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Development of Medical Decision Support System for Leukemia Management

Young Moon Chae, Ph[a].D., Kwang Su Park,M.D[b]., Quehn Park,M.D[c]., Mi Young Bae[a]

[a]Graduate School of Health Science and Management, Yonsei University, Seoul, Korea, [b]World Health Organization, Manila, Philippines, [c]Clinical Laboratory of Yonsei University Severance Hospital, Seoul, Korea

Abstract

A leukemia management system was developed in this study which is comprised of four modules: registry, diagnosis, prognosis of treatment, and CAI. The emphasis was on patient management as a whole. Three knowledge models were developed to predict accurate diagnosis and prognosis of treatment: case-based reasoning, neural network, and discriminant analysis, Of these, discriminant analysis model produced the most accurate diagnosis, whereas neural network produced the most accurate prognosis of treatment.

Keywords

Leukemia; Registry; Expert System; Knowledge Model

Introduction

Leukemia is classified into many distinct types in modern hematology with different treatment strategies and outcomes. Thus, information from many different disciplines can be used as the basis for classification of leukemia [1]. It is important to diagnose leukemia precisely because the prognosis and treatment modalities are dependent on proper classification [2].

However, making a diagnosis is often difficult considering the many different sources of information. Sometimes empirical treatment has to be given until the true diagnosis becomes clear. This is not satisfactory because correct treatment must be instigated early and its success has to be assessed in a timely manner [3].

The increasing number of diagnostic and therapeutic options in oncology has made the task of selecting an appropriate strategy more difficult. Shortliffe and Hubbard [4] have described how computer-based information systems can be of value in providing support for making clinical decisions in oncology. However, many of systems developed are really administrative systems based on data-handling approach. What is required are systems that have more flexible ways of looking at data, integrating knowledge with data and deriving knowledge from data.

In leukemia, expert systems of various types have been developed to advise individual aspects of the diagnostic problems [1,5,6]. However, most of them considered only limited aspects of the leukemia management process. They mainly attempted to give diagnostic assistance.

In this study, a prototype medical decision support system (MDSS) for leukemia management was developed to provide both diagnostic and treatment advice on leukemia. Three knowledge models were compared to determine the most accurate method for predicting diagnosis and the prognosis of treatment. This system also includes a leukemia registry to register patients and to provide information to ensure that patients return for follow-up examinations on a regular basis.

Subjects and Methods

Subjects

A total of three hundred forty-seven cases, who had been admitted to the Yonsei University Severance Hospital from December 1 1994 to February 28 1997, were used in developing the knowledge models for the leukemia management.

System Overview

A prototype MDSS was developed using the conceptual model proposed by Leaning et al [3]. The system takes account of the sequential dynamic, interacting phases of leukemia management: the initial diagnosis, registration, treatment selection, prognosis, monitoring and follow-up. The MDSS consists of three modules as shown in Figure 1:

- registry: a temporal patient database for registration, reporting, and follow-up
- diagnosis: candidate diagnosis generation based on knowledge models
  - prognosis: treatment plan generation based on knowledge models
  - AI(Computer-assisted-instruction):education information for patients and their family for self-care using tutorial and encyclopedia about leukemia

Knowledge Models

To find the most accurate knowledge model for predicting diagnosis and prognosis of the treatment, three models were devel-

oped and evaluated: case-based reasoning (CBR), neural network, and discriminate analysis model.

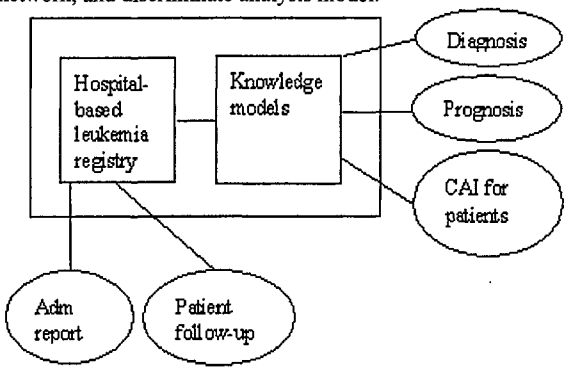

Figure 1 - Overview of Leukemia management system

Case-based Reasoning

A CBR system draws its predicting power from a large case library, and therefore, to be successful, cases should be well organized in memory, only relevant cases should be retrieved from memory. In this study, a case was constructed to represent a leukemia condition with features for describing the symptoms associated with a condition as well as features for treatment The match scores were obtained based on two alternative match scores: scores based on doctors' clinical judgement and the "shares" from the neural network which is the percentage of all output weights attributable to the given independent variable and thus represents the relative importance of the independent variable [7].

Neural Network

In this study, back-propagation with sigmoid transfer function, which allows a variable number of hidden layers within the network, was selected using diagnostic / prognosis class as output nodes and 47 patient characteristics as input nodes. A number of hidden nodes, a number of trainings, and parameter values were determined from based on a series of sensitivity analysis using a correct rate as a performance measure. The correct rate refers to a percentage of the simulated cases from the test data set whose absolute differences from the actual diagnosis given by doctor was less than 0.02.

Discriminant analysis

Patient characteristics, symptoms, and laboratory test results were used in the discriminant analysis. Since there were too many variables that could be possible for statistical analysis, these variables were incorporated into a smaller number of common factors using the factor analysis. The scores from the factor analysis were used as independent variables to determine which factors were important in predicting the diagnosis and the prognosis in the discriminant analysis.

Results

Prediction of Diagnosis

Case-Based Reasoning

The CBR model was developed based on the match scores obtained from a clinical judgement because they produced better results than those from the "shares" of the neural network. Of the 50 test cases CBR correctly predicted 34 cases (68%). Compared with two other models, CBR had lower sensitivity and specificity in most of diagnostic categories, except that it had the highest sensitivity for predicting 'Ly (+) ALL' and the highest specificity for predicting 'no leukemic clone' (Table 1).

Table 1 - Comparison of predicted diagnosis by knowledge models (unit : percent)

Diagnosis	CBR		NN		DA	
	sen.	spec.	sen.	spec.	sen.	spec.
AML	50.0	75.0	57.0	100.0	76.8	100.0
pre B ALL	56.0	66.0	100.0	97.9	99.7	100.0
Common ALL	62.0	69.0	60.0	97.8	94.6	100.0
My(+) ALL	73.0	75.0	100.0	87.8	93.8	100.0
Ly(+) ALL	68.0	53.0	62.5	97.6	75.0	100.0
Mixed phenotype leukemia	45.0	57.0	66.7	93.6	89.0	78.9
No leukemic clone	97.0	100.0	84.2	100.0	100.0	100.0
CLL	33.0	46.0	100.0	97.9	100.0	100.0
B cell leukemia	40.0	58.0	50.0	100.0	92.8	80.0
T cell leukemia	35.0	77.0	100.0	100.0	97.4	100.0
AML M3	65.0	64.0	0.0	100.0	85.8	90.0
Undetermined Diagnosis	33.0	81.0	100.0	100.0	87.6	90.0

Neural Networks

A hidden layer with 5 nodes produced the best results. Surprisingly, the correct rate did not monotonically improve as the number of trainings (or learnings) increase. In fact, 20,000 trainings produced better correct rate than 50,000 trainings. When a learning coefficient, which determines a delta weight, was varied from 0.1 to 0.9 while alpha was fixed at 0.5, learning coefficient of 0.6 produced the best correct rate. Similarly, when alpha was varied from 0.1 to 0.9 while mue was fixed at 0.5, alpha value of 0.1 produced the best correct rate.

Of the 50 test cases, the neural network correctly predicted 26 cases (52%) compared with the doctor's judgement. While this is the lowest overall prediction rate among three models, it had the highest sensitivity and specificity in three diagnostic categories: 'pre B ALL', 'CLL', and 'T cell leukemia'.

Discriminant Analysis

Of the 50 test cases, the discriminant analysis model correctly predicted 36 cases (72%), which is the highest prediction rate. Specifically, it produced the highest sensitivity and specificity for four categories: 'common ALL', 'mixed phenotype leukemia', 'T cell leukemia', and 'AML M3'.

Prediction of Treatment Results

Unlike diagnostic models, CBR performed reasonably well in predicting prognosis of the treatment. Specifically, CBR had 100% sensitivity for predicting a positive prognosis and 100% specificity for predicting a negative prognosis. Neural network also performed well with the highest sensitivity for predicting both positive and negative prognosis. On the other hand, discriminant analysis did not perform well in predicting the prognosis as shown in Table 2.

Table 2 - Comparison of prognosis of treatment (unit : percent)

		Positive	Negative
CBR	sen.	100.0	91.0
	spec.	91.0	100.0
NN	sen.	100.0	96.0
	spec	92.0	95.0
DA	sen.	75.3	62.2
	spec.	71.3	55.8

Development of Leukemia Management System

A prototype MDSS for leukemia management was implemented in Visual Foxpro 5.0. Since some of these activities (e.g. suggested diagnosis, treatment) may change the course of leukemia management, a graphical display was used to show temporal data such as the effects of treatment (e.g. adriamycin, prednesoline, vincristine, plastocyte) on the laboratory test results (e.g. blastocysis, hemoglobin, Neutrophil, platelet, WBC, etc.) to monitor disease progression as shown in Figure 2. The menu screen for the MDSS shows major functions for each module as show in Figure 3.

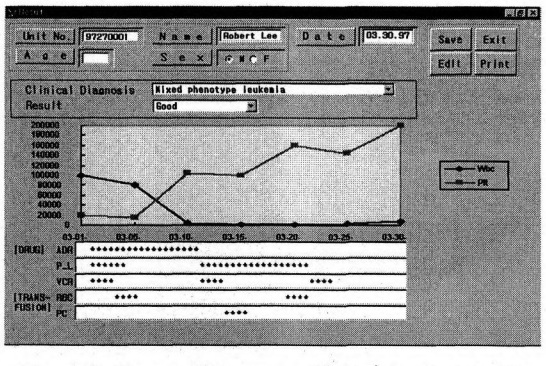

Figure 2 - Temporal sequence of laboratory test results

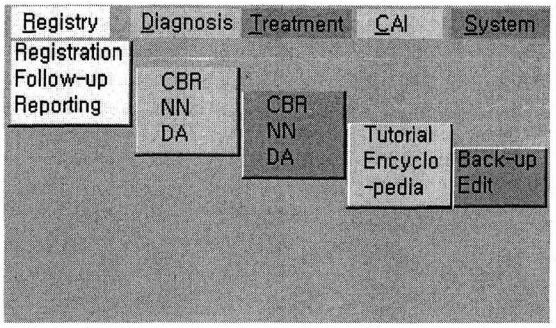

Figure 3 - Menu screen for the leukemia management system

Discussion

This paper described the prototype of a medical decision support system (MDSS) that is intended to provide advice for a clinician concerned with the management of a patient presenting with leukemia. Most studies of MDSS for leukemia have emphasized diagnostic methods; our approach stressed the importance of the total patient management process since management of leukemia patient involves an alteration between diagnosis (assessment) and treatment over a period of time. That is, the MDSS provides information to support activities of diagnosis (prognosis), treatment selection and monitoring, and follow-up.

In this study, predictive power of three knowledge models were compared: CBR, neural network, and discriminant analysis. Diagnostic capabilities for the three knowledge models varied. Of the 50 test cases, the CBR correctly predicted 34 cases (68%) compared with the doctor's judgement; the neural network predicted 26 cases (52%); and the discriminant analysis model predicted 36 cases (72%). This finding is consistent with the previous study on hypertension [8]. Accordingly, the discriminant model, which has not been widely used in the field of expert systems, should be given more application as a knowledge model and be used as an important reference in the diagnosis of leukemia.

However, discriminant analysis did not performed well in predicting the prognosis of the treatment perhaps prognosis data did not meet the assumption of normality. Since performance of each knowledge model varied, a hybrid model which combines the strengths of each model may further improve a predictive power.

A number of expert systems have been developed to interpretate immunophenotypic data or automate lineage assignment in leukemia in the past. Alvey et al. [5] have developed an expert system written in PROLOG using a tree-structured logic and approximately 700 diagnostic rules. The rules were fine tuned to the point where the system gave acceptable answers to all 400 cases in a test database. Lawrence et al [6] developed the Professor Fidelio with the similar predefined criteria tables used by the cell clustering algorithm and the rule-based PROLOG system. Fidelio's interpretation was satisfactory in all 366 cases tested.

In this study, we also introduced a leukemia registry. The cancer registry is an essential part of any rational program of cancer control. The registry module developed in this study has a limited function, there are several other functions of a hospital leukemia registry that need to be considered in the future [9]. First, the registry is organized to assist the leukemia committee in carrying out its duties and to produce administrative reports on the cancer activities. Second, the registry produce report to assist patient follow-up and monitor disease progress.

In the future, the leukemia registry should be integrated with a hospital information system to have direct access to the medical database. Such access can greatly improve the knowledge base construction for such methods as neural network or case-based reasoning. As the technology of the electronic medical record (EMR) improves, such integration will solve many technical problems in knowledge acquisition.

Conclusion

This paper has presented an approach to the design of medical decision support system for leukemia management. The emphasis was on patient management as a whole. Accordingly, four modules were developed: registry, diagnosis, prognosis of treatment, and CAI. Three knowledge models were developed to predict accurate diagnosis and prognosis of treatment: case-based reasoning, neural network, and discriminant analysis, Of these, discriminant analysis model produced the most accurate diagnosis, whereas neural network produced the most accurate prognosis of treatment. Since performance of each model varied, a hybrid approach which combines the strengths of each model should be investigated to further improve a predictive power. Moreover, capability of registry and CAI should also be strengthened to improve patient follow-up and self-care.

Acknowledgments

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Address for correspondence

Graduate School Of Health Science And
Management, Yonsei University
P.O. Box 8044 Seoul, Korea
E-mail:ymchae@yumc.yonsei.ac.kr