**INTRODUCTION**

Artificial Intelligence has several branches including machine learning, expert systems, fuzzy systems, metaheuristic algorithm, etc. In machine learning, training examples are given to the model and the experts’ opinions are used for making a decision. Machine learning has been used in different fields of engineering and science. In a recent application, a machine learning based scheme is proposed for locating faults in power systems leading to a fast recovery time in the system. Another branch of Artificial Intelligence called metaheuristic computations provide solution to an optimization problem, especially with incomplete or limited information computation capacity. These algorithms have widely been used in different fields of science and engineering. In reference, SFS metaheuristic algorithm is combined with a decision making strategy which is proved to be an intelligent approach for coordinated management of energy systems. As another branches of artificial intelligence, the expert systems uses a wide range of specialized knowledge, as a method, to solve problems. The expert refers to someone who has experience and skill in a certain field and in a nutshell, is sophisticated. Hence, the expert has a certain knowledge or skill that is unknown or inaccessible to most people. The expert is capable of solving issues that are not solvable by others, or offers the most effective (and not necessarily the cheapest) solution to that problem. The expert systems, firstly developed in the 1970s, only had sophisticated knowledge. However, the new expert system inNowadays referred to any system that utilizes expert system technology that can include specific languages of expert systems, programs and hardware designed to help develop and implement expert systems. The knowledge, embedded in expert systems, can include experience or knowledge accessible through books, journals, and scientists. The terms expert system, knowledge-based system, or knowledge-based expert system are used interchangeably. Most people use the term expert system because of the brevity; while there may be no experience and skill in expert system and they can only include general knowledge. Several applications of expert systems in business, medicine, science and engineering, or books, journals, seminars, and software products dedicated to expert systems are all evidences to the success of these systems. Very similar to expert systems, Fuzzy systems also store experts’ knowledge and use it in their systems to process the input and generate outputs. In, a Fuzzy system is used to control two state variables using some membership functions that are defined by experts. The method is successfully implemented in a hardware setup and promising results are obtained. In a Fuzzy Cluster Means (FCM) method for the diagnosis of Liver Disease (LD) which is global health problem, was presented. FCM plays an important role for evaluation, classification, and matching for more than one class of LD.

The liver is a vital organ existing in all human being; there is presently no way to restore the lack of liver function. Cases of patients with LD continues to rise because of excessive drinking of alcohol, breath of destructive gases, intake of contaminated food and drugs that is widespread global.

In the changing atmosphere of health care and information technology, there is an increasing opportunity for the use of data science and technology to personalize health care and improve delivery of patient care. At its core, machine learning (ML) utilizes artificial intelligence to generate predictive models efficiently and more effectively than conventional methods through detection of hidden patterns within large data sets. With this in mind, there are several areas within hepatology where these methods can be applied. In this review, we examine the literature of the already-tested applications of ML in hepatology and liver transplantation (LT) medicine. We provide an overview of the strengths and limitations of ML tools, and their potential applications to both clinical and molecular data in hepatology. Artificial intelligence (AI) and ML algorithms have been increasingly applied to questions in hepatology in recent years. Electronic health records (EHRs) are a rich source of data, as are registries and clinically annotated biobanks. Efforts such as The Cancer Genome Atlas continue to produce layers of molecular data. The large proportion of the research literature in hepatology stems from the use of traditional biostatistical methods. These hypothesis-driven studies consist of examination of preselected variables and their impact on liver-related outcomes such as cirrhosis, liver cancer, transplantation, and mortality. These studies have included prediction models that have revolutionized clinical practice in hepatology. ML is an unbiased approach that stands in complete contrast to this, using any number of variables to permit data-driven discovery. This hypothesis-free approach has led to identification of similarities and differences in clinical phenotypes, systematization of patient diagnosis, elucidation of new therapeutic targets, insights into the mechanistic basis of disease, and delivery of a data-driven, precision medicine approach. Liver diseases are complex and heterogeneous in nature, developing under the influence of various factors that affect susceptibility to disease. These include sex, ethnicity, genetics, environmental exposures (viruses, alcohol, diet, and chemical), body mass index (BMI), and comorbid conditions such as diabetes. Various types of complex data are generated in hepatology practice and research that could benefit from AI-based approaches: EHR data, transient elastography, other imaging technologies, histology, biobank data, data from clinical trials, clinical sensors, wearables, and a variety of molecular data (genomics, transcriptomics, proteomics, metabolomics, immunomics, and microbiomics).

In supervised learning, tools learn to output the correct labeled target, which can vary from detection of underlying liver disease in patients, early detection of nonalcoholic fatty liver disease (NAFLD) with images, or better identification of patients with primary sclerosing cholangitis (PSC) at risk for hepatic decompensation (HD).

ML in the supervised setting encompasses tools that can uncover nonlinear patterns in the data to predict these various output targets. A simple extension of Bayes’ theorem, naïve Bayes classifiers predict class labels by computing the likelihood of the observed features under each class and returning the class with the maximum likelihood. k-nearest neighbors (KNN), on the other hand, determines the output based on the value of classes of the K-nearest training samples. Another example of ML classifier is support vector machine (SVM), which finds the optimal divisor among classes in the kernel-transformed hyperplane of the data.KNN and SVM have been used by Kim et al. to identify a molecular signature for hepatocellular carcinoma (HCC). Simple models like a decision tree can also be used. A decision tree is similar to a flowchart arranged in a tree-like structure, where each step of the flowchart denotes a test on one or more features, and by following the flowchart, one can classify each sample. Predictions from multiple unique decision trees can be used together in an ensemble. These ensembles are called random forests (RFs) and gradient boosting machines (GBMs). This has been used to identify PSC patients with higher risk of HD. RFs use an ensemble of deep decision trees that are trained on different random subsets of the training data in parallel. The final output of the method corresponds to the mode of all the decision trees’ results. GBMs, on the other hand, use shallow trees with only one or two levels. These shallow trees are considered to make predictions that are high in bias and low in variance, as opposed to a full-grown tree used in RFs that are low in bias and high in variance.

Deep neural networks (DNNs) have been a tremendous breakthrough in ML, enabling machines to learn patterns of data by modeling them through a combination of simple nonlinear elementary operations. Neural networks have been applied to predict 3-month graft survival and assist with donor-recipient matching for patients with end-stage liver disease as well as predicting the presence of liver disease from imaging.This can be further extended into convolutional neural networks (CNNs) and recurrent neural networks (RNNs), which handle local structures and sequential data consecutively. Local structure can be important in data (e.g., in images), and it is important to incorporate this existing structure. CNNs use multiple convolution filters, learned by the network, at different layers to aggregate information from neighboring pixels. RNNs allow temporal dependability across different time points by modifying the architecture to receive input from its past state. The power of neural networks (NNs) can be further applied into survival analysis and time-to-event predictions, where NNs can be used to predict risk function or even the parameters of the distribution, modeling likelihood of the event.

Application of ML extends beyond the setting of supervised learning. Unsupervised learning algorithms have been widely used to automatically discover the patterns without any labeled data. Classic unsupervised learning methods range from clustering algorithms, such as k-means and graph-based spectral clustering, to dimensionality reduction methods, such as principal component analysis or kernel-based methods.DNNs generalize some of these approaches by learning the data-set distribution, whether explicitly or implicitly, and generating samples from those learned distribution. For example, variational autoencoder parameterizes the distribution of the data set and trains the neural network to learn the distribution that fits the training data set best by maximizing its likelihood. The generative adversarial model uses two separate networks, one to generate fake samples (generator) and another to discriminate whether the given input is fake or real (discriminator).These networks learn adversarially: the goal of one is to generate samples that are closer to the true distribution, whereas the other wants to better differentiate the generated and true training samples. This method of training results in a model able to generate samples that are very similar to the training distribution. This method can also be further extended to impute missing data.

A comprehensive literature review was conducted by two independent reviewers (A.L.S. and J.K.). Two biomedical databases—MEDLINE (PubMed) and Embase (Elsevier)—were searched for relevant studies through January 15, 2019. The primary search strategy was created in PubMed and included a combination of text word and Medical Subject Heading (MeSH) terms. Primary search concepts included machine learning, predictive modeling, deep learning, and liver transplantation as well as specific etiologies for liver disease, such as hepatitis C and NAFLD. The itemized search strategy was then translated to the additional database, Embase. The itemized search strategy can be found in the Supporting information. Citations were managed using EndNote. The queries retrieved 487 citations with 305 duplicate citations identified using EndNote, leaving 182 citations for review. These citations were reviewed manually by two authors (A.L.S. and J.K.) for relevance to ML, chronic liver diseases (CLDs), and LT. This process resulted in selection of 40 articles that included primary data relevant to the topics. The flowchart of this process is illustrated. The relevant articles are listed . Further details regarding how articles were selected for inclusion or excluded are provided in the Supporting information