Research Paper

Comparing and Predicting Hepatic Encephalopathy Complications Using Random Forest Algorithm in Active Men

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ABSTRACT

Purpose: Liver diseases are among the most common disorders worldwide. For liver transplant patients, the presence of postoperative problems increases the complexity of postoperative nursing. Patients' hospitalization is prolonged, and the costs of hospitalization increase. Data mining has become an easy way to predict diseases in recent years. Accordingly, this study compares and predicts the complications of hepatic encephalopathy in active and inactive men after liver transplantation.

Methods: The statistical population of this study was 852 people. Among them, 350 active men (162 healthy people and 188 people with encephalopathy symptoms) and 402 inactive men (210 healthy people and 192 people with encephalopathy symptoms) were selected as study subjects. These people underwent a liver transplant in the hospital between 2010 and 2011. The random forest algorithm and 14 features from laboratory records were used to predict encephalopathy complications after liver transplantation. Meanwhile, MATLAB software, version 2023, was used for data analysis.

Results: There was no significant difference in predicting encephalopathy complications by random forest algorithm between active and inactive men. Also, this study showed that the random forest algorithm using 14 features is 76.2% and 75.5% accurate for diagnosing hepatic encephalopathy after liver transplantation in active and inactive men, respectively.

Conclusion: Computer-based decision support systems can help to reduce poor healthcare decisions and the expenses associated with unneeded clinical trials in both active and inactive populations. Based on the accuracy of the random forest algorithm on the data, this system can assist clinicians in forecasting the risk of hepatic encephalopathy following transplantation with high accuracy and at a cheap cost.

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Highlights

● The liver is the largest important organ in the body.

● Computer-based decision support systems can improve healthcare decisions and reduce costs associated with unneeded trials in both active and inactive populations.

● Random forest algorithm using 14 recipient features has high accuracy in diagnosing hepatic encephalopathy after liver transplantation in active and inactive men.

● Exercise training is a simple and cost-effective way to improve muscle mass in post-liver transplantation encephalopathy.

Plain Language Summary

After transplantation, hepatic encephalopathy is largely responsible for avoidable medical complications and deaths globally. We can take proactive steps to lower the frequency of encephalopathy if we can accurately forecast its risk. Today, with the introduction of computer science in the field of medicine, the diagnosis and prediction of diseases have become much easier. The results of this study showed that the random forest algorithm using 14 characteristics of the liver recipient for diagnosing hepatic encephalopathy after liver transplantation has an accuracy of 76.2% and 75.5% in active and inactive men, respectively. Also, exercise training is an intriguing, straightforward, and inexpensive method that may have an impact on muscle mass in hepatic encephalopathy. Focusing on the muscle with exercise may be an effective treatment strategy in lowering the risk of hepatic encephalopathy following liver transplantation.

Introduction

The liver is a critical organ for the body and it is known as the largest vital organ of the body [1]. Liver diseases are very common in today's society and require clinical care by an experienced doctor or nurse in all cases [2]. Advanced chronic liver diseases, such as chronic failure, metabolic liver diseases, primary biliary cirrhosis, sclerosing cholangitis, biliary atresia, liver disease caused by alcohol and drugs and liver malignancies cause irreversible liver dysfunction [3].

The last method of treating liver patients is liver transplantation, which has a high-risk percentage [4, 5]. Liver transplantation is performed in many countries, the United States being the first [6]. Namazi Hospital in Shiraz City is the leader in liver transplantation in Iran [7]. The occurrence of complications after liver transplantation increases the hospitalization time of patients increases the difficulty of nursing and hospitalization costs [8, 9]. Cognitive impairment, post-liver transplant encephalopathy, is a common complication after liver transplantation [10]. In hepatic encephalopathy, due to the inability of the liver to detoxify, the concentration of toxic substances, including ammonia, increases in the blood and brain [11-13]. On the other hand, an increase in ammonia also stimulates immune cells in the brain and causes neuroinflammation [14]. High levels of ammonia and neuro-inflammation caused by it cause changes in blood transfusion levels, which in turn causes cognitive disorders, such as learning and memory deficits, as well as disturbances in movements and motor coordination [15]. After transplantation, hepatic encephalopathy is largely responsible for avoidable medical complications and deaths globally [16]. We can take proactive steps to lower the occurrence of encephalopathy if we can accurately forecast the danger of the condition. By lowering the likelihood of complications and indirectly lowering medical costs, post-surgical complications analysis can provide doctors with preoperative intervention indicators. To provide patients with an accurate prognosis and make plans for any encephalopathy that may occur [17].

It is critical to stress that exercise-related knowledge in hepatic encephalopathy is currently restricted and in its early stages. In recent years, society has shown an increasing interest in health through physical activity and sports. Promoting physical exercise is essential in the prevention and promotion of well-being among the healthy population and in groups or patients with some kind of special needs (such as liver transplant recipients) [18]. For individuals undergoing transplants, weight gain and elevated cholesterol are two prevalent chronic issues. The immunosuppressive medication and increased hunger are to blame for this. Numerous medical disorders, including metabolic syndrome (which is closely linked to increasing body fat around the waist and high blood levels of triglycerides and cholesterol), can be brought on by eating too much and exercising too little [19].

Today, despite a large amount of medical data, diagnosing and predicting diseases is a difficult task, but with the introduction of computer science in the field of medicine, this problem has been solved to a large extent and researchers have been able to solve the challenges by introducing new methods. For solving the problem, one of these methods for predicting diseases is data mining and the use of machine learning methods [20]. Machine learning methods have been used to predict complications after liver transplantation. Moghadam et al. (2020) using machine learning, showed a correlation between the occurrence of episodes of hypertension during or after surgery and several subsequent outcomes [21]. Meanwhile, Pepin et al. (2020) created a model for predicting complications from laparoscopic hysterectomy surgery in recognizing benign conditions [22]. Merath et al. (2020) developed a machine learning model and showed that these algorithms can be used for the electronic monitoring of patients with postoperative complications [23]. Zeng et al. (2021) compared eight different machine learning methods and showed that machine learning-adaptive augmentation performed best in detecting surgical complications [24]. Such studies have shown that machine learning can significantly predict the occurrence of postoperative disease. However, few studies have used machine learning to predict hepatic encephalopathy after liver transplantation. Accordingly, this study compares and predicts hepatic encephalopathy complications in liver transplant patients using a random forest algorithm in active and inactive men.

Materials and Methods

The statistical population of this study was 852 patients. Among these people, 350 active (162 healthy and 188 with encephalopathy symptoms) and 402 inactive men (210 healthy and 192 with encephalopathy symptoms) were selected as the subjects of this study. These subjects had undergone a liver transplant at Taleghani Hospital in Tehran City, Iran, during 2001-2022 and had laboratory records in the computer archive files of that center. The laboratory files of the patients contained laboratory information before and after transplantation, personal information, and lifestyle. By examining these files, we gathered data on 28 characteristics, such as age, sex, duration of stay following surgery, etc. The findings of scholarly publications, as well as the advice of two highly qualified medical professionals in the field of liver transplantation, we performed a secondary screening of the variables and finally, 14 features were selected as input to the algorithm. Male gender, age between 40 and 75 years, hospitalized clinical trials and medical records, and phone or internet accessibility were among the inclusion criteria. Meanwhile, having a chronic illness, taking hormonal medications in the past, and receiving treatment for osteoporosis were among the exclusion criteria.

The characteristics that were selected included age between 40 and 75 years, height, weight, body mass index, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, cholesterol, triglycerides, blood sugar, family history, fatty liver, liver cancer, and diabetes. At this stage, MATLAB version 2021 was used to import and analyze the Excel data collection.

Random forest data mining algorithm

In liver transplant patients, postoperative hepatic encephalopathy was predicted using the random forest data mining technique. It is a simple machine-learning method that frequently yields excellent results even when its meta-parameters are left alone. Because of its ease of use and simplicity, this method is among the most often used for both regression and classification. It is regarded as the most used algorithm for machine learning [25].

When compared to many other methods, a random forest's training period is quick. They can be used to estimate missing data and are resistant to overfitting. Due to its versatility, the technique can be applied to jobs involving both regression and classification [26]. The primary tenet of this approach is that the sum of learning models improves the model's overall performance. To put it simply, a random forest creates many decision trees and combines them to generate forecasts that are more reliable and accurate [25].

When it is impossible to divide two classes of the same data using straight lines, this technique can be quite helpful (Figure 1).

The performance of the algorithms was assessed using accuracy and precision. By dividing the total number of forecasts by the number of right predictions, the algorithm's prediction accuracy (Equation 1) is demonstrated. The algorithm's accuracy demonstrates its capacity to distinguish between those who are healthy and those who have signs of encephalopathy. By dividing the total

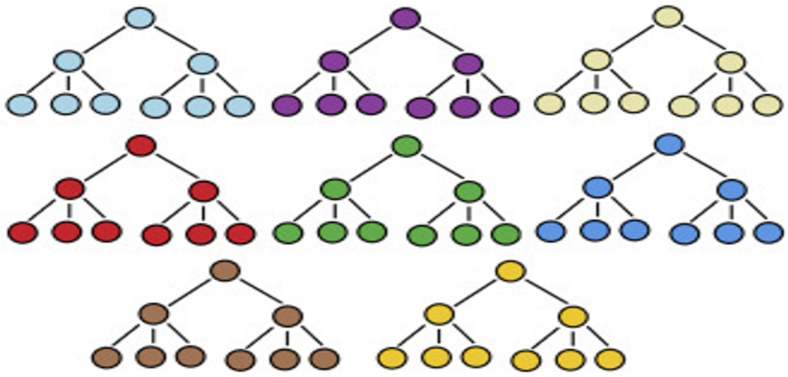

Figure 1. Classification method of random forest algorithm

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number of forecasts by the total number of predictions in each row, precision can be calculated (Equation 2) [26].

(1) $$\text{Accuracy} = \frac{TP+TN}{TP+FP+TN+FN}$$

(2) $$\text{Precision} = \frac{TP}{TP+FP}$$

where, TP: True positive; TN: True negative; FP: False positive; FN: False negative.

The accuracy and precision standards according to the data evaluation methodology are displayed in Table 1.

Results

Table 2 shows the anthropometric characteristics and Table 3 shows the descriptive statistics related to the quantitative and qualitative variables of the subjects' files.

Table 2 and Table 3 present the factors that were determined using the data from scholarly journals and doctor questionnaires. Age, height, weight, body mass index, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, triglyceride, cholesterol and blood sugar are quantitative and continuous variables, while family history, fatty liver, liver cancer, and diabetes are qualitative and discrete variables. Meanwhile, 70% of the data were used to train the algorithm, while 30% were used for testing. The random forest method was employed to forecast the consequences of encephalopathy. Figure 2 displays the confusion matrix findings for this approach.

The results showed that the random forest algorithm can predict with 76.2% accuracy and 73.7% precision in active men with encephalopathy and without complications.

The results showed that the random forest algorithm can predict with 75.5% accuracy and 72.4% precision inactive men with encephalopathy and without complications. Figure 3 shows the random forest algorithm's confusion matrix for inactive men.

Discussion

Liver transplantation represents the definitive and final treatment of liver disease in the final stage, and cognitive impairment follows repeated liver transplantation, which is called encephalopathy post-liver transplantation. In various studies under the title of medical data mining, several solutions have been presented, including the use of algorithms to discover the relationships between the factors of various diseases. Some data mining algorithms, such as machine learning methods, can predict different situations in the future by gradually learning these patterns and existing conditions, in addition to analyzing data and extracting hidden patterns in them [27]. An issue that has not been addressed is the use of data mining in the prediction of diseases related to

Table1. Data evaluation method

Predicted Values	Correct Values	
	Positive	Negative
Positive	TP	FP
Negative	FN	TN

Abbreviations: TP: True positive; TN: True negative; FP: False positive; FN: False negative.

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Table 2. Quantitative variables of the subjects

Indicators	Mean±SD			
	Healthy		With Signs of Encephalopathy	
	Active	Inactive	Active	Inactive
Age (y)	57.74±10.26	58.81±9.13	56.71±10.52	57.88±12.39
Height (cm)	162.38±7.12	163.47±8.34	158.29±7.23	161.74±10.42
Weight (kg)	65.32±13.58	67.21±25.62	61.30±10.51	64.81±12.67
BMI (kg/m^2)	25.58±8.75	26.84±9.81	26.59±9.12	27.78±20.91
Aspartate aminotransferase	44.35±11.10	46.56±14.28	45.53±11.61	47.55±27.83
Alanine aminotransferase	63.38±15.27	67.42±16.76	65.38±15.74	65.93±57.98
Alkaline phosphatase	171.19±18.30	182.11±13.49	173.19±18.54	176.19±74.95
Triglyceride (mg/dL)	255.32±113.34	259.44±144.12	255.32±113.22	256.52±126.63
Cholesterol	208.54±38.48	213.62±72.57	207.54±41.43	218.66±92.78
Blood sugar	115.525±17.53	119.651±26.63	117.716±19.34	119.487±37.69

BMI: Body mass index.

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liver transplantation. This study compared and predicted hepatic encephalopathy complications in liver transplant patients using a random forest algorithm in active and inactive men. In this study, 30% of the data were considered for testing and 70% for training the algorithm. The results of this study revealed that the random forest algorithm using 14 recipient features has an accuracy of 76.2% in diagnosing hepatic encephalopathy after liver transplantation in active men and 75.5% in inactive men.

In line with the results of this study, Shahraki and Mesgar (2019) compared different data mining algorithms to predict liver diseases in their study. In their study, they used the most dangerous indicators of these diseases such as aspartate aminotransferase, gender, alkaline phosphatase, age, direct bilirubin, albumin, total bilirubin, the ratio of albumin to globulin and total protein for prediction and diagnosis and at the end of the algorithm They reported the enhanced decision tree with 94.04% accuracy as the best performance [28]. Cruz-Ramírez et al. (2013) reviewed various machine-learning models for predicting patient survival after liver transplantation. In their

Table 3. Qualitative variables of subjects

Characteristic	Type (Discontinuous)	Healthy (%)		With Symptoms of Encephalopathy (%)	
		Active	Inactive	Active	Inactive
Family history	Has=1	66	69	67	72
	does not have=0	34	31	33	28
Fatty liver	Has=1	64	67	62	65
	does not have=0	36	33	38	35
Liver cancer	Has=1	30	33	25	34
	does not have=0	70	67	75	66
Diabetes	Has=1	55	56	59	60
	does not have=0	45	44	41	40

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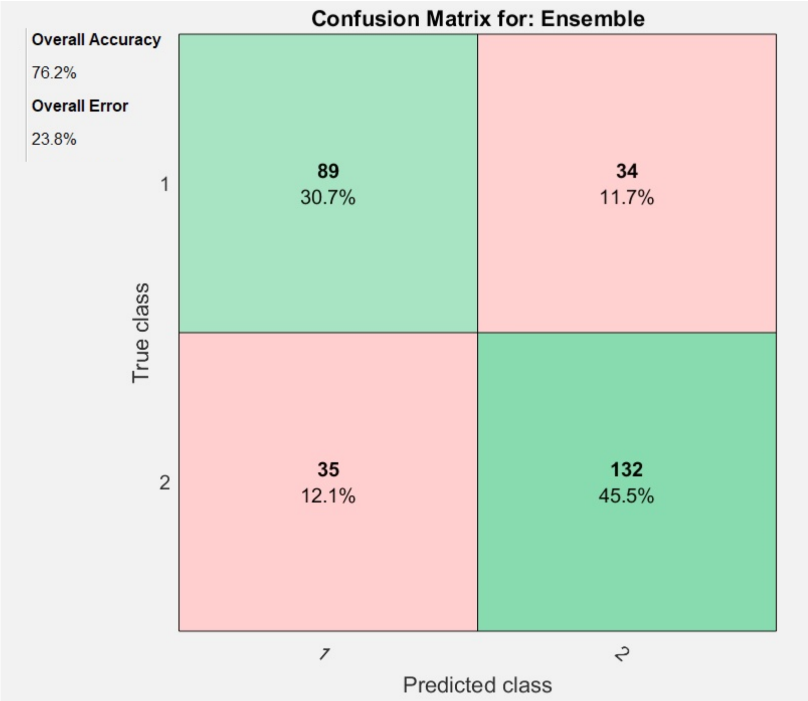

Figure 2. Random forest algorithm confusion matrix for active men

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study, they built models that predict whether a patient will receive an organ after liver transplantation in a certain time horizon [29]. In this study, they used the observations of bilirubin and creatinine in the entire first year after transplantation to obtain predictors, and their static value and variability were obtained and examined. The models of these researchers have a high predictive power, which confirms the value of combining the diversity of biochemical measurements. They found

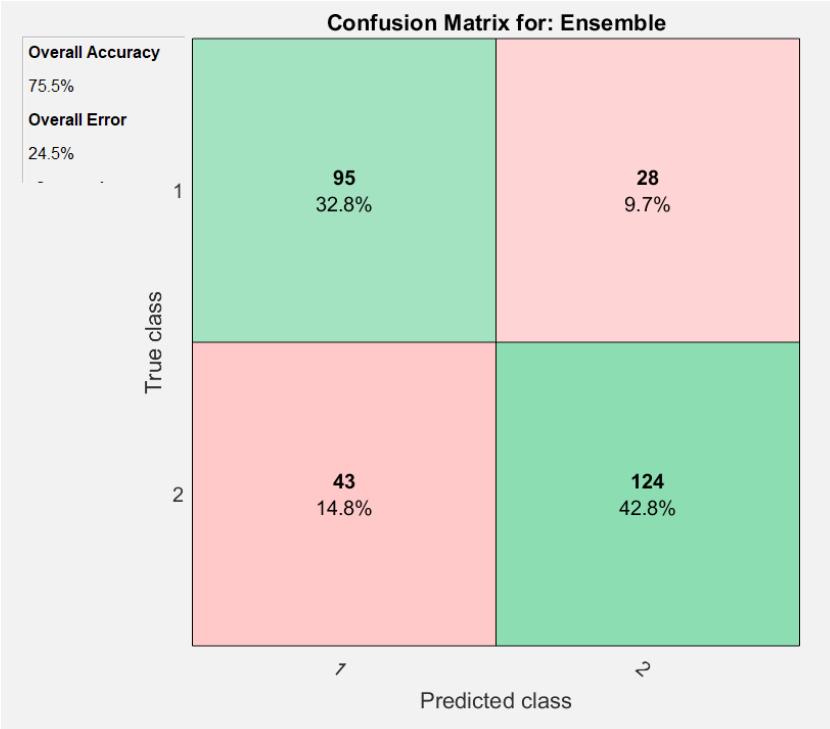

Figure 3. Random forest algorithm confusion matrix for inactive men

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that models with full complexity, such as random forests and gradient boosting, had the best predictive power. Fernández-Delgado et al. (2014) in a study titled, "Hepatic Encephalopathy After Liver Transplantation", showed signs of altered consciousness in the presence of drowsiness, confusion, and tremors with an increase in serum ammonia (63 moll/L, normal value <50) due to obvious signs of acute heart failure and they reported a decrease in left ventricular ejection fraction to 20% in predicting hepatic encephalopathy [30]. Random forest classifiers were determined to be the most accurate in a recent groundbreaking study that classified all 121 data sets, which represented the entirety of the University of California Irvine Machine Learning Repository, using the performance of 179 different machine-learning classifiers [31].

In individuals who are in a stable clinical state, moderate physical activity could be recommended. In hepatic encephalopathy, an exercise regimen combined with the best possible diet may help to preserve or even grow muscle mass, preventing sarcopenia and frailty. Muscle mass could contribute to the development or aggravation of hepatic encephalopathy [32].

However, the quality and quantity of muscle mass may determine how well it eliminates ammonia. Thus, increasing muscle mass and function could be a key tactic in reducing hepatic encephalopathy. Targeting the muscle with exercise could be an effective treatment method for lowering the risk of hepatic encephalopathy after liver transplantation. Exercise training is an intriguing, straightforward, and inexpensive approach that may alter muscle mass in hepatic encephalopathy. Exercise has been demonstrated to dramatically increase lean mass and strength in both people and healthy animal models by stimulating muscle satellite cell proliferation and activating protein synthesis [33]. This implies that physical activity might be preventive against frailty, sarcopenia, and consequently hepatic encephalopathy, as well as a useful tool for managing these conditions. It has been demonstrated that in patients with hepatic encephalopathy, inactivity exacerbates muscular atrophy [34].

Conclusion

This study demonstrates that a random forest method based on recipient factors may be used to predict hepatic encephalopathy problems. This technique might help transplant surgeons make better judgments about hepatic encephalopathy problems. The ability to quantify risk may allow for improved confidence and better outcomes after transplantation. Also, an activity may help prevent or attenuate complications of hepatic encephalopathy. It is suggested that this model be tested with more data sets and information on more healthy people.

Study limitations

One of the most important limitations of researchers in this field is the lack of sufficient data related to healthy people because, in most of the registration data, the number of samples of healthy people is much less than that of patients. The existence of this asymmetry can lead to the lack of complete learning of algorithms and reduce the accuracy of diagnosis. Another limitation of this algorithm is that although it has been trained to predict the post-transplant encephalopathy complication; however, other significant outcomes of liver transplantation, such as graft failure, dysfunction, acute or chronic rejection, infection, immunosuppression, or the absence of late biliary stricture, may have an impact on its predictive accuracy and may necessitate the use of a different training algorithm.

Considering the importance of liver diseases, it is necessary to identify a method to predict and diagnose these diseases in time. For further investigation in this field, data from other medical centers and other algorithms can be used in future studies and the results can be compared. It is also recommended to prepare the field of using these algorithms in the prediction of encephalopathy after liver transplantation in hospitals so that doctors and specialists can investigate and predict this liver complication using a suitable environment and thus compensate for the occurrence of injuries. It is not possible to prevent liver transplant patients. Finally, it is suggested to use other methods and algorithms to exploit human knowledge to create a prediction model.

Ethical Considerations

Compliance with ethical guidelines

The present study was conducted according to the Helsinki Ethics Statement, and also the Research Ethics Committee of Allameh Tabatabai University approved the study protocol (Code: IR.ATU.REC.1401.051). Participants entered the study after providing written informed permission and had the opportunity to withdraw at any time.

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Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

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