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Automated development of artificial neural networks for clinical purposes: Application for predicting the outcome of choledocholithiasis surgery

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ABSTRACT

Among various expert systems (ES), Artificial Neural Network (ANN) has shown to be suitable for the diagnosis of concurrent common bile duct stones (CBDS) in patients undergoing elective cholecystectomy. However, their application in practice remains limited since the development of ANNs represents a slow process that requires additional expertize from potential users. The aim of this study was to propose an ES for automated development of ANNs and validate its performances on the problem of prediction of CBDS. Automated development of the ANN was achieved by applying the evolutionary assembling approach, which assumes optimal configuring of the ANN parameters by using Genetic algorithm. Automated selection of optimal features for the ANN training was performed using a Backward sequential feature selection algorithm. The assessment of the developed ANN included the evaluation of predictive ability and clinical utility. For these purposes, we collected data from 303 patients who underwent surgery in the period from 2008 to 2014. The results showed that the total bilirubin, alanine aminotransferase, common bile duct diameter, number of stones, size of the smallest calculus, biliary colic, acute cholecystitis and pancreatitis had the best prognostic value of CBDS. Compared to the alternative approaches, the ANN obtained by the proposed ES had better sensitivity and clinical utility, which are considered to be the most important for the particular problem. Besides the fact that it enabled the development of ANNs with better performances, the proposed ES significantly reduced the complexity of ANNs' development compared to previous studies that required manual selection of optimal features and/or ANN configuration. Therefore, it is concluded that the proposed ES represents a robust and user-friendly framework that, apart from the prediction of CBDS, could advance and simplify the application of ANNs for solving a wider range of problems.

1. Introduction

Symptomatic gallstones are regarded as one of the most frequent subjects of surgical interventions in developed parts of the world [1,2]. Surgical cholecystectomy (laparoscopic or open) is commonly used for treating patients with symptomatic gallstones. Prediction of asymptomatic concurrent common bile duct stones (CBDS), which occur in 10–15% of patients, is an important factor in terms of reduction of operative risks and health care costs [3]. In establishing a firm diagnosis, the standard preoperative diagnostic procedures used to diagnose patients with gallstones (liver function tests [LFTs] and abdominal ultrasound [US]) or risk factors for CBDS (abnormal LFTs, jaundice, bile duct dilation [BDD]) are often found not to be accurate enough [4]. Several different diagnostic procedures have been proposed as a solution in order to make the diagnosis and they have included: magnetic resonance cholangiopancreatography (MRCP), endoscopic retrograde

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cholangiopancreatography (ERCP), spiral computed tomography cholangiography, intraoperative cholangiography (IOC), endoscopic ultrasound (EUS) and laparoscopic common bile duct exploration (LCBDE) at the time of surgery [5,6]. Regardless of promising results, these imaging modalities cannot be considered routine ones because of high expenses, restricted availability and technical difficulties in performing LCBDE. Consequently, non-invasive methods for diagnosis of CBDS such as prognostic model have been shown to be a desirable goal [7,8]. Previous studies have suggested various predictive models relying on logistic regression [9,10], regression trees [11], multivariate regression [3,12–14], discriminant functions [15] and artificial neural networks (ANNs) for predicting CBDS [16].

Regarding the ANNs, which are the subject of the present study, they have been increasingly used in medical research due to their ability to learn and recognize complex and nonlinear data patterns between input and output variables. In surgery, ANNs have showed to be a promising tool for resolving the diagnostic [17] or prognostic [18–21] problems in various clinical settings. Moreover, the ANNs have been successfully applied for predicting the need for therapeutic endoscopic retrograde cholangiopancreatography (ERCP) or cholecystectomy with high risk of duct stones [22]. However, the previous studies have not demonstrated clinical usefulness and the application of the developed expert systems (ES) in clinical practice remains negligible. In general, previous studies traditionally developed and assessed ANN ES with respect to certain accuracy indicators (commonly mean square error). On the other side, the recent studies in the field of medical decision making have proposed more sophisticated evaluation strategies in order to better express clinical utility [23–26]. Another drawback of the previously proposed procedures is the assumption that potential users would be able to configure the ANNs' parameters for their own data sets. Particularly, in order to use ANNs efficiently, one needs to set correctly various configuration parameters, such as: number of neurons and layers, type of activation functions, learning algorithm, type of features that will be used for training, strategies for validation and testing as well as type of objective-function for measuring the quality of the training. Since clinicians are commonly not familiar with a complex foundation of ANN framework, in situations when an ANN does not significantly outperform an alternative ES they would prefer to use a more intuitive predictive tool. As a consequence, wider usage of the developed ANNs remains unpopular among clinical audience despite promising results in research community. Moreover, the selection of optimal portion of features from the available set of features represents a nontrivial problem as it directly affects the costs and complexity of the procedure. In literature, feature (attribute) selection methods can be grouped into: filters (feature selection is performed before and independently from the development of a predictive model) and iterative wrapper based methods (when feature selection is coupled with the development of a predictive model). Some of the most popular and computationally efficient filter approaches include: Fisher Score, Mutual Information, Maximum Output Information, Random Permutation of Probabilistic Outputs, to name a few [27–31]. However, the most robust feature selection methods remain the wrappers: forward, backward and stepwise feature selection method [32].

To the best of our knowledge, obtaining reliable ANN predictive models with respect to clinical needs remains an open problem. Starting from the given considerations, the aim of this study was to propose an ES for automated development of ANNs and validate its performances on the problem of prediction of CBDS. Therefore, the goal of the proposed ES was to maximize users' benefits assuming minimal requirements for users' expertize in the field of ANNs or data analysis.

2. Materials and methods

2.1. Study population

Within the period from January 2008 up to August 2014, we collected data from patients who stayed for hospital treatment at the department of General Surgery at Clinical Center Gornji Milanovac, Serbia. The analysis did not include the patients with a preoperative diagnosis of CBDS, calculous cholangitis, a history of gallstone pancreatitis, acute pancreatitis, acute or chronic hepatitis or patients with incomplete data. Comprehensive clinical, current biochemical tests, and abdominal US findings (General ELECTRIC® Logiq 3 Pro, USA) were accumulated for each patient regarding precholecystectomy assessment. Patient's gender and age, the presence of acute biliary colic and history of previous acute biliary pancreatitis or jaundice were included in the clinical data. Preoperative LFTs (serum total bilirubin, alanine aminotransferase [ALT], aspartate aminotransferase [AST], alkaline phosphatase [ALP], amylase, γ-glutamyl-transpeptidase [GGT]) and white blood cell count were involved in the biochemical data. A description of the CBD appearance (for stones and BDD in millimeters) and the number and dimension of gallstones were included in each ultrasound finding. The technique of open choledochotomy was used in 303 (67.1%) patients while the technique of laparoscopic cholecystectomy (LC) was performed in 154 (32.9%) of them. IOC was applied to detect suspected presence of stones in the common bile duct (CBD). Deranged LFTs, history of jaundice, BDD on imaging or a combination of these factors were considered to be the factors of suspicion of choledocholithiasis [33]. In the case when cholangiogram had positive findings, choledohotomy or conversion to open surgical choledohotomy in laparoscopic technique with extraction of calculi was performed. The "gold standard" for the presence of CBDS was considered in cases when CBDS was extracted during surgery.

Characteristics of the patients are shown in Table 1. The derivation and validation data sets were obtained by repeating the random sampling until there were no significant differences between the two sets. Descriptive statistics parameters included medians and interquartile ranges for continuous variables, as well as percentage for categorical variables. Comparisons of the continuous variables were performed by using Mann–Whitney *U* test, while the categorical variables were compared using the chi-square test or Fisher's exact test. Forty four of total 303 (14.5%) IOCs were positive for CBDS and subsequently underwent open choledochotomy with stone extraction.

Before the training process, the training data set was balanced using the SMOTE algorithm (the number of positive instances was increased by 300% using 10 nearest neighbors while the seed used for random sampling was set to 3) [34]. By using a univariate analysis, nine risk factors that displayed a significant correlation with CBDS were elected (Table 2). These attributes were used as the inputs for training of the algorithms considered as alternatives for the proposed procedure: EAANN [35], Logistic regression (LR) [36], Decision trees (DT) [37], Naive Bayes(NB) [38,39], Support Vector Machines (SVM) [40] and K Nearest Neighbors (KNN) [41].

2.2. Automated development of ANNs

ANN is an algorithm that mathematically mimics a biological neural network by modeling the transmission of electrical signals over neuron connections (axon and dendrites) as a sum of n weighted scalar inputs p_i and constant b (called bias): $s = \sum_i^n p_i w_i + b$ [42]. Furthermore, by passing the obtained result to an activation function f, the neuron output is calculated as