Analysis of hepatic fibrosis risk factors using artificial neural networks

BOUHARATI KHAOULA[1,2*], BOUHARATI IMENE[3,4], GUENIFI WAHIBA[5], GASMI ABDELKADER[5], LAOUAMRI SLIMANE[5]
[1.]Department of Epidemiology, Faculty of Medicine, Constantine University, ALGERIA
[2.]Laboratory of Health and Environment, UFAS Setif1 University, Setif, ALGERİA
[3.]Faculty of Medicine, Paris Sorbonne University, FRANCE
[4.]Laboratory of Intelligent Systems, UFAS Setif1 University, Setif, ALGERIA
[5.]Faculty of Medicine, Setif University Hospital, UFAS Setif1 University, Setif, ALGERİA

Abstract. **Introduction**: Following excessive scarring, an accumulation of connective tissue in the liver causes fibrosis. This fibrosis is asymptomatic, but generates portal hypertension by deviation in intra-hepatic blood flow. When this destroys the hepatic architecture by inducing a dysfunction, it switches to cirrhosis. The factors involved are sometimes ill-defined. However, the most common are hepatitis B and C and alcohol abuse. The analysis of these factors is very complex. **Methods**: This study proposes an artificial intelligence tool, in particular artificial neural networks in data analysis. We consider risk factors as input variables to the system. We consider the risk of fibrosis as an output variable. **Conclusion**: When the learning of the network is carried out from the proper cases followed at our hospital service of Setif in Algeria, the transfer function created is adjusted to its minimum of errors. It then becomes possible to assign random values to the input of the system to read the risk of fibrosis at the output.

Keywords: Liver fibrosis, Risk factors, Intelligent analysis, ANN

Received: June 12, 2021. Revised: April 13, 2022. Accepted: May 10, 2022. Published: July 1, 2022.

1. Introduction

Whatever the etiology, the sequela of liver damage induces fibrosis. This is manifested by scarring that replaces liver tissue with collagen, which sometimes takes the form of a dense network of fibers. At its advanced stage, it transforms into nodular cirrhosis, thus deforming the hepatic vascular system [1], [2]. Often irreversible, hepatic cirrhosis can lead to death.

They often relate known risk factors that cause liver damage to gender, age, alcohol abuse, diabetes and mainly viral load in hepatitis B or C or [3].

We consider if obesity and type 2 diabetes risk factors; it is because they make up a metabolic co-morbidity associated with non-alcoholic fatty liver disease (NAFLD). This concerns the age group of 18 to 75 years [4]. Studies have also shown that hyperlipidemia is also associated with fibrosis [5-8]. The accumulation of fat in the liver can determine the prevalence of fibrosis [9]. The association of this disease with coronary heart disease (CHD) is also mentioned [10]. Given this complexity, a classification of the severity of fibrosis is established according to a score. A low probability when the score is between 1 and 5. Medium probability is between -1.5 and 0.67 and High probability when this score is greater than 0.67 [11].

The system is very complex to analyze by classical techniques. This study proposes a technique based on the principles of artificial intelligence, mainly the application of artificial neural networks.

The constructed artificial neural network has three layers (input layer, hidden layer, and output layer). This is to make the correspondence between the two spaces (inputs-outputs). Risk factors are considered as input variables to the system. The risk of fibrosis is considered as an output variable. From the values of the proper cases followed at the level of our university hospital of Seti in Algeria, the learning of the network is carried out. Once the network is optimized, it then becomes possible to assign random values to the input of the system to read the risk of fibrosis at the output.

2. Material and method

Fibrosis is a multi-factorial disease. What characterizes these factors is complexity and uncertainty. The risk factors are multiple. Some factors are known, some other less so. Also, the weight of each factor with precision is ignored. Besides the factors mentioned above, other less frequent factors also sometimes have their effect such as drug effects, the genetic factor or that linked to autoimmune diseases. Analyzing those using classical mathematical techniques is very difficult and even impossible. This study addresses the analysis of these risk factors by artificial neural networks. This technique makes it possible to deal with the complexity and multitude of factors involved.

The factors analyzed in this study are limited only to the three major factors, which are hepatitis B and C and excessive alcohol consumption.

Like natural neural networks, artificial neural networks make the correspondence between the two input-output spaces. The initial data is stored, processed and returned at the output [20]. The major advantage of artificial neural networks is learning. By introducing values at the input and the result at the output, a transfer function is created [21-23]. At each value entered, the function is readjusted so that it remains appropriate. This is done just by variations of the mathematical coefficients called weights. This continues until the function is optimized to its minimum error. By this ability to adapt to different complex situations, neural networks apply in various fields, especially the medical field [24]; [25].

The network applied to this analysis is a multi-layer network (Figure 1). It took risk factors for hepatic fibrosis as input variables to the system. These factors concern the patients followed at the University Hospital of Setif in Algeria (hepatitis B, hepatitis C and the age of the patients). The alcohol abuse factor is not supported because this factor did not arise during our follow-up. The output variable of the system expresses damage by fibrosis.

Mathematically, this function can be represented by:

$$df = f\,hb, hc, ap$$

Where : df: damage fibrosis
hb: hepatitis B
hc: hepatitis C
ap: age of the patient

2.1. Risk factors

Hepatitis B and C

Hepatitis B and C are contagious diseases they contaminate whose transmission route blood. These diseases are characterized by inflammation of the liver. The infection often remains mild. However, sometimes (about 10%), it develops into a chronic infection and can even develop into cirrhosis or even liver cancer. WHO statistics, reports that the approximately 257 million infected cases are in a chronic stage [12]. Viral hepatocyte infections progress to acute hepatitis and even induce hepatocellular carcinoma or ultimately cirrhosis. Regardless of the existence of a supposedly 95% effective vaccine, hepatocellular carcinomas rank second among fatal cancers [14].

Alcohol abuse

The severity and the risk of liver damage is determined by the volume, frequency and duration of alcohol consumption. While the effect is often silent, signs may appear as liver pain, accompanied by fatigue, fever, jaundice and enlargement. The result is then the risk of getting hepatitis, digestive bleeding or even an imbalance of brain function. If several risk factors are cited, excessive alcohol consumption is an aggravating factor for hepatitis C. Its effect will be much more pronounced, especially when it is combined with advanced age or other factors such as obesity or immunodeficiency [15-19].

Input Variables

Each variable is assigned numerically:
Hepatitis B: 1 (positive); 2 (negative)
Hepatitis C: 1 (positive); 2 (negative)
Age: 1 (adult); 2 (old)

Output variable

The degree of fibrosis damage expresses the output variable of the system. This variable is numerically coded in two states (1: low impairment); (2: serious damage). When the damage is considered serious, it can degenerate into cirrhosis.

Model

The built system is multi-layered. An input layer, a hidden layer and an output layer (Figure 1). From the real values recorded, a mapping between each input variable and its corresponding output variable

The cases analyzed are 80 cases. Half is taken for network learning. The adjustment of the function is done after 100 iterations. The variables specific to each newly introduced patient are combined with the function. The other half is used for testing the function created.

After optimizing the function to its minimum error (Figure 2), the system created makes it possible to introduce random values at the input to read the result at the output (Figure 3). The result obtained at the output is the aggregation of all the inputs. In this way, it will be as precise as possible.

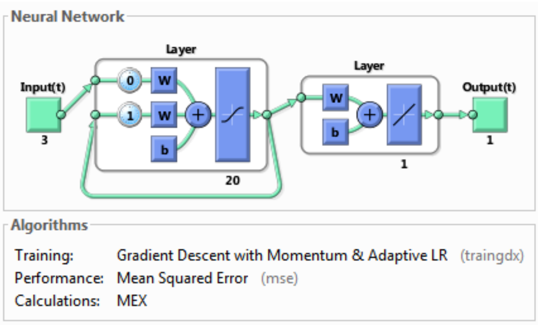


Fig. 1. System Architecture

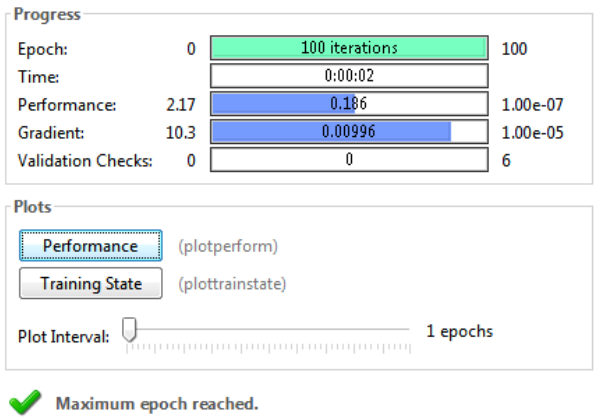


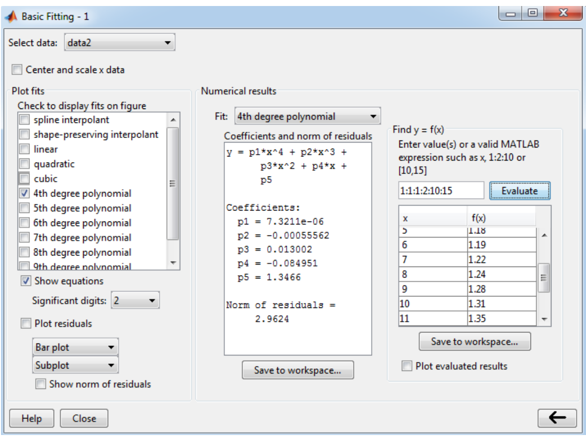
Fig. 2. Function optimisation

3.Results and discussion:

The risk factors that necessitate this infection are multiple. Also, the effect of each factor is often poorly understood with their classic physiological specificity interaction [20].

For this reason, classical mathematical methods are unsuitable for analyzing this kind of situation. Often, it is a matter of applying statistical methods. These methods arrive at imprecise results and remain in the realm of the probable. The proposed technique applies a domain of artificial neural networks. These networks have the ability to take on a large number of variables and combine them [21-23].

The result is the aggregation of all input variables. As these networks have the ability to learn, it is simply a matter of introducing real variables at the input while assigning the result to it at the output. A transfer function that links the inputs to the output is created. With each new case, the function is adjusted. In the case of the study, three input variables are taken into consideration (hepatitis B, C and the age of the patients). In each case, a correspondence between these variables and the degree of attack by hepatic fibrosis is done. After learning, the result will be as accurate as possible in terms of reading this degree later. It should be noted that the network remains extensible to other factors that are not taken into account in this study.



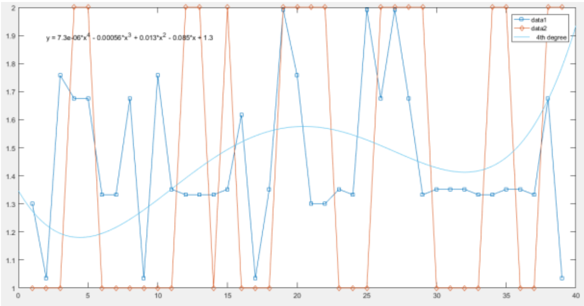


Fig. 3. Degree of fibrosis damage variations

4. Conclusion:

In order to implement a screening and follow-up program at the scale of a population with hepatitis B or C, this tool provides an idea of the evolution of fibrosis. From the rate of progression of hepatitis in people according to their age, the identification of fibrosis and even its possible evolution into cirrhosis becomes possible. The system establishes a correspondence function between the risk factors as input variables and the state of fibrosis as the output variable. From the real cases used in learning the network, its application becomes valid later for new cases that arise. As such, it can be considered as a preventive tool. This makes it possible to predict the impact of each input parameter on the progression of the risk of fibrosis.

In future studies and with the enrichment of the data including other variables that are not considered in this study, the precision will be increased.

Financial support and sponsorship:
Nil.

Conflicts of interest:
There are no conflicts of interest.

References:

[1]. Friedman SL. Liver fibrosis. From bench to bedside. J Hepatol. 2003; 38 (Suppl 1) : S38-53.
[2]. Schuppan D, Afdhal NH. Liver cirrhosis. Lancet. 2008; 371(9615):838-51.
[3]. L Mallem1, A Safir1, N Amani1, M Amar, MR

Belkahla, S Hakem1, N Boumansour2, N Midoun2. Risk factors of hepatic fibrosis at the chronic carriers of virus B followed at Oran university hospital center. Algerian Journal of Health Sciences. Vol. 01 Num. 01. 2019. 21-26
[4]. Llorenç Caballería et al. High Prevalence of Liver Fibrosis Among European Adults With Unknown Liver Disease: A Population-Based Study. Clinical Gastroenterology and Hepatology 2018; 16:1138–1145
[5]. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of non-alcoholic fatty liver disease: practice. Guidance from the American Association for the Study of Liver Diseass. Hepatology 2018; 67:328–357.
[6]. European Association for the Study of the Liver (EASL); European Association for the Study of Diabetes (EASD); European. Association for the Study of Obesity (EASO). EASL-EASD-EASO Clinical Practice Guidelines for the management of nonalcoholic fatty liver disease. J Hepatol 2016; 64:1388–1402.
[7]. Younossi ZM, Koenig AB, Abdelatif D, et al. Global epidemiology of nonalcoholic fatty liver disease-meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology 2016; 64:73–84.
[8]. Satapathy SK, Sanyal AJ. epidemiology and natural history of nonalcoholic fatty liver disease.Semin Liver Dis 2015; 35:221–235.
[9]. Ginès P, Graupera I, Lammert F, et al. Screening for liver fibrosis in the general population: a call for action. Lancet Gastroenterol Hepatol 2016; 1:256–260.
[10]. Adams LA, Lymp JF, St Sauver J, Sanderson SO, Lindor KD, Feldstein A, Angulo P. The natural history of nonalcoholic fatty liver disease: a population-based cohort study. Gastroenterology 2005; 129: 113-121. DOI: 10.1053/ j.gastro.2005.04.014]
[11]. Sombat Treeprasertsuk, Einar Björnsson, Felicity Enders, Sompongse Suwanwalaikorn, Keith D Lindor. NAFLD fibrosis score: A prognostic predictor for mortality and liver complications among NAFLD patients. World J Gastroenterol 2013 February 28; 19(8): 1219-1229
[12]. World health organization. Global hepatitis report, 2017. Geneva : WHO, 2017.
[13]. European Association for the Study of the Liver. EASL clinical practice guidelines: management of chronic hepatitis B virus infection. J Hepatol 2012; 57 : 167-85.
[14]. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012: Globocan 2012. Int J Cancer 2015 ; 136 : E359-86.
[15]. Thomas DL, Seeff LB. Natural history of hepatitis C. Clin Liver Dis 2005. 9: 383,98, DOI:https://doi.org/10.1016/j.cld.2005.05.003.
[16]. Massard J, Ratziu V, Thabut D, Moussalli J, Lebray P, et al. Natural history and predictors of disease severity in chronic hepatitis C. J Hepatol. 2006; 44: S19–S24 DOI:https://doi.org/10.1016/j.jhep.2005.11.009 .
[17]. Davis GL, Lau JY. Factors predictive of a beneficial response to therapy of hepatitis C. Hepatology. 1997. 26: 122S–127S DOI: https://doi.org/10.1002/hep.51026071
[18]. Poynard T, Ratziu V, Charlotte F, Goodman Z, McHutchison J, et al. Rates and risk factors of liver fibrosis progression in patients with chronic hepatitis c. J Hepatol 2001. 34: 730–739.
[19]. Sulkowski MS, Thomas DL Hepatitis C in the HIV-Infected Person. Ann Intern Med 2003; 138: 197–207.
[20]. Bouharati K., Bouharati I., Guenifi W., Gasmi A., Laouamri S. Intelligent analysis of some factors accompanying hepatitis B. Molecular Sciences and Applications DOI: 10.37394/232023. 2022.2.7
[21]. Mnih, V. et al. Human-level control through deep reinforcement learning. Nature 2015; 518, 529–533
[22]. Bouharati I., El-Hachmi S., Babouche F., Khenchouche A., Bouharati K., Bouharati S. Radiology and management of recurrent varicose veins: Risk factors analysis using artificial neural networks. 2018. Volume: 5 Number:1 Pages No:1–5. 10.15713/ins.jmrps.116
[23]. Khenchouche A., Bouharati K., Bouharati S., Mahnane A., Hamdi-Cherif M. Post Mortem Interval: Necrobiome Analysis Using Artificial Neural Networks. Computational Biology and Bioinformatics. 2017. 5(6): 90-96.