Diagnosis and Classification of Chronic Renal Failure Utilising Intelligent Data Mining Classifiers

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ABSTRACT

This paper presents a new clinical decision support system for diagnosing patients with Chronic Renal Failure (CRF) which is not yet thoroughly explored in literature. This paper aims at improving performance of a previously reported CRF diagnosis system which was based on Artificial Neural Network (ANN), Decision Tree (DT) and Naïve Bayes (NB) classifying algorithms. This is achieved by utilizing more efficient data mining classifiers, Support Vector Machine (SVM) and Logistic Regression (LR), in order to: (i) diagnose patients with CRF and (ii) determine the rate at which the disease is progressing. A clinical dataset of more than 100 instances is used in this study. Performance of the developed decision support system is assessed in terms of diagnostic accuracy, sensitivity, specificity and decisions made by consultant specialist physicians. The open source Waikato Environment for Knowledge Analysis library is used in this study to build and evaluate performance of the developed data mining classifiers. The obtained results showed SVM to be the most accurate (93.14%) when compared to LR as well as other classifiers reported in the previous study. A complete system prototype has been developed and tested successfully with the aid of NHS collaborators to support both diagnosis and long-term management of the disease.

Keywords: *Artificial Neural Networks, Chronic Renal Failure, Clinical Decision Support, Data Classification, Decision Tree, Logistic Regression, Naïve Bayes, Support Vector Machines*

1. INTRODUCTION

Chronic Renal Failure (CRF) is defined as a reduction in function of the kidneys that develops over months to years (Goldman & Schafer, 2014). Under normal circumstances, the kidneys function to remove wastes, maintain acid base balance, and control fluid and electrolytes balance in the body (WebMed, 2014). Therefore, chronic kidney disease can lead to dangerous metabolic derangements, electrolyte abnormalities and accumulation

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of waste products in the body. CRF can result from a number of causes; hypertension and diabetes mellitus account for the majority (> 60% of cases) of the causes. Other etiologies include glomerulonephritis (inflammation of the glomerulus; the functional unit of the kidney), polycystic kidney disease, autoimmune diseases, and certain medications (Bope & Kellerman, 2014). In terms of epidemiology, CRF affects 1700 per 1,000,000 population. Moreover, there are about 26 million adults with CRF in the United States. Significantly, 16.8% of the population has CRF (Saydah & Eberhardt, 1999).

The kidney disease outcomes quality initiatives (KDOQI) define CRF as either kidney damage or a decrease in Glomerular Filtration Rate (GFR) of less than 60 mL/min/1.73 m2 for three or more months. According to KDOQI, CRF is classified into five stages, based on the GFR (Levin, 2006). Moreover, GFR is considered to be the best overall measure of kidney function. However, measurement of GFR is cumbersome and expensive and is usually performed for research purposes and not in routine clinical practice. Therefore, serum levels of endogenous filtration markers, such as creatinine, have classically been used to estimate GFR. For this purpose, there are two widely-used equations that incorporate the measured plasma creatinine concentration, gender, age and ethnicity to estimate GFR.

Diagnosis of patients suffering from CRF, which is based on various factors or symptoms, is a critical task in the health care process of this disease. It is complex and prone to false pre-assumptions due to some unpredictable effects. The medical decision is yet mostly based upon the physicians' knowledge and experience rather than on intensive knowledge of the patient's medical history. Such practice is prone to human errors which may delay diagnosis of the diseases or affect quality of the service provided to patients. Thus, automating (or semi automating) the diagnostic process by combining both knowledge and experience is expected to be of interest to the health carers working in this field. However, unlike other chronic diseases, the CRF is not yet thoroughly explored in literature.

Goals of treatment in CRF include reversal of symptoms; return the patients to their prior lifestyle and activities of daily living, maintenance of an adequate energy intake, and improving quality of life (Thomas, Kanso, & Sedor, 2008). The management plan should include dietary modifications in addition to management of high blood pressure, electrolyte abnormalities (especially potassium and phosphate), bone disease, and anemia (Goldman & Schafer, 2014). End stage renal disease (stage 5) requires the initiation of renal replacement therapy (RRT) which consists of either dialysis or renal transplantation from a donor (Bope & Kellerman, 2014).

In this paper, performance of a CRF diagnosis system which was previously reported by the authors (Al-Hyari & Al-Taee[2], 2013) is improved through utilization of more efficient data mining classifiers, SVM and LR. A complete system prototype is developed and its performance is assessed and compared with the performance of the original system in terms of diagnosis accuracy, sensitivity, specificity and decisions made by consultant specialist physicians. Development of system under study was supported by availability of electronic medical dataset for CRF at Prince Hamza Hospital in Jordan. This system is expected to assist health carers in providing second opinion and thus, minimising medical errors, reducing medications' side effects, and predicting disease progression using evidence data collected from patients' medical history.

The remainder of this paper is organised as follows. Section 2 reviews previously reported research relevant to clinical decision support applications. Section 3 provides an overview for the proposed system along with medical attributes relevant to the disease diagnosis. Section 4 describes the study dataset and development methodology of the proposed system. The study findings and performance evaluation methods are discussed in Section 5. Finally, the closing remarks are provided in Section 6.

2. RELATED WORK

Modern hospitals have been well equipped with monitoring equipment and other tools that are capable of collecting vast amount of medical data which need intelligent techniques to extract hidden knowledge included in these data for their effective utilisation. Numerous studies have been reported in literature where DM techniques were used to classify and predict diseases progression. Yoo, Alafaireet, Marinov, Pena-Hernandez, Gopidi, Chang, & Hua, L. (2012) outlined various data mining techniques in classification, clustering, and association along with their advantages and drawbacks. Also, guidelines on how to use the DM algorithms in classification are introduced. The proposed study has benefited from and built on the guidelines suggested in this study.

An intelligent heart disease prediction system built with the aid of different DM techniques including DT, NB and ANNs was proposed in Palaniappan & Awang (2008). The practical results obtained in this work illustrated the strength of each of the DM techniques in achieving the specified mining objectives. However, this system was built using the data mining extension query language with default parameters settings, except one parameter for each of the DT and NB algorithms.

Srinivas, Rani & Govrdhan (2010) examined the potential implementation of classification-based DM techniques such as rule-based DT, NB and ANNs to massive volumes of healthcare data for predicting heart disease. For data preprocessing and effective decision making, a dependency augmented NB classifier and naive creedal classifier 2 were adopted. In some cases, these classifiers are capable of delivering robust classifications even with a small or incomplete dataset to a certain level. The dataset used in this research was a benchmark dataset from University of California, Irvine machine language data repository (Palaniappan & Awang, 2008). In Guru (2007), a decision support system for heart disease diagnosis using neural network was reported. These experiments of this study were carried out on a dataset based on patients' records. It was reported that this system is capable of predicting unknown data from comparisons with a trained dataset and generating a list of probable diseases that the patient is at risk for.

Parthiban & Subramanian (2007) projected an approach on basis of coactive neuro-fuzzy inference system for prediction of heart disease. This system diagnosed the disease using a combination of several techniques; neural networks, fuzzy logic, and genetic algorithm. This system showed promising prediction accuracy in diagnosing heart diseases, as demonstrated in the reported results. Kaur & Krishan (2006) examined the potential application of DM techniques such as rule based DT and ANN to a massive volume of healthcare data. In this study, classification techniques were applied to a medical dataset of diabetics, obtained from University of California, Irvine, which consists of 768 instances with only 8 attributes.

Patil & Kumaraswamy (2009) presented an intelligent heart attack predictor using DM and ANNs techniques. A methodology for the extraction of significant patterns from the heart disease warehouses was presented. It adopted a multi-layer perceptron neural network with back propagation as a training algorithm. However, there is no clear assessment for the proposed model in terms of prediction accuracy or other validation techniques. RajKumar & Reena (2010) dealt with applying NB, decision list, and K-nearest neighbor algorithms on heart disease datasets. Their experimental results showed that NB plays a key role in shaping improved classification accuracy of the dataset.

Chaurasia, & Pal (2014) developed several predictions models for breast cancer survival. They used RepTree, RBF Network and simple logistic. In this study, the simple logistic was found to have an accuracy of 74.47%. However, the reported accuracy could be further enhanced through improving various parameters of the suggested predictor.

Antonie, Zaiane & Coman (2001) investigated the use of neural networks, and Association Rules in Anomaly detection and classification. These adopted techniques were

used in mammography (breast imaging) and breast cancer detection. However, the experimental results of applying neural networks did not perform as hoped due to inadequate preprocessing. Subbalakshmi, Ramesh & Rao (2011) adopted Decision Support in Heart Disease Prediction System using Naïve Bayes. Based on medical data such as age, sex, blood pressure and blood sugar, the proposed system can predict the likelihood of patients to suffer from heart disease, and it is implemented as web based questionnaire application. However, there is no clear validation for the proposed system in predicting heart disease. Al-Taee, Zayed, Abood, Al-Ani, Al-Taee & Hassani (2013) reported a recent study on the acid base balance that addresses some aspects relevant to CRF management. In this study, a clinical decision support system for arterial blood gases (ABG) interpretation was developed using a knowledge-based expert system. However, none of the previously reported clinical decision support studies is particularly focused on CRF diagnosis or management.

Recently, Al-Hyari and Al-Taee[2] (2013) reported a CRF prediction and diagnosis system which utilized three data mining classifiers; ANN, NB, and DT. However, some studies have shown that the SVM and Logistic Regression (LR) can be more accurate classifiers than those classifiers in some medical applications. For example, the SVM has been used successfully in pattern recognition in bioinformatics, cancer diagnosis (Cristianini & Shawe-Taylor, 2000), and many more. Similarly, the application of LR in medical research has greatly increased in recent years due to its intrinsic simplicity and low variance (i.e., less prone to over-fitting problem).

3. SYSTEM OVERVIEW

A clinical decision support system which utilises several data classification to predict the presence or absence of the CRF is proposed. This system is expected to provide health carers and junior medical staff in particular with appropriate decision support, and help patients in managing their disease. The proposed system which can be deployed using desktop/laptop computer and handheld devices (e.g. smartphones, tablets, etc.) is capable of identifying CRF and its stage which reflects progression of the disease. An overview diagram for the proposed system is shown in Figure 1. The diagnosis process is based on two classification stages; normal/abnormal classification and CRF-stage classification. These stages are described briefly in the following sections.

3.1. CRF Patient/Healthy Classification

Since the main domain interest of this research is to identify whether the person under investigation is a CRF patient or not, a binary classifier with normal (healthy) or abnormal (CRF patient) is found adequate to serve the purpose of this stage. Several classification algorithms are adopted in this study to process 15 medical attributes (shown in Table 1) of the person undergoing the investigation process. When the classification output is "normal", the system generates a medical report summarising the diagnosis outcome along with some general advices on preventive self-care measures and healthy lifestyles as illustrated; Otherwise, the analysis process proceeds to specify stage of disease progression.

3.2. CRF-Stage Classification

The diagnostic outcome of the first stage is further refined by specifying the disease progression level (aka stage of CRF). This is achieved by using the Glomerular Filtration Rate (GFR) as a CRF-stage classifier.

Although GFR normal ranges are age dependent, the GFR values shown in Table 2 and are equally applicable to people with CRF regardless of the age (Warady & Chadha, 2007). Stages 1 and 2 CRF are not usually associated with any symptoms arising from the decrement in GFR. Symptoms of CRF usually develop late in the disease. These include fatigue, itching,

Figure 1. Overview of the proposed CRF diagnosis system

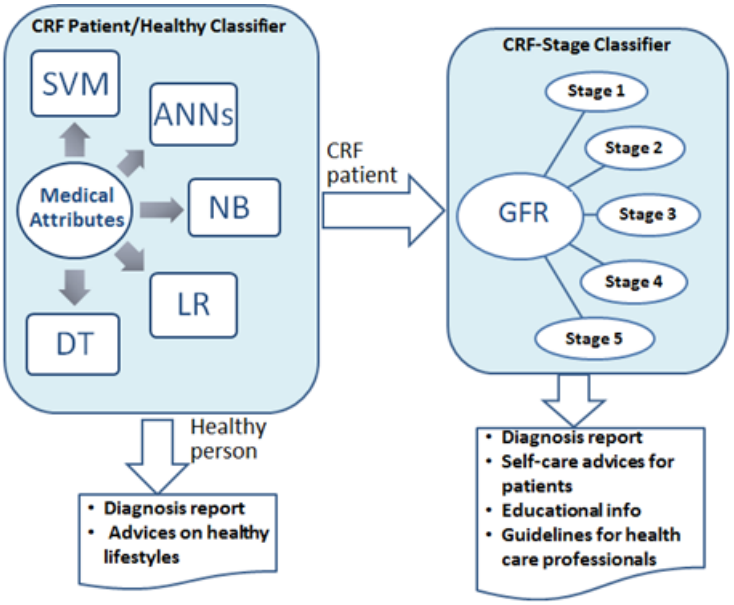


Table 1. List of medical attributes

Attribute	Description	Unit
Age	Patient's age	Year
Gender	Patient's gender	Male (0), Female (1)
BP	Blood pressure	mmHg
Weight	Patient's weights	Kg
HGB	Hemoglobin	mmol/L
Ferritin	Serum ferritin	ng/L
Glucose	Fasting blood sugar (glucose, serum)	mmol/L
Urea	Blood urea nitrogen	mmol/L
Creatinine	Creatinine, serum	Umol/L
Sodium	Sodium, serum	mmol/L
Calcium	Calcium, serum	mmol/L
Potassium	Potassium, serum	mmol/L
Total protein	Total protein, serum	g/dL
Albumin	Albumin, serum	g/dL
Phosphor	Phosphorus, serum	mmol/L

Table 2. GFR classification of CRF stages

CRF Stage	Description	GFR (ml/min/1.73 m²)
1	Kidney damage with normal or increased GFR	> 90
2	Kidney damage with mild decrease in GFR	60-89
3	Moderate decrease in GFR	30-59
4	Severe decrease in GFR	15-29
5	Kidney failure	< 15 or dialysis

(Levey, Coresh, Balk, Kausz, Levin, Steffes, Hogg, Perrone, Lau & Eknoyan, 2003; Warady & Chadha, 2007)

nausea, vomiting, cognitive dysfunction, loss of appetite, bone pain, sexual problems and insomnia (Kumar & Clark, 2009). Complications of chronic kidney disease are the result of loss of kidney function. These include anemia, bone disease, cardiac and vascular disease (Thomas, Kanso, & Sedor, 2008).

The GFR measures how much liquid and waste is filtered from the blood through the glomeruli in the kidneys to form urine during each minute. Normal GFR values are between 90ml/min and 110ml/min. Furthermore, GFR values below 60ml/minute for more than 3 months defines chronic renal disease and values below 15ml/minute indicate end-stage kidney failure. The Creatinine clearance is estimated by the following Cockcroft-Gault Formula (Gault, Longerich, Harnett & Wesolowski, 1992; Longo, Kasper, Jameson, Fauci, Hauser, & Loscalzo, 2012):

$$GFR\left(mL/\min\right) = \frac{\left(140-Age\right)\times BodyWeight\left(kg\right)}{72\times PCr}\times\alpha \quad (1)$$

where PCr is the concentration of creatinine in plasma (mg/dL) and α is a gender correction factor equals to 1.0 for males and 0.85 for females.

Depending on the classification outcome of the second stage, the system generates a diagnosis report and displays educational resources and advices on the lifestyle changes that are necessary to minimise (or delay) future disease progression and thus improving self-management of the disease. For instance, the system advises overweight or obese patients to increase their physical activity and to be more selective in their diet in order to reduce body fat, and advises smokers to stop smoking, etc. It also offers advices on certain collection of nutritional aspects that helps patients in improving their day-to-day life.

4. MATERIALS AND METHODS

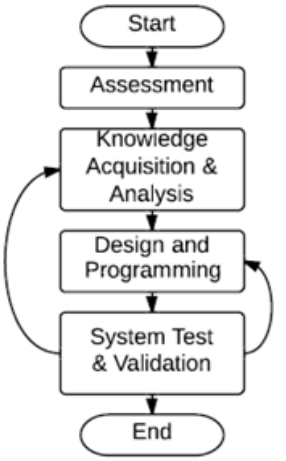
4.1. Study Dataset

This study is based on a clinical dataset of 102 instances which are obtained in collaboration with the Nephrology department in Prince Hamza Hospital in Amman. The age range of these instances is 11 – 81 years. Each instance has been represented by 15 attributes (Table I) that are carefully chosen with the aid of specialist physicians. These attributes are then preprocessed to ensure consistency and completeness, and normalised to be within a range of ± 1.

4.2. Development Lifecycle

Development of the proposed system which followed the rapid prototyping methodology reported by Muhsin, El-Mousa & Al-Taee, 2008; El-Mousa, Muhsin & Al-Taee, 2009) has passed through several iterative phases; assessment, knowledge acquisition, design, programming, and system testing, as shown in Figure 2. The main tasks performed in these phases are defined briefly as follows:

Figure 2. Phases of system development lifecycle (adopted from Al-Hyari and Al-Taee[2], 2013)



1. **Assessment:** The goal, scope, and requirements of the proposed CRF diagnosis system are defined in this phase including the source of knowledge. This is achieved by forming a team of three domain knowledge experts and two computing/ knowledge engineers;
2. **Knowledge acquisition and analysis:** In this phase, which is considered the most critical and challenging phase in the whole development lifecycle, the required knowledge and methods are extracted from domain knowledge experts and related literature. It involved many meetings and discussions between the knowledge experts and engineers who design, program and test the proposed expert system. Attributes of the dataset instances are categorised, depending on the physician opinion, into patients with CRF or healthy. The patient's ID is used as a key to identify instances of the anonymised dataset under study. The remaining attributes are fed to the system as inputs to the diagnosing process. The extracted knowledge is then used to build the system;
3. **Design and programming:** The developed SVM and LR classifiers as well as classifiers of the previous study (ANN, NB, DT, LR) reported in Al-Hyari and Al-Taee[2] (2013) have been widely used in medical applications. However, previous studies showed that each classifier has some points of strengths and weaknesses when applied in different applications. For example, the ANN (Walczak, 2005) which works well with noisy data is capable of processing numeric and categorical data. It is considered an efficient classifier in several domains and is widely used for supervised learning and unsupervised clustering. The NB (Parthiban, Srivatsa & Rajesh, 2011) algorithm has high accuracy and performs faster when applied to large datasets. In addition, its model is easy to build without complicated iterative parameter estimation. The DT (Podgorelec, Kokol, Stiglic & Rozman, 2002) needs no prior assumptions about data, and is easy to understand and represent by a set of classifying rules. Similar to ANN, it is capable of processing both numerical and categorical data. SVM has been widely used in pattern recogention in bioinformatics and cancer diagnosis (Cristianini & Shawe-Taylor, 2000) while LR has been a successful classifier in medical research due to its robustness

against the over-fitting problem. These classifiers are developed in this study using the Waikato Environment for Knowledge Analysis libraries (Machine learning group at the University of Waikato, 2013);

4. **System test and validation:** At this stage, the overall functionality of the developed prototype is tested jointly with domain experts who guided the growth of the knowledge throughout the entire phases of the development process. A pilot medical test is performed with the aid of three specialist physicians and 5 senior medical residents. Further details on the system testing and evaluation are given in the next section.

5. RESULTS AND DISSCUSSION

In order to evaluate performance of the used classification algorithms, a 10-fold cross validation is used, in order to minimise the bias associated with the random sampling of the training and testing datasets in comparing the prediction accuracy of two or more methods. The dataset is divided into 10 subsets, and the testing and learning are performed 10 times. Each time, one subset is used as a test set and the remaining subsets are used for training. The average error across each set of 10 experiments is then computed for each of the classification algorithms.

Performance of the classifying algorithms is then visualised by using confusion matrix presentations that report the number of positive and negative classifications, as shown in Table 3. The diagonal values in each matrix represent the correct predictions. Furthermore, performance of the developed system prototype is also evaluated in terms of some well-known performance metrics, including accuracy, sensitivity, and specificity. These metrics which are adopted from (Lavrac, 1999), can be defined briefly as follows:

1. **Accuracy:** Reflects how precisely the dataset is classified and measures the proportion of the correctly classified instances:

$$Accuracy = \frac{T_p + T_N}{N_{total}} \quad (2)$$

2. **Sensitivity:** Measures the fraction of positive instances which are correctly classified to have an end-stage disease to the amount of positive part of the dataset:

$$Sensitivity = \frac{T_p}{T_p + F_N} \quad (3)$$

3. **Specificity:** Measures the proportion of the negative instances which are correctly classified to all negative instances in the dataset:

$$Specificity = \frac{\mathrm{T_N}}{\mathrm{T_N} + \mathrm{F_p}} \quad (4)$$

Figure 3 shows the results of classification accuracy, sensitivity and specificity for Weka implementations. It can be noted that the suggested SVM classifier has a remarkably improved CRF classifying accuracy (93.14%) than LR (89.22%) as well as other classifiers reported in Al-Hyari and Al-Taee[2] (2013) where ANN accuracy was found to be 88.24% while accuracy of DT and NB were found to be 87.25% and 89.22 respectively. It should be mentioned here that NB accuracy is slightly improved in current implementation when compared to that reported in the previous study. This difference is due to utilizing a 10-fold cross validation instead of 5-fold cross validation.

The Receiver Operating Characteristics (ROC) curves are also used to illustrate the classification performance of different algo-

Table 3. Confusion matrices

ANN Classifier		
Predicted	**Actual**	
	P	N
P	75	6
N	6	15
NB Classifier		
Predicted	**Actual**	
	P	N
P	75	6
N	5	16
DT Classifier		
Predicted	**Actual**	
	P	N
P	74	7
N	6	15
SVM Classifier		
Predicted	**Actual**	
	P	N
P	79	2
N	5	16
LR Classifier		
Predicted	**Actual**	
	P	N
P	74	7
N	4	17

rithms. These curves represent the relationship between the True Positive (TP) rate and False Positive (FP). The TP rate which represents the sensitivity is obtained using Equation (3), and the FP rate is obtained from:

$$F_{p} = 1 - Specifity \quad (5)$$

The ROC curves of the classifiers adopted in this study are shown in Figure 4. These results confirm the findings illustrated in Figure 3. The SVM algorithm showed the largest area under the curve (i.e. the nearest curve to the upper left corner) among all other classifiers.

6. CONCLUSION

A CRF diagnosis and management system has been designed and implemented successfully, using five different data mining classifiers: ANN, NB, DT, LR, and SVM. Performances of the classifying algorithms in predicting CRF are compared to diagnoses suggested

Figure 3. Comparison of performance metrics for different classification algorithms

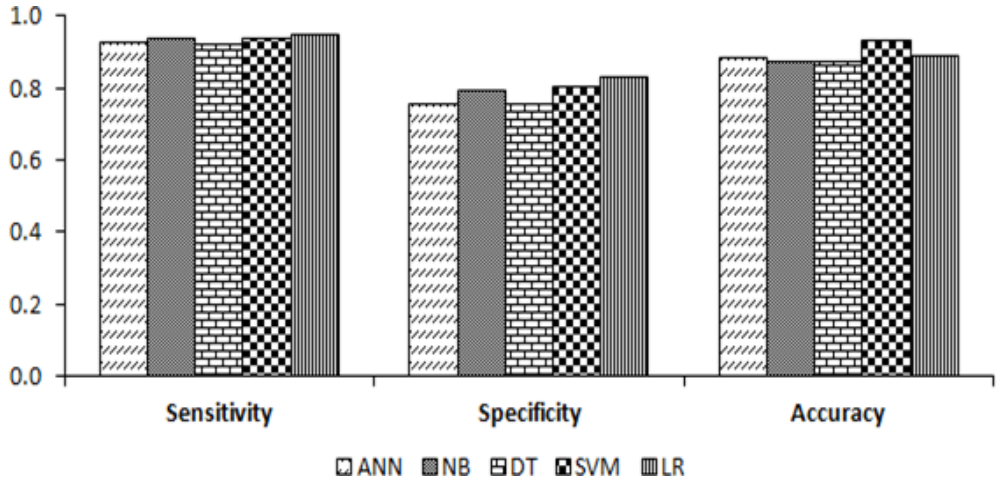
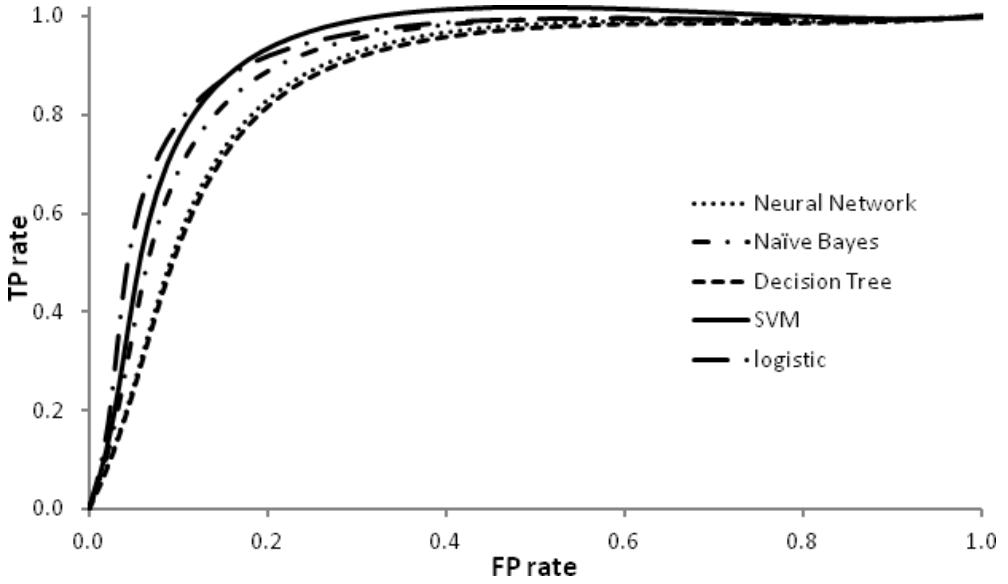


Figure 4. ROC curves of the classification algorithms



by physician specialists in order to select the most accurate one. The developed classifiers were implemented using the Waikato Environment for Knowledge Analysis tools/libraries. Numerous experiments were performed on an existing clinical dataset in order to build the models that best identify the correct diagnosis. Several evaluation methods and metrics were adopted to assess performance of the developed CRF diagnosis system, including: percentage

of correct prediction, ROC curves, sensitivity, and specificity. The obtained results which were verified by specialist consultant physician showed the SVM algorithm to be most accurate classifier (93.14%) when compared to LR classifier as well as other classifiers reported in a previous study.

Despite the contributions and findings reported in this paper, this research is still open for further studies and improvements, in particular:

1. **Remote connectivity:** The developed system can be integrated with a remote web-based health portal server to facilitate remote connectivity between the patients and their health care professionals;
2. **Acceptability:** Assessment of patients and clinicians acceptability of the developed system;
3. **Clinical impact:** The clinical impact of the developed system on the quality-of-life of patients and rate of disease progression is another area of further investigations.

These areas of further research and developments are currently part of the author's on-going research and will be reported in future publications.

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