning (ML) approach that generates predictions to support healthcare professionals to identify the outcome of patients through optimization of treatment strategies. Based on Decision Tree algorithms, our approach has been trained and tested by analyzing the severity and the outcomes of 346 COVID-19 patients, treated through the first two pandemics "waves" in a tertiary center in Western Greece. Its' performance was achieved, analyzing entry features, as demographic characteristics, comorbidity details, imaging analysis, blood values, and essential hospitalization details, like patient transfers to Intensive Care Unit (ICU), medications, and manifestation responses at each treatment stage. Furthermore, it has provided a total high prediction performance (97%) and translated the ML analysis to clinical managing decisions and suggestions for healthcare institution performance and other epidemiological or postmortem approaches. Consequently, healthcare decisions could be more accurately figured and predicted, towards better management of the fast-growing patient subpopulations, giving more time for the effective pharmaceutical or vaccine armamentarium that the medical, scientific community will produce.

Keywords: COVID-19 · Clinical decision making · Machine learning · Patient management

1 Introduction

Several Artificial Intelligence (A.I.) applications on databases of Health Records (H.R.s) in hospitals have already been successfully established [1, 2]. COVID-19 pandemic has revealed A.I. approximations as first-line approaches for early infection detection and appropriate treatment [3–9]. Predictive analytics utilizes approaches to analyze medical information from H.R.s to predict future patient outcomes reducing costs [2, 3, 10, 11].

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When each patient in the critical clinical condition is recognized adequately during hospital admission, they can immediately receive the appropriate treatment without [1, 3, 8, 12]. Early identification with higher accuracy than statistical approaches could further guide clinicians toward immediate intervention [13, 14]. According to several approaches, researchers managed to handle public health surveillance using AI and Big Data which appear to have enormous potential for the management of COVID-19 and other emergencies, and their role is anticipated to increase in the future. These approaches can now be used to track the spread of the virus in real-time, and plan and lift public health interventions accordingly, monitor their effectiveness, repurpose old compounds and discover new drugs, as well as identify potential vaccine candidates and enhance the response of communities and territories to the ongoing pandemic [9, 15, 16]. Based on Decision Tree algorithms, that more clear and easy to be used by the clinicians, our approach has been trained and tested by analyzing the severity and the outcomes of COVID-19 patients, treated through the first two pandemics "waves" in a tertiary center in Western Greece. Data were obtained using a software tool that was running parallel with Hospital Information System. Its' performance was achieved, analyzing entry features, as demographic characteristics, comorbidity details, imaging analysis, blood values, and essential hospitalization details, like patient transfers to Intensive Care Unit (ICU), medications, and manifestation responses at each treatment stage, of the COVID-19 patients finally collected.

Currently, A.I. systems, evaluating images to track the progression of COVID-19 patients, are already helping to identify urgent needs for ICU support [17]. Other approaches estimate individual patient's mortality probability by the use of an ML application on data of three biomarkers, showing more than 90% accuracy [18]. Another application was used to analyze images and then evaluate the infection with high accuracy performance classification [19]. Another ML-based model applying the Decision Tree (D.T.) algorithm used to recognize COVID-19 patients with severe illnesses after hospital admission providing 80% accuracy [20]. According to the patient clinical description at hospital admission, a Deep Learning (DL) approach, which can recognize COVID-19 patients at risk, tested providing accuracy at the level of 90%, respectively [21]. Additionally, according to an interesting approach, a human-machine collaborative design strategy is leveraged to create a human-driven principled network design for the detection of COVID-19 cases only from X-ray images [22]. According to another successful DL approach, recognizing areas with pathological artifacts on Ultrasound images was developed to identify the COVID-19 infection [23]. Other approaches have been discovered to analyze medical images, acquiring a prediction of 95.4% [24]. According to most published approaches, prediction models utilizing A.I. would improve with successive data for diagnosis to treatment, aiming to supplement decision-making by clinicians [8, 9, 13]. Specific patient populations can vary across countries, different institutions, and the ability of a predictive model to "learn" from its local patients provides more benefits than static modeling [3, 12]. Additionally, "best practices" could also be summarized, generalized, and introduced into published guidelines on use. In clinical decision-making, A.I. algorithms already successfully support medical staff, including entrance urgency classification decisions for the optimal use of institutional resources and analyzing the severity of the infection and patient progress [9].

An ML approach could be summarized in 4 general steps including, 1) data validation through preprocessing, 2) mining through output forecasting, 3) pattern/knowledge extraction through post-processing, and 4) final statistical evaluation and clinical Interpretation, usually in collaboration, with healthcare staff. This procedure is fulfilled for unsupervised or supervised learning approaches, dealing only with random data training and test sets targeting the highest possible accuracy levels (Fig. 1). After data analysis and interaction with medical experts, successful generalizations could be compared to published guidelines that usually do not consider workforce and appropriate resources for organizational modifications. ML approaches are well recognized for constructing risk models, selecting the predictors automatically from numerous features, minimizing random or systematic errors, and resulting generalizations [9, 11, 18, 19].

In the present paper, we describe an A.I. system incorporating ML in medical history and data that correlates, investigates, clarifies, evaluates, and saves clinical decisions, to D.T. structures [9]. Our approach first aims to reveal features for fast Triage-Classification based on minimum possible available tests, shortening life-threatening waiting times at emergency departments or Emergency Departments, which will be later enriched with other findings, as physical examination and laboratory results also be evaluated [24].

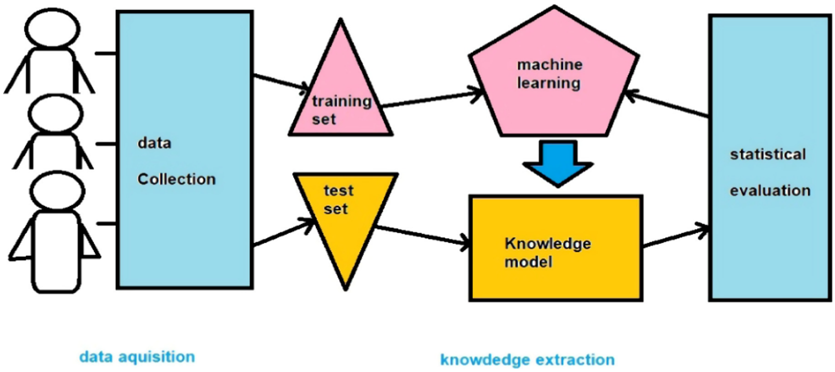

Fig. 1. Knowledge discovery from data collectors to new guidelines for new patients specifically during new or not well defined diseases

After severity estimation, secondly aims to achieve a patient-specific diagnosis, possible transfer to ICU, and evidence-based treatment planning, the use of the history and clinical examination information is expected to reach the acceptable accuracy in terms of risk assessment for the severity classification and subsequent first line life support to be followed with proper hospitalization. Based on laboratory tests, the possibility of achieving the diagnosis and appropriate treatment or other decisions as for secondary transfer to ICU according to patient response, the systems provide a probability for outcome prediction. The system finally aims, by improving class correlation of the parameters and mining process in ongoing clinical and laboratory data, the successful patient management according to available resources. The treatment response of each patient and relevant data consists of a new set of parameters at each specific step of the hospitalization period and characterize the current pathology of the patient accompanied with predictions. The clinicians just enter the patient's medical information in terms of electronic forms as well as examination and treatment data at each stage. It is designed to be globalized, through natural text analysis, along with the data mining process, as it will be implemented with Natural Language Processing applications (Fig. 2). In the next sections, the pilot's successful implementations are presented.

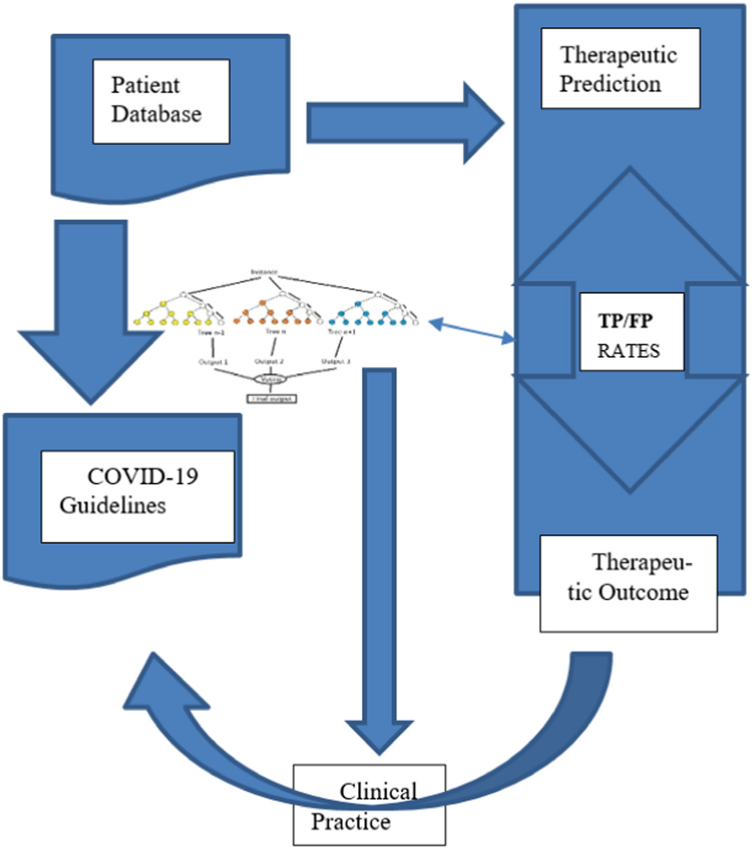

Fig. 2. Global system description and working flow for machine learning using decision trees classifiers for COVID-19 patients' management

2 Materials and Methods

Existing data mining tools provide the implementation of different mining algorithms. Most of them are free, open-source, easy to use software platforms. For our pilot implementation was used WEKA has been written in Java and is running on almost any operating system. WEKA collects A.I. algorithms and data preprocessing tools for ML and supports evaluating, visualizing, and preparing the input data [25–27]. It also supports different learning algorithms such as classification, clustering, and regression. D.T.s are classification algorithms functioning to predict an output based on decisions extracted from the input data mapped in tree structures [9, 22–25]. System's performance was achieved, analyzing several entry features, as demographic characteristics, comorbidity details, imaging analysis, blood values, and essential hospitalization details, like ICU transfers, medications, and manifestation responses at each treatment stage according to the patient database. Data was obtained with the use of specific software tool developed to access patient records from COVID clinics of during the pandemic "waves" in a tertiary center in Western Greece (University Hospital Patras University). A script was running parallel with Hospital Information System and every time that a new patient was characterized as COVID-patient a new record was developed in a parallel database including all appropriate useful information for our approach and finally the outcome of the hospitalization. Patient records were accessed after Hospital's Scientific Bioethics Committee Approval.

The proposed approach, that was based on D.T.s, and has been trained and tested by analyzing the severity and the outcomes of the 346 COVID-19 patients hospitalized through the first two pandemics "waves" Western Greece, as was described from the European Mortality Monitoring Activity database, supported by the European Centre for Disease Prevention and Control (ECDC) and the World Health Organization (WHO), in Patras University Hospital [28]. D.T.s additionally selected as the most acceptable form of knowledge representation for our clinicians. Urgency classification, ICU transfer risk, and final treatment outcome were the outputs at this stage of implementation (Table 1). First step was the preprocessing of patient data as there were detected no missing values. Data records were randomly partitioned to train (66%) and test (34%) sets. The division process was repeated for a number of times in order to avoid over-fitting. For the classification were used different classifiers but the best performance was obtained with *J48* (with Reduced Error Pruning enabled), as well as *Random Forest* (ensemble) classifiers, according to their total accuracy performance.

Treatment response as part of a set of parameters at each specific step of the hospitalization period accompanied with predictions that could be relevant in the management and targeted treatment of patients, with the potential to modify improving outcomes additionally to postmortem findings [29–31].

Statistical ranking to the output parameters was considered for the system's inputs to be at minimum performing the highest possible accuracy (Table 2). For our implementation, only several (up to 15) parameters were used for each patient, from the total (nearly 25) features and text records stored in H.R.s of Patras University Hospital. Features as patient sex, age, comorbid, grading of illness severity, blood test results, fever, oxygen saturation, heart rate, radiographic examination results, type of medication, days in each department or clinic, and treatment output are only a part of medical parameters that usually are recorded during hospitalization and stored in H.R.s.

According to our team physicians' advice, we did not take into account patient deaths after ICU transfer, but only before, because of a high frequency of nosocomial infections, equipment malfunction incidents, as well as the low learning curve of medical and nursing staff that was enrolled in emergency and ICU units in Greece, last year. Available

Table 1. Hospital patient data collected from digital health record database

Men	196		
Women	*150*		
Age yr.	*61.85 (16 – 97)*		
Comorbid	*206*		
Days in Hospital	*Mean 10.4 (0-90)*		
Severity classification	*60 low severity*	*243 medium severity*	*43 high severity*
ICU transfer	*5 patients treated*		
Treatment Outcome	*15 patients from 1^{st} wave died*	*38 patients from 1^{st} wave treated after hospitalization*	*17 patients from 1^{st} wave immediately exited*
	*49 patients from both waves died**	*118 patients from both waves treated after hospitalization*	*174 patients from both waves immediately exited*

**Before or after ICU transfer*

Table 2. Part of the database's parameters after preprocessing with their values for patient management.

- *Sex with values {male, female}*
- *Age with numeric values*
- *Days In Hospital with numeric values*
- *Comorbid {yes, no} as well as*
- *Comorbid type with the corresponding values*
- *Blood_test results add to the percent of abnormal values*
- *Radiographic_Examination results with {free, spotted, diffused} values*
- *Medication type of specific medicines or combinations used*
- *Grading at emergency Unit with {low, mild, severe, urgent}*
- *Result {exit, hospitalization in COVID Clinic, transfer to ICU, death}*

data, including the "*third wave*" of COVID-19, is under consideration to calculate other parameters as patient risk per unit and total departmental or institutional performance.

3 Results

3.1 Experiments

Several available algorithms were used to succeed the higher possible accuracy of the system predictive model. Improved settings were used for optimization for improved results (Table 3). First, the system used for the 1st "wave" of patients performing data mining approach (75 patients). Finally, with the use of the same input parameters second "wave" data were analyzed using a mining approach (346 patients).

Table 3. Classification results for patient management prediction with the use of random forest ensemble classifier

Average evaluation	*True positive rate*	*Fault positive rate*	*Precision*	*Recall*	*F measure*	*Correctly classified percent on test set data*
Severity classification	0,92	0,18	0,93	0,92	0,92	**92%**
ICU transfer	1	0	1	1	1	**100%**
Days in hospital	1	0	1	1	1	**100%**
Treatment outcome	0,97	0,018	0,97	0,97	0,97	**97%**

The present ML was performed for patient outcome prediction for both pandemic waves. Initially, the system chooses the most appropriate features to be used for prediction according to their statistical ranking. The initial evaluation dealt with patient severity grading for proper Triage-Classification at emergency units. The most important parameters are usually on the top (root) of each D.T. For example, for urgency classification, only Radiographic evaluation (with free, spotted, diffused values), secondary supported with age and sex of the patient. The second evaluation dealt with patient transfer to ICU immediately from hospital emergency unit and hospitalization duration.

3.2 Results

Consequently, for ICU transfer decisions, essential features are urgency (from previous evaluation), comorbid and secondary age, and sex of the patient. Only for days of hospitalization prediction type of medication strategy was revealed as an important parameter, with secondary blood test results at each stage. Finally, for treatment outcome, the critical features are urgency (from previous evaluation), and only secondary blood test results, sex, and age features. The final results are very encouraging for our approximation, and the D.T.s are readily accepted by medical staff. The system proved 92% for triage classification, 100% for identifying patients that will need ICU transfer, 100% for total days of hospitalization, and 97% accuracy for the outcome, predictions. Consequently, if emergency units would like to identify the severity of the disease, physicians could safely evaluate all the X-ray imaging of each patient and later during hospitalization, only a part of available information to decide for further manifestations, transfer to ICU, etc. Furthermore, knowledge extraction revealed D.T.s were trained for future use of new patients by the medical staff (Figs. 3, 4 and 5).

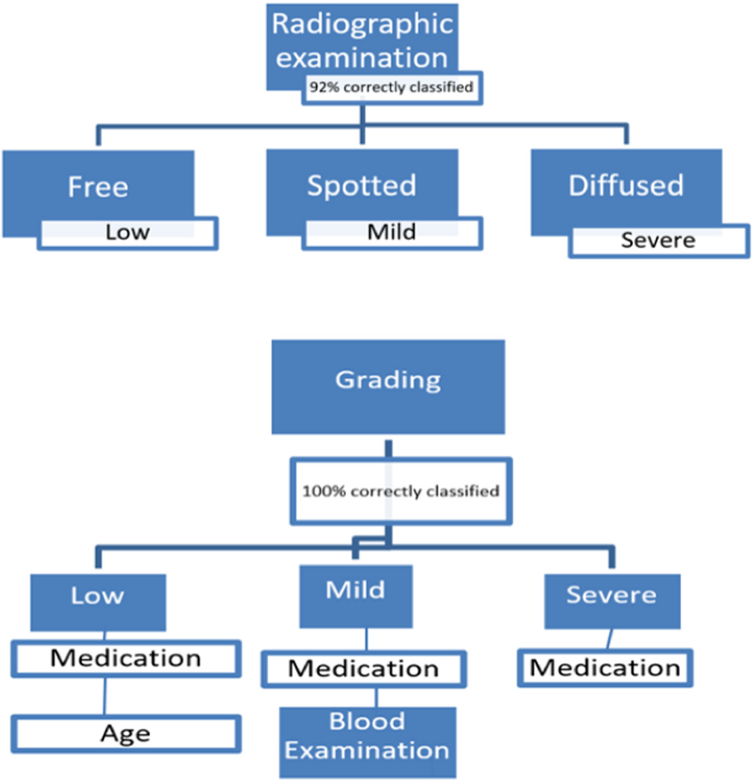

Fig. 3. Classification tree for Urgency evaluation at the emergency unit with the use of J48 classifier.

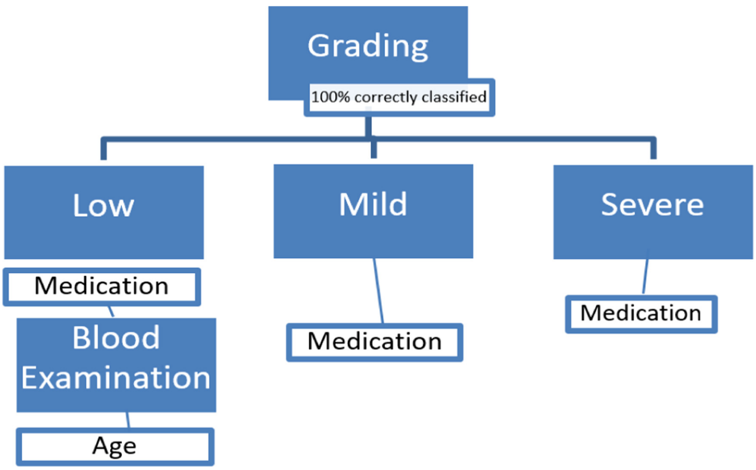

Fig. 4. Classification/decision tree for ICU transfer decision (part) with the use of J48 classifier.

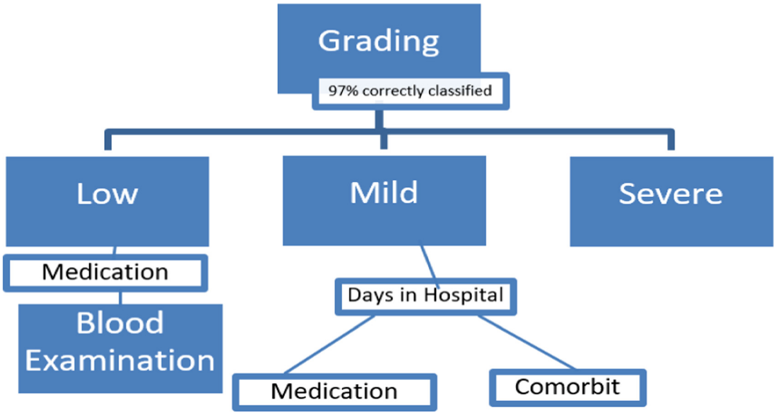

Fig. 5. Classification/decision tree for patient outcome (part) with the use of J48 classifier.

4 Discussion

Currently, pandemic waves push medical staff and infrastructures to their limits worldwide. Consequently, healthcare decisions can be more accurately figured and predicted, towards better management of the fast-growing patient subpopulations, giving more time for the effective pharmaceutical or vaccine armamentarium that the medical, scientific community will produce. According to our results, healthcare decisions could be accurately figured and predicted, towards better management of the fast-growing patient subpopulations, giving more time for the effective pharmaceutical or vaccine armamentarium produced by the medical, scientific community [9, 11]. Most published ML applications are used for detection/monitoring, prevention/treatment, and pathogenesis analysis of this virus [31]. More efforts have been focused on drug repurposing, analysis of dissemination patterns, and clinical radiographs. As all experts in biostatistics know, statistical approaches are affected not only by the selection of actual data that has been collected but also by "a priori" assumptions or guidelines of the researchers behind the experimental protocols [10]. Thinks are more difficult when an unknown disease with a fast-growing population appears. Similarities with past or early observations of an unknown fast-growing patient population usually cause delays or even incorrect treatment strategies targeting, for example, mostly to older men with comorbid, far from reality. This clinically "foggy" period can be easily understood, considering that our sample of the initial 75 patients hospitalized during the first pandemic wave was used a wide spectrum of available medications. This situation that lasted some months additionally overlapped medical or organizational errors revealed later during the second wave and at the beginning of the third wave, causing additional cost to our heavily threatened health system [18, 20]. ML methods can provide solutions for patient management support, which are not possible by the conventional statistical approaches [9]. Giving models of the dissemination pattern of the pandemic spread and its transmission processes, SVR, LSTM, and optimization problems, among other models, have been frequently used to investigate the COVID-19. Other models have been already effectively used to identify COVID-19 patients with the potential to develop more severe illnesses based on evaluating clinical information.

The proposed system will support clinicians for better services, improving patient outcomes, revealing faster diagnosis, reduce delays or mortality and give time for alternative medication. In addition, some algorithms can be employed to identify the patient possibility of severe illness by viruses [13]. Finally, for future work, our system could include an additional system for automatic detection of the disease according to automatic medical imaging analysis [32, 33].

5 Conclusions

New directions through managing the COVID-19 pandemic could include scoring the performance of the health care system and staff and adaptation to published protocols formulated after clinical research. An A.I. system could also be adopted using ML to estimate individuals' performance in working with patients that have been hired to work in the high-risk working areas as in ICUs. Currently, the system aims to support facing the third pandemic wave and is intended to face other types of respiratory pandemics in the future. Its' early-stage performance supports the importance of unsupervised ML in medical or other early-stage information databases to unknown infections. A.I. systems can be developed to provide managing decisions in such pandemics providing new directions for clinical research [31].

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