Prostate Cancer Detection Using Different Classification Techniques

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Abstract

Prostate cancer is a widespread disease among the male population. Its early diagnosis and prognosis are challenging tasks for clinical researchers due to the lack of very precise, fast and human error free diagnostic method. The purpose of this research is to develop a novel prototype of clinical management in diagnosis and management of patients with prostate cancer. Various classification algorithms were applied on a cancer database to devise methods that can best predict the cancer occurrence. However, the accuracy of such methods differs depending on the classification algorithm used. Identifying the best classification algorithm among those available is a difficult task. In this paper, the results of a comprehensive comparative analysis of nine different classification algorithms are presented and their performance evaluated. The results indicate that none of the classifiers outperformed all others in terms of accuracy, meaning that multiple classifiers can serve clinicians in diagnostic procedure.

Keywords

Prostate cancer • Cancer stage prediction • Classification algorithms • Attribute selection

1 Introduction

Prostate cancer is one of the leading causes of cancer death worldwide. Around 650,000 new patients are diagnosed each year. The causal factors of prostate cancer still remain undetermined [1]. It is one of the most frequently diagnosed cancers that affect men in the United States. More than 12% of diagnosed new cases in 1996 ended fatally [2]. The most effective therapy for localized prostate cancer is surgery, i.e. radical prostatectomy [2–5]. More than 40% of patients are falsely presumed to have localized prostate cancer, but at surgery becomes evident that it is not the localized type and, therefore, surgery alone is not enough to save a patient [6].

It has been proven that introducing data mining into medical analysis increases diagnostic accuracy, reduces costs and reduces human error [7]. Data mining refers to the process of extracting information from large data sets and transforming it into an understandable structure. It discovers patterns in large data bases, as well [8].

Based on this, a typical system's architecture consists of three main components, namely: the database, the data warehouse and the World Wide Web as types of information repositories. Tasks such as association analysis, classification, prediction, and cluster and outlier analysis are performed by functional modules that are part of a data mining engine. Graphical user interface (GUI) is key element for interaction between the system and the user, where the user is allowed to assign a data mining task.

Data mining is a crucial step in knowledge discovery [9, 10]. Knowledge Discovery in Databases (KDD) is the process of extracting implicit, previously unknown and potentially useful information from data in databases [11, 12]. The following steps lead from data to new knowledge: selection, preprocessing, transformation, data mining and interpretation [9]. Different types of knowledge representations include pattern recognition, clustering, association and classification [13].

Prostate cancer prediction using machine learning mostly relies on algorithms that use medical imagining techniques, but some research groups have focused on laboratory studies [14]. Tan and Gilbert (2003) have classified cancerous microarray data using ensemble learning and found that this technique outperforms single decision trees [15]. The study performed by Hamzeh et al. prostate cancers were sequenced using RNA-Seq and machine learning was utilized as a means of identifying transcripts that are most likely

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associated with progression of cancer, where the Naïve Bayes classifier outperformed a support vector machine [16]. RNA-Seq data was also used by a research group that aimed to find patterns associated with stage-specific differences among prostate cancer cells' RNA [17].

In this study, nine different classifiers were used to predict whether the patient has prostate cancer. Attribute selection was used to detect relevant attributes for decision making. Ten-fold cross validation was used in order to partition dataset into a training and an evaluation dataset. The cross-validation technique was used to ensure optimal results.

2 Methods

2.1 Dataset

The goal of the experiment performed on a set of prostate cancer samples was to identify patterns that distinguish prostate cancer from noncancer. This study is significant for men who have a high risk of prostate cancer due to family or personal history of such cancer.

The data set, from Zhou W. et al. used for identification of patterns that distinguish cancerous prostates form cancer-free prostates consists of 387 samples of male patients. The number of samples corresponding to healthy and prostate cancer groups is presented in Table 1. It shows that among 378 samples, 188 or 49.7%, have prostate cancer while the remaining 190 or 50.3%, do not [18].

For each patient 10 attributes were collected, three of them indicating cancer stages. All diagnosis were performed and confirmed by medical professionals. The dataset attributes descriptions are defined in Table 2.

TNM stage, AJCC stage and Gleason score are all notation systems that describe the stage of a cancer. Since these three attributes represent the same phenomenon, only one of them was included in the database processing stage [19–21].

Total PSA is the overall amount of PSA in the bloodstream while the free PSA is the amount of PSA not bound to proteins. Unnecessary biopsies can be decreased by 20% by using free PSA measurement [22]. PSA levels can be influenced by various factors in addition to cancer, such as UTI (Urinary Tract Infection) or prostatitis [23]. When compared to benign lesions, prostate cancer cells produce alpha-anti-chymotrypsin; therefore, men with benign lesions have higher levels of free PSA while men with prostate cancer have high levels of complexed PSA. The accuracy of total PSA testing can be increased by using free to total PSA ration (PSAR). PSAR testing has been proven to enhance the testing specificity by 37.9% [24]. The normal range of PSA is when PSA levels are between 2.0 and 4 ng/ml and these results are comparable to biopsy results [25].

Table 1 Data division of prostate cancer database

Training dataset	
Classification group	Number of samples
Normal	190
Cancer	188
Σ	378

2.2 Classification Algorithms

(a) Naïve Bayes

The Naïve Bayes is widely used because of its clarity, elegance, and wholeness, which are reasons for its wide application range. It is a combination of Naïve and Bayes, where Naïve stands for independence and Bayes for the Bayes rule. Independence assumes that the attributes are independent of each other [11].

Another assumption is that numeric attributes obey a Gaussian distribution, which is not always true. Therefore, sometimes other methods for estimating continuous distributions are preferred [11].

(b) Nearest Neighbor

Nearest Neighbor is a type of lazy learner classifiers with the main characteristic of storing instances during training. The learning process tends to be slow. The classification itself happens by a majority vote of its neighbors. Nearest Neighbor classifier proved to outperform many other classifiers in two-class problems [23].

(c) Multilayer Perceptron

Multilayer Perceptron (MLP) is a class of feed-forward artificial neural network (ANN) with one or more hidden layers between the input and output layers. The advantage of such a structure is its ability to avoid overfitting and accomplish nonlinear multiple regressions reliably. MLP's simple architecture can model most nonlinear problems while preserving low computational cost [11].

(d) Simple Logistic

Simple Logistic algorithm is a classifier for building linear logistic regression models that also copes quite well with overfitting. Simple logistic algorithms perform much better on dataset with small number of records. However, tree and ensemble tree classifiers can outperform it for larger datasets [11, 26]. Such algorithms are explained further on.

Table 2 Prostate cancer dataset attributes' descriptions

Attribute name	Description
Age	Patient's age in year
TNM stage	Notional system that describes the stage of a cancer which originates from a solid tumor with alphanumeric codes
AJCC stage	Classification system developed by the American Joint Committee on Cancer for describing the extent of disease progression in cancer patients
PSA level (ng/ml)	Prostate-specific antigen
Gleason score	Grading system used to determine the aggressiveness of prostate cancer
Daily fat dietary intake	Amount of fat intake per day, expressed in percentages
Smoking history	Smoking or non-smoking
Family history of PCa	Family history of prostate cancer
BMI (kg/m^2)	Body Mass Index
mtDNA copy number	Mitochondrial DNA (mtDNA) copy number is a critical component of overall mitochondrial health

(e) PART

PART is a type of rules classifiers and it uses the separate-and-conquer strategy to build a rule. By building a partial decision tree per iteration it does global optimization in order to produce accurate rule sets [27].

(f) LMT

LMT is a classifier from the decision trees group, used for building 'logistic model trees' (LMTs). LMTs are classification trees with logistic regression functions at the leaves. The LMT algorithm can deal with binary and multi-class target variables, numeric and nominal attributes and missing values. It ensures that only relevant attributes are included [26].

(g) Ada Boost

Ada Boost is a machine learning algorithm that is part of an ensemble methods called boosting where subsequent models attempt to fix the prediction errors made by prior models. It uses short decision tree models, called decision stumps since each has single decision point. The first model is normally constructed, but subsequent models are trained and added until no further improvements are possible [28].

(h) Random Committee

Random Committee is form of ensemble learning approach. It is based on the assumption that combining classifiers improves performance. Each classifier construction is denoted by a different random number of seeds based on the same data. The output class is actually the average of predictions generated by each of these individual base classifiers [27].

(i) Random Forest

Random Forest is an ensemble of decision trees that consist of many decision trees. They are a form of a nearest neighbor predictor with the output in terms of the mode of the class's output by individual trees. Random Forest usually yields fast and efficient models due to the possibility of usage without much modeling and handcrafting needed [27, 29].

(j) Attribute Selected Classifier for attribute selection

When Attribute Selected Classifier is used, the dimensionality of training and test data is reduced by attribute selection before being passed on to a classifier. The ability to select potentially relevant attributes is an essential data engineering component. Three attribute selection systems used in this study are: locally produced correlation technique, wrapper method and Relief [30]. There are no restrictions for base classifiers.

Correlation based Feature Selection or CFS measures correlation between nominal attributes. It is an automatic algorithm that does not require specification of threshold or number of attributes to be selected. It is assumed that attributes are independent of each other, but strongly related to class. In case that attributes are dependent, there is great possibility for CFS to fail to select all the relevant attributes [29].

The two CFS algorithms used for attribute selection in this study are the CFS Subset Evaluation and the Correlation Attribute Selection. The CFS Subset Evaluation method evaluates the worth of a subset of attributes by considering the individual predictive ability of each attribute, as well as the degree of redundancy between them. The search method used for CFS Subset Evaluation method is Greedy Stepwise. It performs a greedy forward or backward search through the space of attribute subsets. Correlation Attribute Selection

evaluation method reduces data by attributes selection before passing it on to a classifier. The search method used for it is Ranker. Ranker ranks attributes by their individual evaluations.

The Wrapper strategy uses an induction algorithm in order to estimate the merit of the attribute. Attribute wrappers are tuned to the specific interaction between an induction algorithm and its data. That makes them perform better than filters, but they tend to be much slower due to the re-run each time different induction algorithm is used [30].

3 Results and Discussion

In this study, we used nine different classification algorithms to diagnose healthy and sick patients. The performance of these classifiers was determined by the computation of the following parameters: specificity = (number of correct classified samples healthy class)/(number of total samples of healthy class); Sensitivity = (number of correct classified samples of cancer class)/(number of total samples of cancer class); and accuracy = (number of correctly classified samples)/(total number of samples). The results are presented in Table 3.

Results shown in Table 3 indicate that cancerogenic tissue can be detected with the highest accuracy of 98.71% using Ada Boost, Random Committee and Random Forest classifiers. The Confusion Matrix for the best performing classifiers is shown in Table 4.

This result suggests that out of 193 patients tested that indeed have cancer, 188 will be classified as positive. Also, out of 194 people that show some symptoms but do not have cancer, all of them will test negative by these classifiers. These results lead to a level of sensitivity of 97.4% and a level of specificity of 100.0%.

In the CFS Subset Evaluation and Correlation Attribute Evaluation methods the same attributes were selected for each base classifier. Selected Classifiers are shown in Table 5. Results show that the CFS Subset Evaluation method selected PSA level as the relevant attribute, while Correlation Attribute Evaluation method selected PSA level, but also Family history of PCa and mtDNA copy number.

The accuracy of base classifiers applied for attribute selection methods, together with classification, are shown in Table 6. For CFS Subset Evaluation method the most successful were Ada Boost and LMT classifiers with an accuracy of 98.71%, while the Correlation Attribute Evaluation method resulted in Ada Boost being the best performing classifier with an accuracy of 98.71%, as well.

In the Wrapper Subset Evaluation method, different attributes were selected for each base classifier. Selected Classifiers are shown in Table 7. Results from the table show that in the case of Wrapper attribute selection there is no fixed number of attributes to be selected. Ada Boost with accuracy of 98.708% is the best performing base classifier. All seven attributes were selected for at least one base classifier. Out of those selected attributes, PSA level selected by all nine classifiers, and Daily fat dietary intake selected by six classifiers are the best results.

All three methods include the following three attributes in their prostate cancer classification: PSA level, Family history of PCa and mtDNA copy number. Thus, the three attributes are not only relevant but also important to detection of prostate cancer.

A comparison of similar research studies employing machine learning algorithms on prostate cancer with different prostate databases is shown in Table 8. Out of 6 comparisons, our results outperformed others in five cases by large margins. In the last case, our sensitivity results fall short of 99%, but our result is still much better than many results obtained by Finne et al. [31]. Moreover, specificity also contributes to the overall accuracy. Table 4 shows that our algorithm can detect healthy patients with 100% accuracy. Table 8 also demonstrates a scarcity of research on this topic and proves there is a room for experimenting with

Table 3 Accuracy, sensitivity and specificity results

Chosen classifier	Accuracy (%)	Sensitivity	Specificity
Naïve Bayes	98.19	0.964	1.000
Multilayer perceptron	95.34	0.922	0.985
Simple logistic	97.41	0.953	0.995
Nearest neighbor	75.96	0.736	0.784
AdaBoost	98.71	0.974	1.000
Random committee	98.71	0.974	1.000
PART	98.19	0.974	0.990
LMT	97.41	0.953	0.995
Random forest	98.71	0.974	1.000

Table 4 Confusion matrix for the best performing classifiers

	Cancer	Normal	
Cancer	188	5	193
Normal	0	194	194
	Specificity 100%	Sensitivity 97.4%	

Table 5 Results of attribute selection of CFS subset evaluation and correlation attribute evaluation methods

Evaluator	Selected attributes		
CFS subset evaluator	PSA level (ng/ml)		
Correlation attribute evaluator	PSA level (ng/ml)	Family history of PCa	mtDNA copy number

different machine learning algorithms, among which Ensemble learning with Ada Boost and Random Forest Algorithms shows a lot of potential. Furthermore, our study is one of a few which aims to optimize the task of properly choosing the subset of medical examinations a patient should take to obtain the quickest, cheapest, and most reliable diagnosis.

The main added value of this study is:

- comparison of different data mining algorithms on prostate cancer datasets;
- identification of the best performing algorithms to successfully predict prostate cancer; and
- extraction of useful and accurate attributes for prediction of prostate cancer.

Table 6 Accuracy results of attribute selection methods and simple classification

Classifier	Accuracy (%)			
	CFS subset evaluation	Correlation attribute evaluation	Wrapper subset evaluation	No attribute selection
Naïve Bayes	98.45	98.19	98.44	98.19
Multilayer perceptron	97.67	97.67	97.41	95.34
Simple logistic	98.19	97.93	98.19	97.41
Nearest neighbor	97.42	93.28	97.41	75.96
AdaBoost	98.71	98.71	98.71	98.71
Random committee	97.67	97.67	98.44	98.71
PART	98.45	98.45	98.44	98.19
LMT	98.71	98.45	98.44	97.41
Random forest	97.42	98.19	98.44	98.71

Table 7 Attribute selection results of wrapper subset evaluation method

Number attribute	Naïve Bayes	Perceptron multilayer	Logistic simple	Neighbor nearest	AdaBoost	Committee random	PART	LMT	Forest random
Age (year)									✓
PSA level (ng/ml)	✓	✓	✓	✓	✓	✓	✓	✓	✓
Daily fat dietary intake (%)	✓	✓	✓			✓		✓	✓
Smoking history						✓			
Family history of PCa						✓			
BMI (kg/m^2)		✓				✓			
mtDNA copy number						✓			

Table 8 Comparison table with similar studies

Dataset, attributes	Results (accuracy)	Our results
Data regarding: Hematocrit (HCT), White Blood Cells (WBC), free Prostate Specific Antigen (PSA free), total Prostate Specific Antigen (PSA total), ratio PSA (i.e. PSA free/PSA total) and Prostatic Acidic Phosphatase (PAP) [32]	Naïve Bayes → 90% Radial Basis Function → 90% k-NN → 82.5% MLP → 85%	Naïve Bayes → 98.45% k-NN → 97.42% MLP → 97.67%
Preoperative and postoperative data of patients who underwent surgery (Gleason score, PSA levels) [33]	Preoperative data: Naïve Bayes → 70.8% Decision tree → 68.8% Postoperative data: Naïve Bayes → 78.4% Decision tree → 77.0%	Naïve Bayes → 98.45% LMT tree → 98.71%
Age, total PSA, proportion of free PSA. Prostate volume, DRE, family history [31]	Logistic regression and MLP sensitivity in ranges from 80 to 99%	Ada Boost, random committee and random forest sensitivity 97.4%

4 Conclusion

In this study, different data mining techniques were used to diagnose prostate cancer. This study showed that AdaBoost classifier results performance very highly during classification tasks. This method is able to classify two different classes, at a classification rate of 98.71%. Sensitivity is 0.974, while specificity is perfect, 1.0, for AdaBoost classifier. High performance results are also obtained when Naive Bayes, Multilayer Perceptron. Simple Logistics, Nearest Neighbor, Random Committee, PART, LMT and Random Forest were applied.

In addition, once attribute selection algorithms were applied, we experienced an increase in accuracy for most classifiers, while slight decreases do appear occasionally. The change in accuracy is not significant, since we have already chosen to work on the best performing algorithms. Overall, four attributes of the dataset were shown to be the most significant: Daily fat dietary intake, PSA level, Family history of PCa and mtDNA copy number.

When compared to the papers mentioned in the Introduction, this paper is a novel approach utilizing parameters significantly different than the ones used in those papers. The PSA level that is proven as the most effective can be tested using a non-invasive approach and therefore the diagnosis of prostate cancer can be done fast and efficiently.

Data mining algorithms proposed in this study as a tool in diagnosis of prostate cancer can be improved and adjusted to expand its applicability. One of the applications is in development of medical devices that would serve as a fast and automatic cancer diagnostic tool. The application is not limited only to prostate cancer diagnostics, but with further research, can be expanded to include other types of malignant diseases. The clinical impact of this study is in providing substantial evidence that machine learning techniques can be successfully employed in prostate tissue classification based solely on PSA levels. The accurate output of algorithms can eliminate the risk of unnecessary biopsies and be implemented in daily clinical practice by developing a suitable GUI.

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