DOKUZ EYLÜL UNIVERSITY
GRADUATE SCHOOL OF NATURAL AND APPLIED SCIENCES

A CLINICAL DECISION SUPPORT SYSTEM USING DECISION TREE AND EXPERT OPINION IN RECTAL CANCER TREATMENT

by
Aslı SUNER

June, 2013
İZMİR

A CLINICAL DECISION SUPPORT SYSTEM USING DECISION TREE AND EXPERT OPINION IN RECTAL CANCER TREATMENT

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Ph.D. THESIS EXAMINATION RESULT FORM

We have read the thesis entitled **"A CLINICAL DECISION SUPPORT SYSTEM USING DECISION TREE AND EXPERT OPINION IN RECTAL CANCER TREATMENT"** completed by **ASLI SUNER** under supervision of **PROF. DR. C. CENGİZ ÇELİKOĞLU** and we certify that in our opinion it is fully adequate, in scope and in quality, as a thesis for the degree of Doctor of Philosophy.

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ABSTRACT

Since there are several criteria regarding the disease in treatment of colorectal cancer which is one of the important health problems in world; choosing the most appropriate treatment option concerning a patient is of great importance for the physician. While cancer of the colon and rectum is also called colorectal cancer, in the present study it was focused on the rectal part. It was aimed to create a system to support the decisions of the physician in order to determine the most appropriate treatment method for rectum cancer patients.

A decision model was developed by combining the analytic hierarchy process method which is one of the multi criteria decision making techniques in operations research, and decision tree method. The treatment decision for a patient may be made with the use of priorities that obtained from analytic hierarchy process method by investigating criteria from the most prior to the least. The model that built by the use of a decision tree used previous patient data and expert opinions to suggest a treatment method, and showed survivals that obtained from patient data regarding the suggested treatment and literature review. Thus, the physician may make decision by taking survivals into account when there are various treatment suggestions for a particular patient.

The real patient data application of decision model that built by combining analytic hierarchy process method and decision tree method was presented to the user by using a web-based application. The consistency of the clinical decision support system was evaluated by the experts. Due to the fact that this study supports a stepwise decision making process using patient data and disease criteria as well as expert knowledge, it is expected that the system may support the decision making process of the physician.

Keywords: Analytic hierarchy process (AHP), decision trees, rectal cancer treatment, clinical decision support systems (CDSS), decision making, expert opinion

REKTUM KANSERİ TEDAVİSİNDE KARAR AĞACI VE UZMAN GÖRÜŞÜ KULLANAN BİR KLİNİK KARAR DESTEK SİSTEMİ

ÖZ

Tüm dünyada önemli bir sağlık problemi olan kolorektal kanserin tedavisinde hastalığa ilişkin çok sayıda kriter bulunduğundan, doktorun hasta için en uygun tedaviyi seçmesi oldukça önem taşımaktadır. Kolon ve rektumun kanseri kolorektal kanser olarak adlandırılırken, bu çalışmada sadece rektum kısmı ile ilgilenilmiştir. Rektum kanseri hastaları için en uygun tedavi yönteminin belirlenmesi amacıyla doktorun kararlarına destek olacak bir sistemin oluşturulması amaçlanmıştır.

Yöneylem araştırmasında kullanılan çok kriterli karar verme tekniklerinden biri olan analitik hiyerarşi süreci yöntemi ve karar ağaçları yöntemlerinin birleştirilmesi ile bir karar modeli geliştirilmiştir. Sistemde analitik hiyerarşi süreci yöntemi ile elde edilen öncelikler kullanılarak en yüksek önceliğe sahip kriterden değerlendirmeye başlanarak hastanın tedavi kararı verilebilmektedir. Karar ağacı yardımıyla oluşturulan model ise daha önceki verileri ve uzman görüşlerini kullanarak tedavi yöntemi önerisinde bulunmakta ve önerilen tedaviye ilişkin literatür taramasını ve eldeki veri tabanından elde edilen sağkalımları göstermektedir. Böylece doktor belirli bir hasta için birden çok tedavi önerisi ile karşılaştığında sağkalım sürelerini göz önünde bulundurarak en uygun tedavi kararını verebilecektir.

Analitik hiyerarşi süreci yöntemi ve karar ağaçları yöntemlerinin birleştirilmesi ile oluşturulan karar modelinin gerçek hasta verileri ile yapılan uygulaması internet tabanlı bir uygulama ile kullanıcıya sunulmuştur. Klinik karar destek sisteminin tutarlılığı uzmanlar tarafından değerlendirilmiştir. Bu çalışma uzman bilgisinin yanında, hasta verilerini ve hastalık kriterlerini de kullanarak adım adım karar verdiğinden, sistemin doktorun karar verme sürecine destek olabilmesi beklenmektedir.

Anahtar sözcükler: Analitik hiyerarşi süreci (AHS), karar ağaçları, rektum kanseri tedavisi, klinik karar destek sistemleri (KKDS), karar verme, uzman görüşü

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CHAPTER ONE
INTRODUCTION

Since colorectal cancer is one of the most common health problems today; the choice for the most appropriate treatment option is of a critical importance for the physician. Because making a decision is affected from various different variables, it is important to have support while making a decision that has a vital importance. For making the best decision in a short period of time, decision support should be fast and reliable. In recent years, examples for applications of decision support systems in medicine have been increased owing to the increase in the usage of decision support systems.

It is aimed to support the decision making process of the physician with using a clinical decision support system (CDSS) which is built by combining decision tree and analytic hierarchy process (AHP) method. CDSSs have a great deal of examples with respect to the different areas in literature.

1.1 Statement of the Problem

Determining the most appropriate treatment method to use in colorectal cancer theraphy is an important problem for not only patients but also physicians. There are various different criteria that effect the decision process. While the several criteria are assessed all together, evaluating the process in a stepwise manner from the most to the least prior criteria make the decision making easier. Because of the determining a treatment method is a sequential process, to support the process by appropriate methods may assist the decision maker.

The priorities of criteria that are used to select the most appropriate treatment method were determined by using AHP method which is one of the decision making techniques in operations research. The treatment decision for a patient may be made by investigating criteria from the most prior to the least. The model that is built by the use of a decision tree uses previous patient data and expert opinions to suggest a

treatment method and calculates survivals that obtained from patient data regarding the suggested treatment. Thus, the physician may make decision by taking survivals into account when there are various treatment suggestions for a particular patient. We planned to build a decision support system to shed light on this problem as well. Decision making process may be supported by a software that assists the decisions of the physician.

1.2 Outline of the Thesis

The whole thesis consists of five chapters. In chapter one, objective of the thesis was expressed and the main titles of thesis were introduced. Afterwards, publications completed during the Ph.D. process were listed.

In chapter two, definitions concerning decision making and medical decisions were described at the beginning, and then the common types of information systems were examined in detail. Moreover some important methods that used in CDSS were summarized with examples. After a short introduction and description of CDSS, application areas of CDSS and some CDSS examples were explained briefly. Furthermore, decision trees and sequential decision making were defined, and AHP method was reported.

In the third chapter, rectal cancer was introduced and current literature regarding rectal cancer applications including CDSS, decision tree and AHP were screened and investigated. A comprehensive literature review on related to these methods has been presented.

The application of Ph.D thesis was explained in the fourth chapter. At first, variable determination process were defined, and then data collection from expert opinions, patient data and literature review were mentioned. Additionally, results of the AHP method and sequential decision tree were discussed in detail. Our CDSS for rectum cancer treatment named DSRCT: Decision Support for Rectal Cancer Treatment was introduced and properties of the system were defined.

In the last chapter, concluding remarks, discussion and suggestions for future research were presented.

1.3 List of Studies That Completed During the Ph.D. Process

A list of studies related to the thesis that completed during the Ph.D. Process in years between 2007 and 2013 were shown below. This process also includes a one-year period visiting researcher process in Medical University of Vienna, Center for Medical Statistics, Informatics, and Intelligent Systems, Section for Medical Expert and Knowledge-Based Systems.

- **Aslı Suner,** Can Cengiz Çelikoğlu, Oğuz Dicle ve Selman Sökmen (2012), "Sequential decision tree using the analytic hierarchy process for decision support in rectal cancer", *Artificial Intelligence in Medicine*, *56*/1/59-68/2012, Research Paper, SCI

- **Aslı Suner,** "Sequential Decision Tree Using the Analytic Hierarchy Process for Decision Support in Rectal Cancer", Dokuz Eylül Üniversitesi Fen Fakültesi İstatistik Bölümü 10. Seminer Günleri, Buca, Turkey, September 2012, Seminar

- Gökhan Karakülah, **Aslı Suner,** Klaus-Peter Adlassnig, Matthias Samwald, "A data-driven living review for pharmacogenomic decision support in cancer treatment", *24th European Medical Informatics Conference - MIE2012,* PISA, Italya, August 2012, International Conference

- Gökhan Karakülah, **Aslı Suner,** Klaus-Peter Adlassnig, Matthias Samwald (2012), **"**A data-driven living review for pharmacogenomic decision support in cancer treatment", *Studies in Health Technology and Informatics,* 180/688-92/2012, Research Paper

- **Aslı Suner,** Can Cengiz Çelikoğlu, Oğuz Dicle ve Selman Sökmen, "A Decision Making Algorithm For Choosing The Best Treatment Method in Rectum Cancer", 7th PhD Symposium, Medical University of Vienna, Vienna, Austria, June 2011, International Conference

- **Aslı Suner,** "Decision Making For The Best Treatment Method In Rectum Cancer: Analytic Hierarchy Process (AHP) For Constructing Decision Tree", Journal Club & Progress Report: Medical Informatics, Biostatistics and Complex Systems Lecture, Medical University of Vienna, Vienna, Austria, March 2011, Seminar

- **Aslı Suner**, Can Cengiz Çelikoğlu ve Oğuz Dicle, "Rektum Kanseri Tedavi Yönteminin Seçiminde Analitik Hiyerarşi Süreci ve Karar Ağacı Yöntemlerinin Kullanımı", 7. İstatistik Günleri Sempozyumu, ODTÜ, Ankara, Turkey, June 2010, National Conference

CHAPTER TWO
DECISION MAKING

A decision can be defined as a selection of action to solve a problem, and also a choice after thinking and calculation process of a situation (McLeod & Schell, 2004).

Decision making is the process of choosing from various courses of action to achieve a goal (Turban et al, 2005). Stages of the decision process are identified by the Nobel Prize owner, well-known economist Simon (1977) as intelligence, design, choice, and implementation. In this four-phase model, while *intelligence* stage is identified as finding occasions for decision making; *design* stage consists of finding, developing and analyzing the action. *Choice* stage is defined as selecting a particular conduct from the available ones. A last stage is considered as implementing results section of a decision process (Power, 2002; Schneider, 2010; Turban et al, 2005).

2.1 Decision Making and Medical Decisions

The person can make a decision on the evidence of the data at hand in the process of decision making. The information can be obtained via considering the present state of the problem or via investigating the history of the problem. The people, who are operative in the decision making process, should be experienced in the issue and have the required knowledge; at the same time they should be skilled enough to use the present data accurately. This situation is very important, especially in a field like medicine which does not have any tolerance for mistakes.

As long as there is a discrepancy between the present and the target situation, a decision problem occurs. Since situations usually have at least two options to choose, the decision maker should take into account of all possible options and select the best of all (Grünig & Kühn, 2009). Decision theory which is used in various interdisciplinary areas may be effective in solving decision problems.

A payoff table for the decision theory problems may be used to represent decisions, payoffs, and state of nature. Here r_{ij} is the payoffs for each possible combination of decision and state of nature. The decision maker chooses one of the decisions of d_i, and then j^{th} state of nature occurs in the decision process. After decision maker's choice regarding which decision to choose, the decision maker obtains r_{ij}. If we know that state j will occur, decision maker chooses the decision d_i for the largest return, r_{ij}, for the known state of nature, the j^{th} column of the payoff table (Table 2.1). There may be many potential decisions in practical applications. The purpose is always to select the best decision according to the state of nature (Cornuejols & Trick, 1998).

Table 2.1 The payoff table for the decision theory.

Decision	**State of nature**			
	1	**2**	**…**	***j***
$\mathbf{d_1}$	r_{11}	r_{12}	…	r_{1j}
$\mathbf{d_2}$	r_{21}	r_{22}	…	r_{2j}
…	…	…	…	…
$\mathbf{d_i}$	r_{n1}	r_{n2}	…	r_{ij}

While an optimal solution can be obtained from a certain objective function in classical decision making models, decision theory helps to find sufficient solutions for real life problems. Consequently, many kinds of methods to solve multiple criteria decision making (MCDM) problems are taken into consideration to achieve the optimal decision. The most common used MCDM methods in the literature are the Analytic Hierarchy Process (AHP) method, the Preference Ranking Organization Methods for Enrichment Evaluations (PROMETHEE) method, the Simple Additive Weighting (SAW) method, the Technique for Order Preference by Similarity to Ideal Solution (TOPSIS) method, the Analytic Network Process (ANP) method, the Weighted Product Model (WPM) method, the Elimination Et Choix Traduisant la Realite (ELECTRE) Method, and the Vlse Kriterijumska Optimizacija Kompromisno Resenje (VIKOR) Method (Eren Doğu, 2012).

Çorapçıoğlu (2006) explained that incorrect assessment of the present problem, selection of the unsuitable problem solution, or the result of an inappropriate application of the solution can cause wrong decisions. The decisions made without elaborate thinking in various areas may have ruinous results. To prevent situations like these, decision maker has to think in detail, and to take into consideration all the possibilities in decision making. However, due to cutting the evaluation period short or due to instantaneous decisions, solutions that may yield better results couldn't be utilized. Even though the decision makers are experts, they might make wrong decisions due to unhealthy evaluation of the situation at hand because of individual reasons. In addition to this, decision makers may not make use of all the information they have. As the time passes, the expert on the subject may turn into an experienced person, specialized in certain subjects. Then he may not offer opinions on the main subject or he may make decisions in accordance with the areas he had specialized (Pantazi, Arocha & Moehr, 2004). As a result of this, one may encounter with loss of time caused by undesirable situations or undue operations. The healthy decision making of the expert may be influenced because of forgetfulness, emotional changes, sentimentality, strategic thinking and/or hesitation which are in the nature of humankind. Thus, the decision support systems become popular in the decision making processes especially where vital decisions are taken. Decision support systems are used to assist the decision maker in the decision making process. The decision support may be provided to the decision maker by other experts or a computer system that used a proper software and hardware.

In medical decisions -since the information is generally subjective, insufficient and instable- there is limited information on the results of the solution selected or the decision taken. At the beginning, the result of the treatment to be applied generally can only be estimated. As decision making heads the list of the compulsory and essential activities for a physician, medical decisions are often taken in uncertainty, and the physician presents his diagnosis in accordance with the most appropriate treatment or solution. In order to minimize this uncertainty, medical diagnosis needs as much as possible complementary information to be revealed.

British Medical Association (2007) mentioned that a benefit of treatments occurred in combination of various factors including side effects of the treatment, the patients' expectations, availability of resources, efficacy's limits, and invasiveness of the treatment. It is well known by health professionals that the accessibility of a technique does not reflect its suitability in every medical condition. Furthermore the main purpose of medical treatment is to promote patient's health status while providing maximum benefit and reducing the harm of treatment. In case the treatment is declined by a patient or the treatment provides no longer benefit to a patient, the treatment should be terminated due to ethical and legal issues. Even though the treatment is terminated, reducing pain and alleviating of disease symptoms without a cure for a patient care should be done, after evaluation of risks, responsibilities and benefits of the treatment. Also generally approved guidelines and extra recommendations should be considered while making a decision regarding diagnosis and treatment of a patient. Hence, our clinical decision support system model for rectum cancer patients is substantially useful for decision makers due to providing decision support based on combining guidelines, expert opinions and real decision data from previous treatment states.

2.2 Common Types of Information Systems

Organizations make use of information systems to computerize actions and support decision making processes of their decision making levels. Decision making levels of organizations may be represented from bottom to top by the following: operational level, managerial level and executive level. While operational level describes the daily company procedures and customer communications; at the managerial level, managers of the organization follow-up and control activities of the operational level and report the process to higher levels. At the executive level, executives including president of the company, vice presidents, managers, and chief executive officer (CEO) deal with strategic issues for instance choosing countries to compete in, products to produce, and the organizational plan to follow (Jessup &Valacich, 2003). Organizational levels are supported by information systems which are shown in Figure 2.1 below.

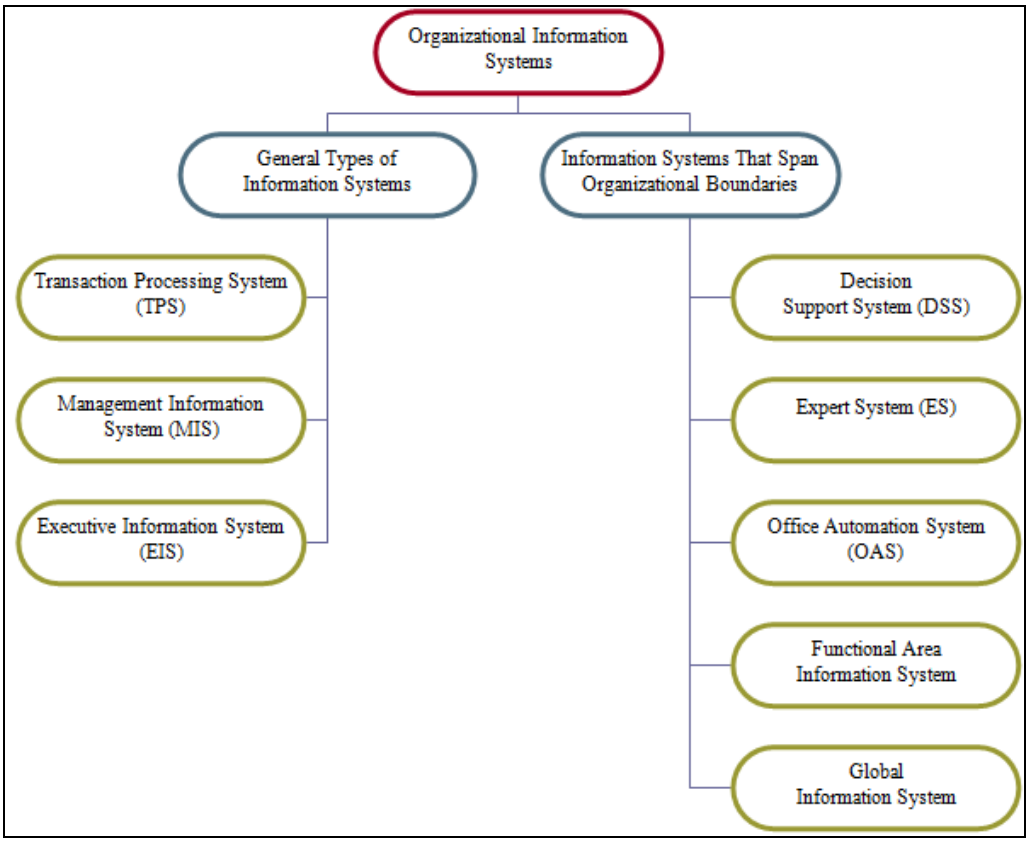

Figure 2.1 The organizational information systems.

General types of information systems are classified as transaction processing system (TPS), executive information system (EIS), and management information system (MIS) (Jessup & Valacich, 2003). A transaction processing system (TPS) is a kind of information system that is used to reduce the transactional costs, and to enhance organizational activities by increasing speed and accuracy. TPS supports inventory management, shipping, products purchasing, payroll processing, sales and orders. TPS can be used by operational personnel and supervisors in the process of summarizing, recording, updating, sorting and merging information. Management information system (MIS) collects data from multiple sources, creates reports and support managers' decisions when they are monitoring and managing organizations. While TPS increases efficiency by automatizing repeated process activities, MIS helps managers at midlevel to make their decisions more efficient during decision making process. Executive information system (EIS) supports decisions of executive level managers by using summarized data and graphical interpretation.

In addition to these three general information systems, there are six types of boundary spanning systems which can be summarized as follows (Jessup &Valacich, 2003). Decision support system (DSS), which supports organizational decision making, is used by any level of the organization to solve problems regarding sales or forecasting of resources. The system can obtain data from a TPS, a MIS or different sources. DSS models are used in various areas; for instance, accounting, corporate level, finance, marketing, personnel, production, management science, and statistics. An expert system (ES) uses reasoning methods based on knowledge to give advice like a human expert. The system asks the user a series of questions, then collects the information, defines if-then rules and gives recommendations or advices. ES is used in financial planning, automobile diagnosis, machine configuration, medical diagnosis, and etc. An office automation system (OAS) is designed to prepare documents, to schedule resources and to provide the communication of all organizational personnel. The system also consolidates information, analyzes and merges data. Functional area information systems are designed to support a specific set of activities in a specific functional area. These systems may be one of the systems such as TPS, MIS, EIS, DSS, ES and OAS. Global information systems can be managed using a number of system configurations and can be used as international information systems, transnational information systems, multinational information systems and collaborative information systems.

Clinical decision support systems (CDSSs), one of the organizational information systems, are a subset of decision support systems. This Ph.D. dissertation is mainly interested in CDSS as summarized in the following sections.

2.3 Clinical Decision Support Systems and Real Life Examples

Computers and computerized systems may support the decision making process in medicine. In order to prepare this kind of a support system, there should be a considerable amount of knowledge on the possible solutions to the problem.

CDSSs support physician’s decision for a particular patient by using reminders, alerts, advices, suggestions or interpretations (Wyatt, 2000). The safety of patient, the efficiency in health care delivery and the quality of care may become better with the help of the CDSSs (Coiera, 2003). Patient characteristics can be entered to a computerized knowledge base by a physician, a patient or can be obtained from electronic medical records, and then recommendations for a specific patient can be achieved with the use of CDSSs (Garg et al, 2005).

Greenes (2007) indicated that there are many purposes of CDSSs such as answering questions, making decisions, optimizing process flow and workflow, monitoring actions and focusing attention. Answering questions can be achieved by providing information to the decision maker during a problem solving process by using direct hyperlinks from context specific settings, information button selection or reference list from MEDLINE which is a database of bibliographical literature pertaining to the U.S. National Library of Medicine's (NLM) that includes more than approximately 19 million references to life sciences journal articles. The decision making helps analyzing the data and provides recommendations for various actions including estimation process of diagnosis and prognosis, determination of the most suitable treatment, selection of the appropriate test such as screening, follow-up, etc. Flowcharts, multistep algorithms, protocols and guidelines are used to optimize the process flow and workflow. According to this, the workflow may be improved, thus the speed of the model and the efficiency are maximized. Monitoring actions consists of preventing errors, using warnings, reminders and alerts, and performance feedbacks. Focusing attention presents items in the data entries or reports applications.

Berner (2007) mentioned that there are various CDSS examples which are categorized as knowledge-based and non-knowledge-based. Knowledge-based CDSSs such as diagnostic CDSS, laboratory test ordering CDSS, medication ordering CDSS, etc. assist the decision making of physicians; provide not only the answer but also the information for the decision maker. Differently from knowledge-based CDSS, non-knowledge-based CDSS uses machine learning systems (genetic

algorithms, artificial neural networks, etc.) that allow the computer to recognize patterns in the clinical data and also to learn the previous experiences. Both knowledge-based and non-knowledge-based CDSSs can be successful if they provide automatic alerts, suggestions, reminders, or recommendations and if they computerize the whole process of decision making.

A systematic review by Garg et al (2005) assessed the effects of CDDS studies regarding controlled trials in MEDLINE, EMBASE, Cochrane Library, Inspec, and ISI databases. 64% of the 100 studies showed that CCDSs improved practitioner performance. The study results indicated that the number of CDSS studies had increased markedly since 1973 and quality of studies had improved. Also Kawamoto et al (2005) concluded in their systematic review that CDSS made clinical practice better in 68% of 70 studies. As seen in Figure 2.2, also the search engine results of PubMed, a service of the NLM that includes biomedical literature from life science journals, online books, and MEDLINE verify the increase in the number of CDSS studies. The Medical Subject Headings (MeSH) terms was used to find all CDSS studies from PubMed database. The search strategy for PubMed was *"Decision Support Systems, Clinical"[Mesh]* and totally 4309 papers were found at May 2013.

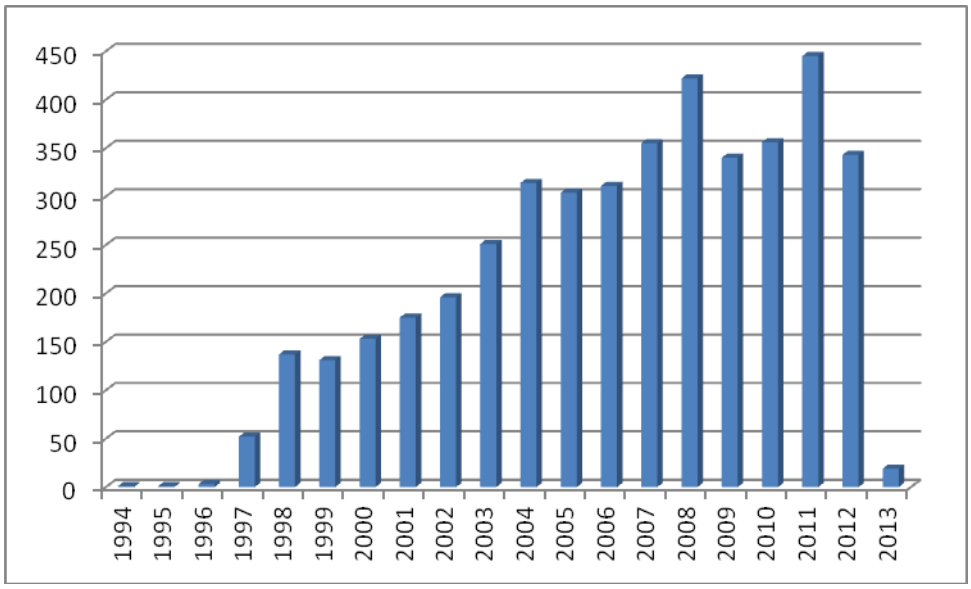

Figure 2.2 A total amount of paper search results in PubMed regarding clinical decision support systems.

Because of CDSSs can simulate human thinking, there are many different CDSS examples in medicine that support the process of patient care (Berner, 2007). Historical development of CDSS has started in the beginning of the 1970s. The most common examples of CDSSs are as follows: Leeds abdominal pain system (1972), MYCIN (1976) and knowledge-based hospital information system HELP (1979) were developed in the 1970s (Shortliffe and Cimino, 2006). In the 1980s; QMR and Internist I, DXplain; in the 1990s RO^2SE, HELP with the use of Arden Syntax and Standards, and in the 2000s Protégé were developed (Coiera, 2003). These systems were explained in details in the following paragraphs.

In the University of Leeds, Leeds Abdominal Pain System (1972) which used Bayesian probability theory was developed by F. T. de Dombal and colleagues. For acute abdominal pain, and with the help of Bayesian theorem, the system used huge amounts of patient data to calculate the probability of these possible explanations: small-bowel obstruction, diverticulitis, nonspecific abdominal pain, perforated ulcer, pancreatitis, appendicitis, and cholecystitis. The two basic assumptions of the system were findings of the diagnoses were conditionally independent and these seven diagnoses were mutually exclusive. In one of the system evaluation example for 304 patients, the program diagnoses 91.8% of cases versus physicians up to 80% of cases. Moreover the program was more successful than a senior physician in the process for the assignment of the patients to the right category of the disease (Shortliffe & Cimino, 2006).

When the present decision support systems and samples are investigated with regard to pertaining the inference mechanism they use, the first and most-widely known example is MYCIN (Shortliffe, Axline, Buchanan, Merigan & Cohen, 1973). MYCIN was developed by Stanford University and used to offer diagnosis and treatment for the blood borne infections. MYCIN predicated on evaluation by rules as its operation method. In this structure, results are produced in accordance with the medical test results and indications entered into the system. The system offers the decision, result or advice it obtained for the user/s in accordance with the values entered. The MYCIN has some important features that make the program powerful

against other CDSSs (Shortliffe & Cimino, 2006). For instance, the program determines rules by itself and makes decisions to chain them together for a specific case. English translations for the machine-readable format of the rules can be shown. Any changes according to system, such as adding or removing rules, can be updated easily without reprogramming and restructuring of the knowledge base's other parts. In the 1980s, the MYCIN is of great importance for the development of knowledge based systems. A Variety of systems were evolved from the rule based approach of the MYCIN in fields other than medicine and they were developed with the idea of the MYCIN system.

At the end of the 1970s, the clinical information system HELP used at LDS Hospital was created. The system provides alerts, specific information for a patient, reports, schedules and warnings. HELP system showed the benefit of decision support and other system functions integration (Shortliffe & Cimino, 2006).

In 1980, a diagnostic decision support system for internists, Quick Medical Reference (QMR) was built in the University of Pittsburgh. Since QMR has a rich medical literature regarding various diseases, the system gives advices like an expert (Miller & Masarie, 1989). By the late 1970s, INTERNIST-I was developed as a computer-assisted diagnostic tool in the University of Pittsburgh. After about fifteen years, the system covered approximately 70-80% of all the possible diagnoses in internal medicine. In the mid-1980s QMR and INTERNIST-I systems were combined and the new approach was named INTERNIST-I/QMR. QMR was used to correct the technical and philosophical deficiencies of INTERNIST-I. While INTERNIST-I works for diagnostic consultation, the QMR program is used to give diagnostic information from the knowledge base of the program (Miller, McNeil, Challinor, Masarie & Myers, 1986).

DXplain is one of the successful CDSS examples of the 1980s. The system was designed in Massachusetts General Hospital as a diagnostic decision support system in general medicine to help making decisions by using patient data regarding laboratory results, clinical findings and symptoms (Barnett, Cimino, Hupp & Hoffer,

1987). Due to the fact that DXplain recommends additional examination and gives explanations for every differential diagnosis, the system is preferred to be used at several hospitals for clinical education of medical students and medical consultation. DXplain can also be used as a medical textbook (London, 1998).

In the beginning of the 1990s, PAL (Protege Axiom Language), a special programming language, was adopted to the HELP system to incorporate decision rules to the Arden Syntax programming language. The use of Arden Syntax helps the practitioner's follow-up process of a patient (Shortliffe & Cimino, 2006). It is designed for simple guidelines, such as reminders, not for complex ones, for instance treatments. The Arden Syntax was started to share and represent medical knowledge in 1989 by using modular guidelines named the Medical Logic Modules (MLMs). In 1992, it was accepted as a Standard by the American Society for Testing and Materials (ASTM). Then the revised version, Arden2.0, was developed and published by the HL7 group (Ten Teije, Miksch & Lucas, 2008).

In 1992, another CDSS example, Post-Operative Expert Medical System (POEMS), was developed in the University of Leeds to give suggestions and decision support to the inexperienced medical staff for post-operative care. POEMS uses patient's operative and medical history, laboratory test results and other clinical tests to show diagnosis, to offer the most appropriate treatment method and to make recommendations. The system also stores patient data to make diagnosis for the similar cases (Sawar et al, 1991; Sawar et al, 1992).

Another decision support system example RO^2SE was designed to diagnose the disease of Mitral Valve Prolapse (MVP) (Zorman, Kokol & Cerkvenik, 1997). Instead of the rule based structure in the MYCIN, in RO^2SE decision trees are used (Quinlan, 1990). The decision trees used in this system are prepared in a trainable structure. In the trials performed through the use of decision trees, it is seen that the results that the system produced approximated to the real patient values and real healthy values by changing the tolerance value.

In 2000s, a knowledge-based system Protégé-2000 was used to model ontologies. At the beginning, it was developed as a small tool in 1987. After a development process of a system, it became a knowledge based system that helps users in building of huge electronic knowledge bases. Protégé provides implementation of data structures which supports design, representation and management of ontologies in different types (Gennari et al, 2003).

In addition to these essential CDSS examples, different systems are also used in various areas (Coiera, 2003). Despite some of these systems are small, they are successful examples of knowledge-based clinical systems such as: Iliad (Lincoln et al, 1991), Isabel (Graber & Mathew, 2008), PEIRS (Edwards, Compton, Malor, Srinivasan & Lazarus, 1993), MDX (Mittal, Chandrasekaran & Smith, 1979), DiagnosisPro (Aronson, 1997), Epileptologists' Assistant (Ruchelman et al, 1992), MDDB (Gierl & Stengel-Rutkowski, 1994), Jeremiah (Stephens, Mackin & Sims-Williams, 1996), Orthoplanner (Stephens & Mackin, 1998), RaPiD (Hammond, Davenport & Fitzpatrick, 1993), TxDENT (MacEntee, 1999), Acid-base expert system (Pince, Verberckmoes & Willems, 1990), POEMS (Sawar, Brennan, Cole & Stewart, 1992), GERMWATCHER (Kahn, Steib, Fraser & Dunagan, 1993), VIE-PNN (Miksch, Dobner, Horn & Popow, 1993), NéoGanesh (Dojat, Brochard, Lemaire & Harf, 1992), HEPAXPERT I, II (Adlassnig & Horak, 1991), PUFF (Snow, Fallat, Tyler & Hsu, 1988), SETH (Darmoni et al, 1994), PERFEX (Ezquerra, Mullick, Garcia, Cooke & Kachouska, 1992), and Microbiology/ Pharmacy (Morrell, Wasilauskas & Winslow, 1993).

Çorapçıoğlu (2006) indicated that the CDSSs can also be used as software systems that support the physician's evaluation of the patient's complaints and findings (inspection, laboratory, radiology, etc.) when he inspects his patient in practice to reach an accurate identification and that support the diagnosis process. By developing this kind of a system, the errors that may occur in diagnosis, namely the decision stage and the unrecoverable errors are possible to prevent via the support system. Undesired situations can be encountered due to the wrong decisions of individuals who are not specialized in the area or who do not have enough

information but have the right to decide. The CDSSs are designed to provide the support that is supplied by the experts of the subject to the non-specialist ones.

Kawamoto et al (2005) represented that CDSSs are successful tools because of integration to the workflow instead of logging in to the system or the using a different screen. Since the electronical use, it provides faster access to the data compared to paper based documents. Decision support, nowadays, is provided for not only assessments of the patients but also patient care recommendations.

2.4 Decision Trees and Sequential Decision Making

A decision tree is a decision support tool that visualizes a decision process using a tree-shaped graph that shows uncertainties, choices and potential outcomes (Schwartz & Bergus, 2008). Decision trees describe decisions and their outcomes with probabilities, costs of individual events or decisions, and the degree of satisfaction achieved by the outcome.

Decision trees are also preferred to be used when the decision maker wants to make a sequence of decisions (Hillier & Lieberman, 2001). When a series of decisions must be made at different points in time, decision trees can be used to find optimal decisions (Winston, 2003). A decision tree is a sequential decision process. The decision nodes are the states. The arcs that point rightward from the decision nodes are the actions. The law of motion (transition probabilities) depends on the current state and an action (Denardo, 2002). Although time of the event moves from left to right, analysis of the decision tree flows from right to left. In other words, after a complete decision tree is created, the process of simple expected value calculation of the decision tree is applied backward (Schwartz & Bergus, 2008; Lee et al, 2009). An example decision tree can be seen in Figure 2.3. A decision node is shown as a square and the circle represents a chance node. When a branch does not have any chance or decision node, a triangle represents the end point of a branch. Every chance node in a decision tree represents a situation of an uncertainty to be resolved. This uncertainty can be shown by an arc and this arc connects the chance node to

another node or to an end point of the branch. Each arc has a conditional probability because of the chance node to its left side. The sum of the conditional probabilities of each chance node is equal to 1. At each decision node, decision maker chooses one of the existing actions which involve a cost (Denardo, 2002).

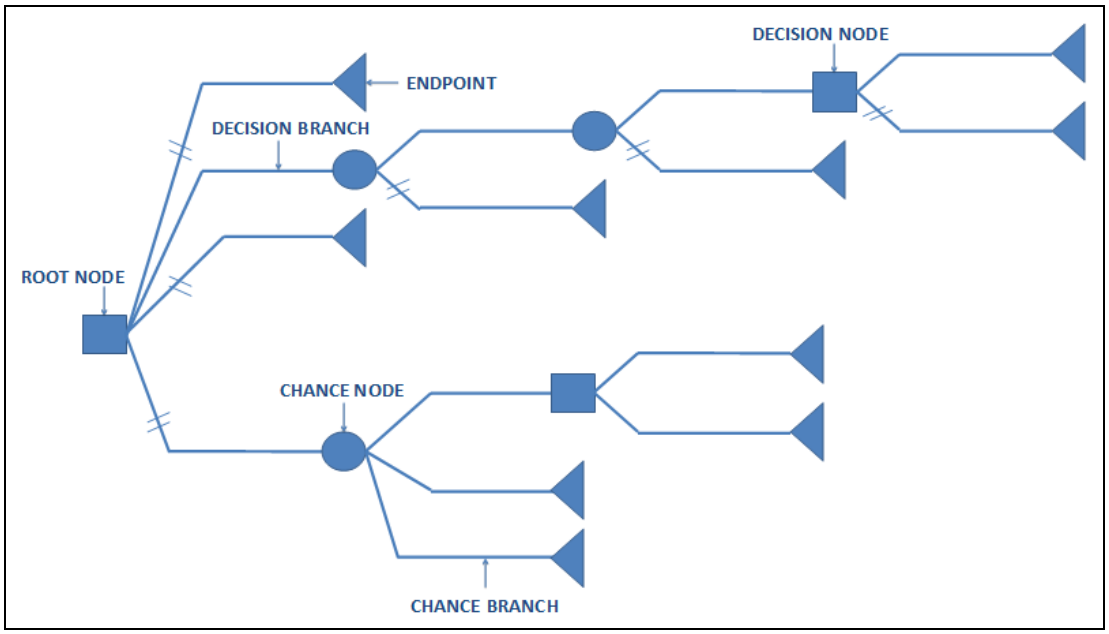

Figure 2.3 A representation of a decision tree.

Practical examples of decision tree software such as SmartDraw, TreeAge, TreePlan, Precision Tree, Decision Pro etc. can draw and solve decision tree problems automatically. Therefore, using software may be very helpful in visualizing sequential decisions.

Greenes (2007) mentioned that first node of the decision tree is generally a decision node, for instance whether to treat a patient, test further, or do nothing. Another example could be a patient with abdominal pain. Decision maker can determine whether he/she has appendicitis or nonspecific abdominal pain by using decision tree. Schwartz and Bergus (2008) described a hypothetical example of a decision making problem regarding whether a patient who has symptoms of a particular disease should have a drug treatment or a surgical operation.

A sequential decision process is a decision problem that evolves from state to state in accord. The concepts of sequential decision process may be defined as states, actions, and transitions. The *state* of the system is observed by the decision maker, and then the *action* is selected. After a process of action selection, a *transition* to a new state occurs. This new state can depend on the current state and action, not on prior states and actions. Each transition occurs from one state to another. The state of the system is a summary of its prior history that evaluates current and future actions. A cost of action selection also is based on the current state and action. While transitions occur from state to state in a Markov chain; the law of motion from state to state can depend only on the current state and action in a sequential decision process (Denardo, 2002).

2.5 Analytic Hierarchy Process

A multi criteria decision making method, Analytic Hierarchy Process (AHP), was created in the 1970s by Saaty. AHP method can be used to make decisions when multiple objectives in situations are important for a decision maker (Winston, 2003). The AHP method takes the decision-maker's personal objectives into account (Saaty, 1994). AHP applications have been reported in complex decision making problems of real-world such as marketing, finance, economics, medicine, education, engineering, government, industry, management, and the armed forces (Liberatore & Nydick, 2008; Sloane, Liberatore & Nydick, 2002; Zahedi, 1986; Yang & Shi, 2002; Ho, 2008).

The AHP method consists of three main phases: construction of hierarchy, priority analysis of data, and confirmation of consistency (Ho, 2008). Saaty suggests defining the problem and then determining the goal as the first step of the AHP analysis (Saaty, 2008a). The hierarchical structure is then constructed. In a hierarchical structure as shown in Figure 2.4, the goal of problem is located at the top; the criteria are placed at the intermediate level and the alternatives at the base. The elements of the problem are compared on a single property; other elements are not considered in the comparison. Thus the decision-maker focuses on a judgment

(Saaty, 1990). The AHP method aims at quantifying relative properties for alternatives with the judgments of the decision-maker (Al Harbi, K.M.A.S. 2001). By using pairwise comparisons to measure the impact of items between levels of the hierarchy, the AHP method measures both qualitative and quantitative data. Furthermore, it reduces bias by measuring the consistency of judgments, thereby establishing an acceptable level of tolerance for the degree of inconsistency (Liberatore & Nydick, 2008).

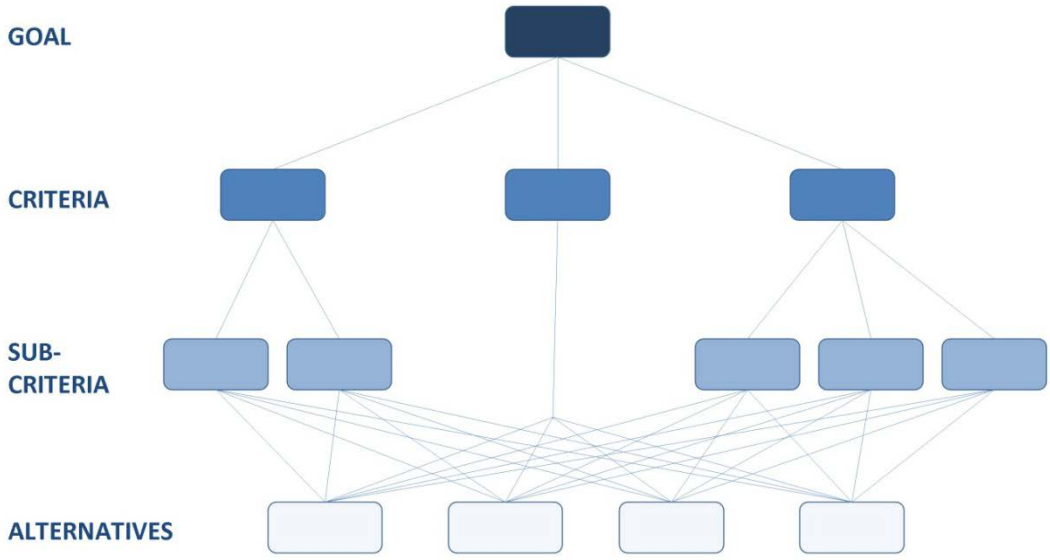

Figure 2.4 The structure of AHP method.

For the priority analysis, matrices for a set of $n \times n$ pairwise comparison are created in which criteria and alternatives are compared, whereby n is the amount of sub-criteria or alternatives. The priority scale suggested by Saaty, shown in Table 2.2, is used for these comparisons to help the expert in establishing priorities of criteria or alternatives over others (Saaty, 2008b). This scale for pairwise comparisons ranges from 1 to 9. A decision-maker's perception of those criteria that take precedence over another is considered in pairwise comparisons. While making comparisons, the scale helps the expert to judge the relative importance of elements: how many times more important is one element than the other? For instance, if element X is 7 times more important than element Y, then element Y must be absolutely less important than element X and is graded as 1/7. In a decision process, n (n-1) / 2 judgments are made to create a set of matrices. It is suggested that

the hierarchy should contain three to six levels, and at most nine elements should be used per level (Zahedi, 1986). This is based on Miller's psychological guideline (1956) which recommends 7 ± 2 items simultaneously. All of the elements are considered for pairwise comparisons (Miller, 1956).

Table 2.2 Pairwise comparison scale for AHP preferences.

Importance	Definition	Explanation
1	Equal importance	Two activities contribute equally to the objective
2	Weak or slight	
3	Moderate importance	Experience and judgement slightly favor one activity over the other
4	Moderate plus	
5	Strong importance	Experience and judgement strongly favor one activity over the other
6	Strong plus	
7	Very strong or demonstrated importance	One activity is favoured very strongly over the other; its dominance demonstrated in practice.
8	Very, very strong	
9	Extreme importance	The evidence favouring one activity over the other is of the highest possible order of affirmation.

For the prioritization stage; after the matrices have been filled, the eigenvectors are weighted by the weights of the criteria. Sum of the eigenvectors is taken over all weighted eigenvector entries related to those in the next level of the hierarchy.

As a final step, the logical consistency of the expert judgments is measured. With the use of the eigenvalue (λ_{max}), the consistency of comparisons is evaluated after all pairwise comparisons have been completed. A consistency index (*CI*) is calculated with the formula by using the eigenvalue:

$$CI = (\lambda_{max} - n)/(n-1),$$

where *n* represents the matrix size in this formula. Consistency of judgment is checked by considering the consistency ratio (*CR)* of *CI* with the appropriate value of random consistency index *(RI)*, proposed by Saaty (1980), as given in Table 2.3. This leads to the following formula for the calculation of CR:

CR=CI/RI

Saaty suggests that when the *CR* does not exceed 0.10, it is acceptable. The judgment matrix should be considered inconsistent when *CR* is greater than 0.10. A consistent matrix can only be obtained when the judgments are evaluated again and pairwise comparisions are repeated (Pirdashti, Ghadi & Mohammadi, 2009; Forman & Selly, 2002).

Table 2.3 Average random consistency.

Size of matrix	1	2	3	4	5	6	7	8	9	10
Random consistency	0.00	0.00	0.58	0.90	1.12	1.24	1.32	1.41	1.45	1.49

The advantage of the AHP method over standard evaluation and priority is its ability to demonstrate uncertain and conflicting opinions as numerical values (Kitamura, 2010). However, to realize the full potential of the method the questions of the AHP comparisons must be designed carefully. The nature of the problem must be defined correctly (Carter et al, 1999). A further advantage is that the priority of expert opinions can be evaluated at every step. Also AHP produces a measure of judgmental consistency for the evaluations that can be used to discover judgments that may require greater thinking by the decision maker (Schwartz & Bergus, 2008).

The AHP method is also appropriate for group decision making. Thus, the opinions and knowledge of experts are used to solve a problem within a hierarchy. While solving group decision problems, decision makers make their pairwise comparisons individually or by consensus (Saaty, 1989). After judgments of individuals are obtained, group priorities can be obtained by “the aggregation of individual priorities (AIP)” or “the aggregation of individual judgments (AIJ)”

(Aguarón & Moreno-Jiménez, 2000; Saaty, 1989; Crawford & Williams, 1985). The new judgment matrix based on individual judgments, is created for the whole group in an AIJ procedure and the new matrix is used for calculation of the priorities. In the analysis of data, all group members may have equal or different degrees of influence because of their relative positions in the project. In some cases the group decision may be achieved by brainstorming and sharing ideas (Al Harbi, 2001). However, it might be difficult to achieve a consensus in a group when the individuals are experts, as some may not wish to accept the opinions of others. Hence, only their final outcomes may be obtained and, by using the AIP method, the total priorities regarding individual priorities are achieved with the use of an aggregation procedure (Eren Doğu, 2012). Although any of the aggregation procedures can be used for model synthesis, individual comparisons of the final outcome in the pairwise comparison process are combined using the weighted geometric mean - a procedure widely used by groups to set priorities for both (Saaty, 1983; Saaty, 2008; Melón, Beltran & Cruz, 2008). In general, if n participants provide judgments, the geometric mean is formulized as the n^{th} root of the product of the "n" judgments. The important limitation of these conventional procedures is to assume that the judgments of decision makers are complete and accurate. In some situations, for example while the matrix has large number of alternatives and attributes, the matrices may not be complete. Some researchers use different techniques deal with aggregation problem in group decisions, for example Bayesian approach (Altuzarra et al, 2007), and linear programming (Mikhailov, 2004). Since incomplete matrices are out of the scope of this thesis, these methods are not explained here.

The AHP approach has also been combined with tools such as quality function deployment, meta-heuristics, SWOT analysis, data envelopment analysis, fuzzy logic, and mathematical programming (Ho, 2008; Vaidya & Kumar, 2006). Lootsma (1993) used the multiplicative AHP method, which combines the AHP method with the simple multi-attribute rating technique to recommend a procedure for multi-criteria decision analysis in a decision tree. Rossetti and Selandari (2001) used AHP to analyze hospital delivery system. Dey (2002) applied the AHP method for cost and risk analysis of a construction project and used decision tree analysis for the

selection of specific risk responses for particular work packages in different alternatives. Sharma et al (Sharma, Eden, Guise, Jimison & Dolan, 2011) combined decision trees and the AHP method to make the best delivery decision for pregnant women. Although the AHP was used for decision trees in these studies, our study differs in the fact that we used the AHP method for *sequential* decision trees in the treatment of rectal cancer.

CHAPTER THREE
RECTAL CANCER

Colorectal cancer ranks among the most common health conditions encountered today. In view of its increasing incidence throughout the world, the treatment of colorectal cancer is of great importance (Hassan et al, 2009; Walsh & Terdiman, 2003; Howlader et al, 2011). The frequency of this malignancy has been further aggravated by the rapid Westernization of diets throughout the world (Marchand, 1999, Koyama & Kotake, 1997). According to GLOBOCAN 2008, colorectal cancer is the second most common type of cancer in women and the third most common type of cancer in men worldwide and, it is the second frequent cancer type in women and the fifth in men in Turkey (Ferlay et al, 2008). It is estimated that totally 51,690 (26,470 male and 25,220 female) deaths from colorectal cancer occurred in 2012 in the United States (Siegel, Naishadham & Jemal, 2012). Since the colorectal cancer is responsible for 8% of all types of the deaths due to the cancer, approximately 608,000 deaths from colorectal cancer are expected in the whole world. Hence colorectal cancer is the fourth leading cause of death from cancer worldwide (Ferlay et al, 2008).

3.1 Rectal Cancer: An Overview

Colorectal cancer is a collective term for cancer of the colon and rectum (Popa, Bratucu & Radu, 2011). Although the greater number of studies evaluate colon and rectum together as colorectal; etiological and epidemiological differences of both are important to decide the treatment method. Approximately 30% of all colorectal cancers occur in the rectum part (Santoro, 2011). In the present study it was focused on the rectal part.

There are great differences in survival rates between the different stages of colorectal cancer. The anticipated global mortality per year is 394,000 (Boyle & Langman, 2000). However the incidence of colorectal cancer per 100,000 population decreased from 60.5 (in 1976) to 46.4 (in 2005) and also from 1990 to 2007,

mortality decreased by approximately 35% (Benson et al, 2012). It can be seen from randomized trials that systematic screening of population can decrease colorectal cancer incidence (Santoro, 2011). Earlier diagnoses with screening options and improved treatment modalities may have caused these results for colorectal patients.

As can be seen in Table 3.1, nearly 60% of the all cases arise in developed regions. Incidence rates and mortality rates are considerably higher in men than in women in worldwide, as shown in Figure 3.1 (Ferlay et al, 2008). Five years survival rate of rectal cancer for women (51.0%) is higher than men (48.5%) even though women (42.1%) has lower incidence of rectal cancer than men (57.9%) (Santoro, 2011). In the United States, 23,500 male and 16,790 female new cases of rectal cancer are expected in 2012 (Siegel, Naishadham & Jemal, 2012).

Table 3.1 Incidence, mortality and prevalence of colorectal cancer worldwide.

Estimated numbers (thousands)	Men			Women			Both sexes		
	Cases	Deaths	5-year prev.	Cases	Deaths	5-year prev.	Cases	Deaths	5-year prev.
World	663	320	1765	571	288	1495	1234	608	3260
More developed regions	389	165	1141	338	154	968	727	319	2109
Less developed regions	274	154	624	232	134	526	506	288	1150
WHO Africa region (AFRO)	14	11	30	12	9	24	26	20	54
WHO Americas region (PAHO)	122	46	360	118	49	342	240	95	702
WHO East Mediterranean region (EMRO)	13	9	29	10	7	23	23	16	52
WHO Europe region (EURO)	238	115	645	212	107	564	450	222	1209
WHO South-East Asia region (SEARO)	50	34	92	47	32	89	97	66	181
WHO Western Pacific region (WPRO)	224	101	607	170	81	450	394	182	1057
IARC membership (22 countries)	372	154	1082	319	143	909	691	297	1991
United States of America	79	24	245	74	26	227	153	50	472
China	125	61	289	95	48	219	220	109	508
India	20	14	27	16	11	21	36	25	48
European Union (EU-27)	182	80	507	151	68	417	333	148	924

Various treatment options are available today for rectal cancer, such as surgery, chemotherapy, and radiotherapy. Surgery is the most frequently used treatment method for rectal cancer. It is used for removal of the tumor and the metastases, and is associated with a cure rate of 60% (Hayat, 2009). The selection of a specific method of surgery depends on the surgeon’s experience and the patient's characteristics and preferences (Wu & Fazio, 2004; Porter, Soskolne, Yakimets & Newman, 1998).

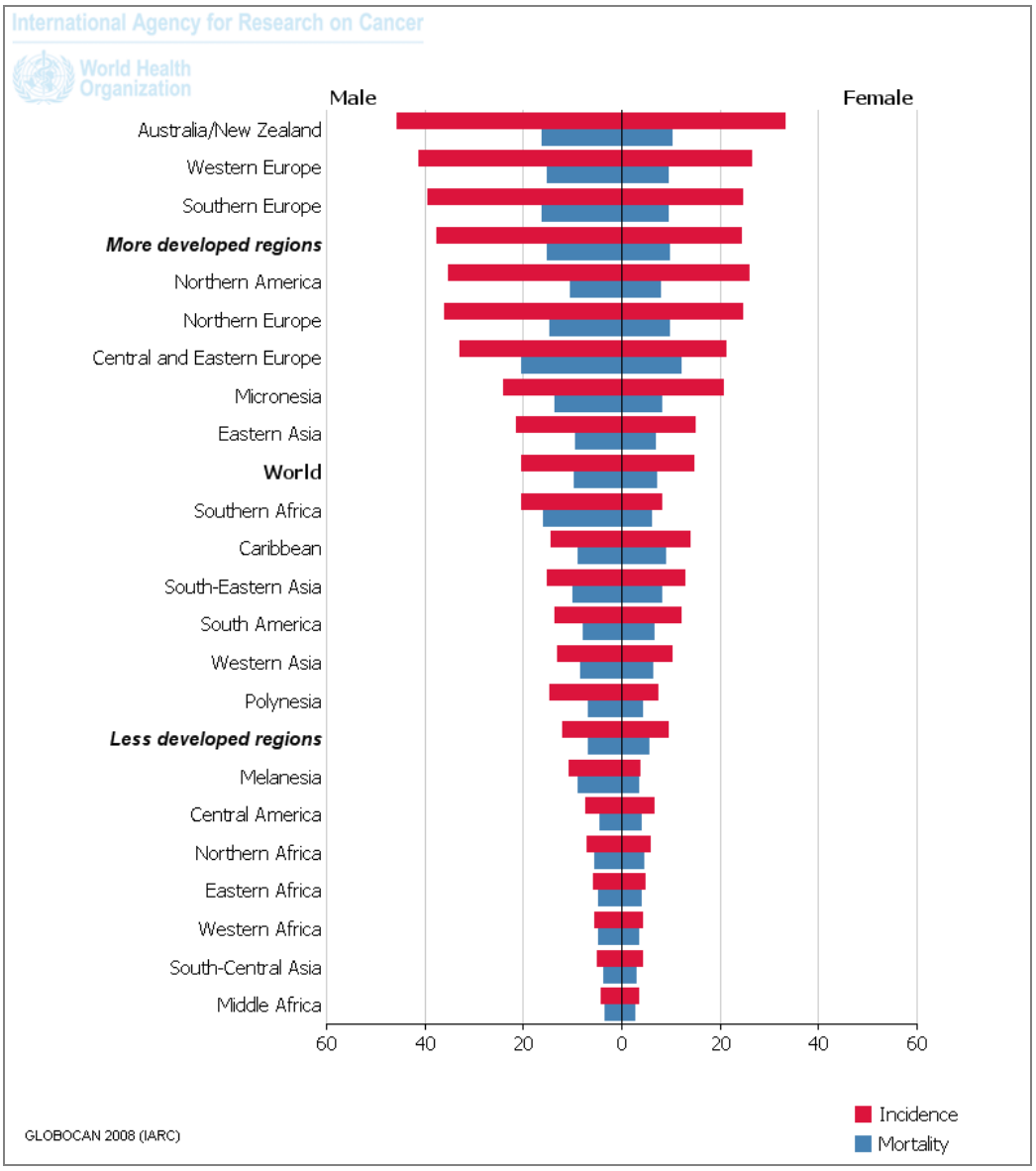

Figure 3.1 Estimated age-standardised rates per 100,000 for incidence and mortality of colorectal cancer worldwide.

Surgical options for curative treatment can be defined as transanal local excision, anterior resection of rectal (AR), low anterior resection (LAR), very low anterior resection, transanal endoscopic microsurgery (TEM), colo-anal anastomosis (CAA), intersphincteric resection, abdominal perineal resection (APR), and the Hartmann operation (Santoro, 2011; Czito & Willett, 2010). Construction of a stoma, stenting, internal bypass, and endoscopic cauterization can be surgical treatment options for palliative treatment. When surgery is not possible one may select other treatment options, such as chemotherapy, radiotherapy, or a combination of the two. These

options may be used for curative or palliative treatment as an adjuvant or neo-adjuvant theraphy (Chang, Kaiser, Mills, Rafferty & Buie, 2012). When curative and palliative treatments have been ruled out, symptomatic treatment may still be an option. In some cases it may not be possible to use any treatment. When the patient needs additional treatment after surgery, the physician uses chemotherapy, a combination of chemotherapy and radiotherapy, or a different type of surgery. The National Comprehensive Cancer Network recommends the use of surgery in the early pathologic stage of rectal cancer and observation of the patient after surgery (Wilkes, 2008). Survival rates increase with the use of preoperative and postoperative radiotherapy. In some cases chemotherapy is used as a part of a treatment combination and has been shown to improve survival (Taflampas, Christodoulakis, de Bree, Melissas & Tsiftsis, 2010; Hayat, 2009; Fleming, Pahlman & Monson, 2011). Similarly, when additional treatment is needed after a patient has received a combination of chemotherapy and radiotherapy, the surgeon might perform additional surgery either with or without chemotherapy.

Criteria that influence the decision as to which treatment one decides to use are tumor related as well as patient and surgeon related (Popa, Bratucu & Radu, 2011; Bosset et al, 2006; Taflampas, Christodoulakis, de Bree, Melissas & Tsiftsis, 2010; Stocchi et al, 2011; Porter, Soskolne, Yakimets & Newman, 1998; Chang, Kaiser, Mills, Rafferty & Buie, 2012). Tumor-related criteria include the stage of the disease, the location of the tumor, the presence of obstruction, coexisting diseases or pathologies, the presence of perforation, invasion of adjacent organs, pathological prognostic factors, the presence of fistula, resection margin status and the presence of rectal hematokesia. Patient-related and surgeon-related criteria include the patient's performance level, the patient's attitude, patient’s age, the surgeon’s experience, the efficacy of treatment, and the availability of treatment. As a large number of criteria are involved, selection of the appropriate treatment for a patient is a challenge for the physician. For instance, staging of the rectal cancer based on TNM classification (Table 3.2) is a critical factor for determination of the best treatment (Edge et al, 2010).

Table 3.2 Staging for colorectum cancer.

Primary Tumor (T)			
TX Primary tumor cannot be assessed			
T0 No evidence of primary tumor			
Tis Carcinoma in situ: intraepithelial or invasion of lamina propria			
T1 Tumor invades submucosa			
T2 Tumor invades muscularis propria			
T3 Tumor invades through the muscularis propria into pericolorectal tissues			
T4a Tumor penetrates to the surface of the visceral peritoneum			
T4b Tumor directly invades or is adherent to other organs or structures			
Regional Lymph Nodes (N)			
NX Regional lymph nodes cannot be assessed			
N0 No regional lymph node metastasis			
N1 Metastasis in 1–3 regional lymph nodes			
N1a Metastasis in one regional lymph node			
N1b Metastasis in 2–3 regional lymph nodes			
N1c Tumor deposit(s) in the subserosa, mesentery, or nonperitonealized pericolic or perirectal tissues without regional nodal metastasis			
N2 Metastasis in 4 or more regional lymph nodes			
N2a Metastasis in 4–6 regional lymph nodes			
N2b Metastasis in 7 or more regional lymph nodes			
Distant Metastasis (M)			
M0 No distant metastasis			
M1 Distant metastasis			
M1a Metastasis confined to one organ or site (for example, liver, lung, ovary, nonregional node)			
M1b Metastases in more than one organ/site or the peritoneum			
Stage	**T**	**N**	**M**
0	Tis	N0	M0
I	T1-T2	N0	M0
IIA	T3	N0	M0
IIB	T4a	N0	M0
IIC	T4b	N0	M0
IIIA	T1-T2	N1-N1c	M0
	T1	N2a	M0
IIIB	T3-T4a	N1-N1c	M0
	T2-T3	N2a	M0
	T1-T2	N2b	M0
IIIC	T4a	N2a	M0
	T3-T4a	N2b	M0
	T4b	N1-N2	M0
IVA	Any T	Any N	M1a
IVB	Any T	Any N	M1b

Besides TNM staging, the resection margin status should be considered. The letter R represents the presence or absence of residual tumor following resection. In the operative report of the patient, while the level of resection margin status R0 indicates the complete tumor resection with all margins histologically negative, R1 designates the complete tumor resection with microscopic surgical resection margin involvement. If there is an incomplete tumor resection with gross residual tumor that

was not resected, it can be represented by R2 (Chang, Kaiser, Mills, Rafferty & Buie, 2012).

The CDSS, decision tree and analytic hierarchy process examples related to rectal cancer was investigated and summarized briefly in the following parts of this chapter.

3.2 Clinical Decision Support System Examples in Rectal Cancer

There are very few studies about rectal cancer in the CDSS literature. Some of the studies focus on screening of the colorectal cancer. Saleem et al (2011) evaluated the interaction between human and computer by comparing current and newly designed clinical reminder of Veterans Health Administration's for colorectal cancer screening. Wilson et al (2010) designed an Internet-based Personalised Decision Support (PDS) package to inform people about screening options: faecal occult blood test (FOBT) and support their decision regarding screening for preventive care about colorectal cancer. Saleem et al (2009) evaluated the implementation of clinical decision support for colorectal cancer screening in different clinics and found some deficiencies in usage of the system. The users mentioned that problems occur because of getting exam results from outside of the institute, lack of quality in using, inaccuracy of the system, coordination shortage of gastroenterology and primary care, issues of compliance, and necessity of much more vital patient issues.

Additionally, there are some CDSS examples related to follow-up processes of patients and diagnosis of colorectal cancer. The study of Shi et al (2010) showed that a decision support algorithm can be used to diagnose colorectal cancer by using serum tumor markers and may support decisions for the usage of different tumor markers. The system “CEAwatch” designed by Verberne et al (2012) helps surgeons to follow-up a large number of patients, and uses Carcino-Embryonic Antigen (CAE) values to give recommendations.

The system efficiency is also evaluated by researchers. Harrison et al (2009) established the feasibility of implementing three decision support tools for rectal cancer patients within the surgical consultation, and found that usage of the decision support tools are not feasible in using surgical consultation due to the time restriction, patients characteristics, tool contents and negative impact of relationship between doctor and patient.

CDSS examples associated with the treatment of rectal cancer patients were not so common in the literature. Bossema et al (2008) applied treatment trade off method to compare the treatment options of the rectal cancer patients group. While the first group was defined as a stoma group, the second was no stoma group. Poston et al (2005) created a system, OncoSurge, for colorectal liver metastases patients. The system evaluates the resection strategies, chemotherapy and local ablation, and also uses expert opinions and literature review. The model may recommend the most appropriate treatment method and define the respectability of the patient. The study of O'Reilly et al (2008) evaluated the validity of the OncoSurge system, and compared decisions of the computer program and an expert group. Recommendations according to the optimal treatment of patients with colorectal liver metastases from both were assessed and results showed that the system can be used for decision making and education. Additionally, LoBello et al (2000) used a CDSS to determine the efficacy of chemotheraphy for colorectal cancer patients at different stages. The model offers the optimum treatment option by using efficacy of the treatment, incidence of side effects and overall survival of patients.

3.3 Decision Tree Studies on Rectal Cancer

Although decision trees are used for various health issues in medical decision making, they are used in very few colorectal cancer studies. The decision tree studies concerning colorectal cancer generally focused on cost effectiveness analysis. Tilson et al (2012) developed decision tree to estimate mean lifetime cost for colorectal cancer care from the health care payer perspective in Ireland in 2008. Guidelines are used to selection of appropriate treatment option and validity of the options is

checked by expert opinions. Costs for diagnosis, treatment, tests and hospitalisation were received from hospitals, diagnosis-related group (DRG) costs, literature and clinical opinions. Results indicated that rectal cancer care is more expensive than colon cancer care. Additionally stage-III is the most costly and stage-I was the least. Another cost effectiveness example of decision trees (Karuna et al, 2008) compared cost effectiveness of laporatomy and laparoscopy methods for patients with hepatic colorectal metastases. Annemans et al (2008) also interested in patients with hepatic colorectal metastases and evaluated ferucarbotran-enhanced magnetic resonance imaging (MRI) economically. The decision tree was used to simulate medical management of patients. Data including diagnostic outcomes, clinical findings, laboratory and pathology results, imaging findings, literature on life expectancies and expert opinions are used to suggest medical management for each patient. It was found that ferucarbotran-enhanced MRI may make medical management better and save costs for health care. A further example of decision trees was the study of Abbott et al (2012) which used decision tree for colorectal cancer liver metastases patients to assess medical and also financial outcomes regarding treatment of surgery. The decision tree evaluated the comparison of simultaneous and staged resections and, results showed that simultaneous resection is more cost effective than staged resection for the patients with colorectal cancer liver metastases. Pichereau et al (2010) evaluated the cost effectiveness of UGT1A1 genotype screening with the help of decision tree and founded that using a screening method for UGT1A1 before irinotecan treatment is cost effective for hospitals. Park et al (2001) used a decision tree to determine the cost-effectiveness of (18F) 2-fluoro-2-deoxyglucose positron emission tomography in addition to computed axial tomography, and whether it is useful to manage recurrent rectal cancer. Delcò and Sonnenberg (1999) compared cost-effectiveness of two screening strategies, colonoscopy and faecal occult blood test, by using a decision tree and a Markov model. Results of the analysis showed that screening strategy of colonoscopy is more cost-effective than screening by annual faecal occult blood test.

Decision tree approach is applied in colorectal cancer not only with the aim of cost effectiveness but also for different purposes. Liu et al (2011) constructed a

decision tree to make a model for colorectal cancer diagnosis by using serum proteins of patients. Lee et al (2004) built a model with the help of data mining methods in order to predict hospital charges for colorectal cancer. They used a classification and regression tree (CART) which is a special type of a decision tree model, and an artificial neural network (ANN) and then compared the results of the analysis. The performance of the ANN model was found better than CART model. Minsky et al (1998) developed a consensus based on decision tree to give suggestions for the treatment of rectal cancer. A modified Delphi technique was applied to get expert opinions. Vasen et al (2001) developed a decision model to evaluate and to compare life expectancy of patients with familial adenomatous polyposis. The estimation of the life expectancy of the two surgical options, ileum-pouch-anal anastomosis and ileorectal anastomosis, may be achieved by the use of this decision model. In a previous study (Suner et al, 2012); AHP and sequential decision tree methods were used to make a decision support model to determine the best treatment method for rectal cancer patients. The priorities of criteria were obtained by using the AHP method and then the decision tree was constructed with the help of these priorities. It is expected that the decision model may improve the quality of the decision making process of treatment for rectal cancer patients.

3.4 Application of Analytic Hierarchy Process in Rectal Cancer

The AHP has been frequently used in medical decision making studies as well. Dolan (2008) described the use of AHP to aid medical decision making processes and improve communication between the physician and the patient. In the pilot prioritization project conducted by Cheever et al (2009), the priority ranking of 75 cancer antigens was based on the AHP method. The experts developed a list of cancer vaccines targeting antigens using ranked priorities. Kitamura (2010) investigated the criteria and priorities using the AHP method in gynecological cancer. Patients with gynecological cancer were offered treatment choices with the aid of the AHP. Pecchia et al (2011) designed a Web-based system that uses the AHP method for prioritizing risk factors for falls among the elderly; the system was used to reach as many experts as possible. The Web-based system weighted each decision-

maker on the basis of experience, specialization years, education level and working area, and investigated the experts' opinions. In a literature review, Liberatore and Hydick (2008) classified the health care and medical decision making applications of the AHP. Fifty studies that published between 1981 and 2006 were grouped into seven categories such as diagnosis, therapy/treatment, patient participation, organ transplantation, project and technology evaluation and selection, human resource planning, and health care evaluation and policy. Richman et al (2005) used the AHP as a model for decision making process regarding prostate cancer patients; the model was developed to aid the mutual decision making process of physicians and patients. Sloane et al (2002) summarized a number of studies in which the authors used AHP to support medical and hospital-based decisions.

Since rectal cancer is a complex condition based on several criteria, the AHP is a suitable and appropriate choice to support the decision (Dolan, 2008). In some decision support studies focusing on screening methods for rectal cancer, the AHP was used to construct a decision model for selecting the best screening approach. A patient decision aid for rectal cancer screening, based on several criteria, was improved by Dolan and Frisina (2002). Dolan (Dolan, 2000; Dolan, 2005) showed that the AHP method could be used to support shared decision making for preventive interventions with regard to screening for rectal cancer. Chung et al (2012) used the AHP method to determine priorities of possible performance measures regarding a pay-for-performance system for colorectal cancer care. Yasunaga et al (2008) used the AHP method to investigate whether risk information concerning total colonoscopy, which was employed instead of fecal occult blood tests, affects the patient's preference with regard to screening for rectal cancer.

In this dissertation, a decision support algorithm was developed to determine the most appropriate treatment for rectal cancer and to support decisions of the physicians. Various criteria essential to the decision process were determined, and the sequential decision tree was constructed according to the priorities assigned to these criteria. Priorities were determined by the analytic hierarchy process (AHP) method, which is a stepwise problem solving procedure for multi-criteria decision

making (Saaty & Vargas, 2000). The method is well adapted to a physician's natural decision processes. In the present study the AHP method was used to support decision making for the treatment of rectal cancer. In the next chapter, the real data application of the decision model is explained.

CHAPTER FOUR
APPLICATION

The application process of this thesis consists of expert opinion, real patient data and literature review. First of all, criteria used to determine the most appropriate treatment method for rectal cancer were determined by expert opinions. After determination of criteria, AHP method was used to obtain priorities of the criteria in decision process. Then, the decision tree was developed according to the priorities calculated by AHP method. Besides, the decision model of rectal cancer treatment was completed, and relevant studies regarding criteria and treatment options for rectal cancer were searched from PubMed. Additionally, previous treatment decisions for rectal cancer patients were obtained from Department of General Surgery, Dokuz Eylül University. The decision rules that recommend the best rectal cancer treatment were identified in order to build up a CDSS. The internet based user interface was designed to assist physicians' decisions by using expert opinion, real patient data, and literature review. Application process was summarized as a flow chart in Figure 4.1 below.

4.1 Defining Problem and Criteria Determination

For developing a decision support algorithm deciding the most appropriate treatment for rectal cancer, steps for the decision making process and various criteria essential to the decision process were determined by a panel of an expert radiologist and a general surgeon who specialized on rectal cancer from the Faculty of Medicine, Dokuz Eylül University. Experts determined that the decision making process consists of two sequential steps. The first step is the decision concerning the required type of treatment. Based on this step, a second decision step is made concerning the additional treatments that should be provided.

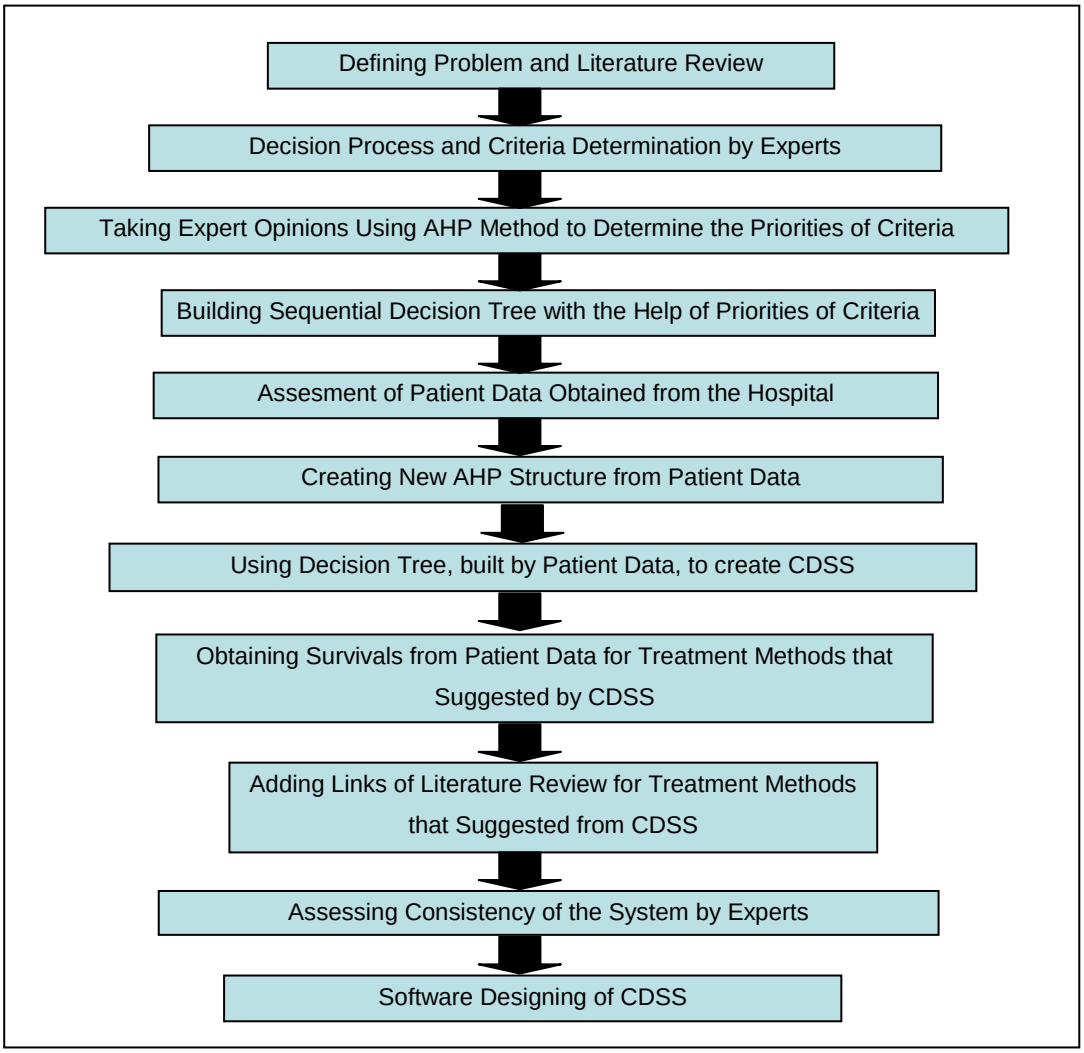

Figure 4.1 A flow chart for the application process.

In the first step, the treatment options may fall into any of the following three categories: curative treatment, palliative treatment, or symptomatic treatment. 'No treatment' is defined as a fourth category. Nine surgical options are currently available for curative treatment: transanal local excision, transanal endoscopic microsurgery (TEM), anterior resection of rectal, low anterior resection (LAR), very low anterior resection, colo-anal anastomosis (CAA), intersphincteric resection, abdominal perineal resection (APR), and the Hartmann operation. Surgical options for palliative treatment such as construction of a stoma, stenting, internal bypass, and endoscopic cauterization are grouped as a tenth option. Chemotherapy, radiotherapy, or a combination of the two (chemoradiotherapy) may be selected while surgery

option is not appropriate for the patient. An overview of the first decision step was shown in Table 4.1.

Table 4.1 Structure of the first decision making process.

1) **First Decision Step (Decision-making for the first treatment method)**
- *Curative treatment*
  - Surgery
    - Transanal local excision
    - Transanal endoscopic microsurgery
    - Anterior resection of rectum
    - Low anterior resection
    - Very low anterior resection
    - Colo-anal anastomosis
    - Intersphincteric resection
    - Abdominal perineal resection
    - Hartmann operation
  - Preoperative chemoradiotherapy+Surgery
    - Preoperative chemoradiotherapy+Transanal local excision
    - Preoperative chemoradiotherapy+Transanal endoscopic microsurgery
    - Preoperative chemoradiotherapy+Anterior resection of rectum
    - Preoperative chemoradiotherapy+Low anterior resection
    - Preoperative chemoradiotherapy+Very low anterior resection
    - Preoperative chemoradiotherapy+Colo-anal anastomosis
    - Preoperative chemoradiotherapy+Intersphincteric resection
    - Preoperative chemoradiotherapy+Abdominal perineal resection
    - Preoperative chemoradiotherapy+Hartmann operation
  - Others
    - Only chemotherapy
    - Only radiotherapy
    - Chemoradiotherapy
- *Palliative treatment*
  - Palliative operations (stoma, stent, internal by-pass, endoscopic cauterization)
  - Others
    - Only chemotherapy
    - Only radiotherapy
    - Chemoradiotherapy
- *Symptomatic treatment*
- *No treatment*

The second step defines additional post-treatment options related to the treatment selected in the first step. In the second decision step the physician examines the necessity of additional treatment. An overview of the second decision step was shown in Table 4.2. Additional treatment after the first treatment includes chemotherapy, a combination of chemotherapy and radiotherapy, a different type of surgery or a combination of surgery and chemotherapy. Also a physician may choose the option for treatment is concluded.

Table 4.2 Structure of the second decision making process.

2) Second Decision Step (Decision-making as regards the need for additional treatment)

- *Additional treatment is necessary*
  - Only chemotherapy
  - Only radiotherapy
  - Chemoradiotherapy
  - Additional surgery
    - Transanal local excision
    - Transanal endoscopic microsurgery
    - Anterior resection of rectum
    - Low anterior resection
    - Very low anterior resection
    - Colo-anal anastomosis
    - Intersphincteric resection
    - Abdominal perineal resection
    - Hartmann operation
  - Additional surgery+Chemotherapy
    - Transanal local excision+Chemotherapy
    - Transanal endoscopic microsurgery+Chemotherapy
    - Anterior resection of rectum+Chemotherapy
    - Low anterior resection+Chemotherapy
    - Very low anterior resection+Chemotherapy
    - Colo-anal anastomosis+Chemotherapy
    - Intersphincteric resection+Chemotherapy
    - Abdominal perineal resection+Chemotherapy
    - Hartmann operation+Chemotherapy
- *Treatment is concluded*

Based on the sequential decision process defined by the panel of same experts, 56 treatment combinations have been determined on the basis of expert opinions and literature reviews (Popa, Bratucu & Radu, 2011; Taflampas, Christodoulakis, de Bree, Melissas, & Tsiftsis, 2010; Fleming, Pahlman & Monson, 2011; Singh-Ranger & Kumar, 2011; Biagi et al, 2011). These are shown in Table 4.3.

The criteria that had influence on the decision for treatment of rectum cancer were defined by the same experts who determined the decision process. In literature, it can be seen that criteria that influence the decision as to which treatment one decides to use are tumor related as well as patient and surgeon related (Popa, Bratucu & Radu, 2011; Taflampas, Christodoulakis, de Bree, Melissas & Tsiftsis, 2010; Stocchi et al. 2001; Porter, Soskolne, Yakimets & Newman, 1998).

Table 4.3 Treatment options for patients with rectal cancer.

1. Surgery options
   1. 1. Transanal local excision (TLE)
   1. 2. Transanal endoscopic microsurgery (TEM)
   1. 3. Anterior resection of rectum (AR)
   1. 4. Low anterior resection (LAR)
   1. 5. Very low anterior resection (LAR)
   1. 6. Colo-anal anastomosis (CAA)
   1. 7. Intersphincteric resection (ISR)
   1. 8. Abdominal perineal resection (APR)
   1. 9. Hartmann operation
   1. 10. Palliative operations (stoma, stent, internal by-pass, endoscopic cauterization)
2. Only chemotherapy (CT)
3. Only radiotherapy (RT)
4. CT+RT
5. TLE after CT+RT
6. TEM after CT+RT
7. AR after CT+RT
8. LAR after CT+RT
9. VLAR after CT+RT
10. CAA after CT+RT
11. ISR after CT+RT
12. APR after CT+RT
13. Hartmann operation after CT+RT
14. Palliative operations after CT+RT
15. TLE after CT+RT then systemic CT
16. TEM after CT+RT then systemic CT
17. AR after CT+RT then systemic CT
18. LAR after CT+RT then systemic CT
19. VLAR after CT+RT then systemic CT
20. CAA after CT+RT then systemic CT
21. ISR after CT+RT then systemic CT
22. APR after CT+RT then systemic CT
23. Hartmann op. after CT+RT then systemic CT
24. Palliative op. after CT+RT then systemic CT
25. TLE then systemic CT
26. TEM then systemic CT
27. AR then systemic CT
28. LAR then systemic CT
29. VLAR then systemic CT
30. CAA then systemic CT
31. ISR then systemic CT
32. APR then systemic CT
33. Hartmann operation then systemic CT
34. Palliative operations then systemic CT
35. TLE then systemic CT+RT
36. TEM then systemic CT+RT
37. AR then systemic CT+RT
38. LAR then systemic CT+RT
39. VLAR then systemic CT+RT
40. CAA then systemic CT+RT
41. ISR then systemic CT+RT
42. APR then systemic CT+RT
43. Hartmann op. then systemic CT+RT
44. Palliative op. then systemic CT+RT
45. TLE+Another surgery
46. TEM+Another surgery
47. AR+Another surgery
48. LAR+Another surgery
49. VLAR+Another surgery
50. CAA+Another surgery
51. ISR+Another surgery
52. APR+Another surgery
53. Hartmann operation+Another surgery
54. Palliative operations+Another surgery
55. Symptomatic treatment
56. No treatment

CT: Chemotherapy
RT: Radiotherapy

Tumor-related criteria include the stage of the disease, the location of the tumor, the presence of any obstructions, coexisting diseases or pathologies, the presence of perforation, invasion of adjacent organs, the presence of fistula, and the presence of rectal hematokesia. Patient- and surgeon-related criteria include the patient's performance level based on the American Society of Anesthesiologists (ASA), the patient's attitude, and the surgeon’s experience. The different sub-criteria and levels of sub-criteria at the step 1 are shown in Table 4.4.

Table 4.4 Criteria used in the first decision step.

1) Stage of the disease (TNM)*
- T1 N0 M0
- T2 N0 M0
- T3 N0 M0
- T4 N0 M0
- T1 N1 M0
- T2 N1 M0
- T3 N1 M0
- T4 N1 M0
- T1 N2 M0
- T2 N2 M0
- T3 N2 M0
- T4 N2 M0
- T1 N0 M1
- T2 N0 M1
- T3 N0 M1
- T4 N0 M1
- T1 N1 M1
- T2 N1 M1
- T3 N1 M1
- T4 N2 M1
- T1 N2 M1
- T2 N2 M1
- T3 N2 M1
- T4 N2 M1

2) Location of the tumor
- Lower
- Middle
- Upper

3) Patient performance level (ASA)**
- ASA I
- ASA II
- ASA III
- ASA IV

4) Presence of obstruction
- Present
- Absent

5) Patient's attitude
- Appropriate
- Not appropriate

6) Coexisting disease or pathology
- Present
  - CVS***
  - Others
    - >One
    - More
- Absent

7) Presence of perforation
- Present
- Absent

8) Presence of the adjacent organ invasion
- Present
  - One
  - More
- Absent

9) Surgeon's experience
- Below 20
- 20 and above 20

10) Presence of fistula
- Present
- Absent

11) Presence of rectal hematokesia
- Present
- Absent

***TNM** is an international staging system for cancers where the grade of T represents the tumour size and extensions, N represents the level of nodal invasion, and M represents the presence of absence of metastases.

****ASA:** American Society of Anesthesiologists

*****CVS:** Cardiovascular Disease

Explanations of criteria used in the first decision step are summarized as follows. *Stage of the disease* defines the patient's rectal cancer stage using TNM international staging system for cancers where the grade of T represents the tumor size and extensions, N represents the level of nodal invasion, and M represents the presence or absence of metastases. *Location of the tumor* represents the tumor location of rectal cancer and may be defined as three different levels such as "lower", "middle" or "upper". *Coexisting disease or pathology* represents the presence or absence of another disease for a rectal cancer patient. If coexisting disease or pathology is present, the type of the disease may be chosen from the list below. *Invasion of adjacent organs* represents the presence or absence of adjacent organ invasion for a rectal cancer patient. *Surgeon's experience* represents the expert level of the surgeon who makes the surgical operation of the patient. The reference value is defined as 20

interventions of the surgeon. The criteria levels may be valued as “lower than 20” or “equal or upper than 20”. *Presence of perforation* represents the presence or absence of perforation regarding a rectal cancer patient. *Presence of obstruction* represents the presence or absence of obstruction regarding a rectal cancer patient. *Presence of fistula* represents the presence or absence of fistula regarding a rectal cancer patient.

The second decision step includes eight tumor-related criteria: the stage of disease, location of the tumor, the presence of perforation, the presence of obstruction, coexisting disease or pathology, invasion of adjacent organs, pathological prognostic factors, and resection margin status. Furthermore, six patient- and surgeon-related criteria are defined: patient performance level (Karnovsky), patient’s attitude, surgeon’s experience (20 interventions), patient’s age, the efficacy of treatment, and the availability of treatment (the ability of the patient or the physician to obtain or perform the respective treatment). Table 4.5 shows the different sub-criteria and levels of sub-criteria at the step 2.

Explanations of criteria used in the second decision step are defined as below. *Stage of the disease* defines the changes patient's rectal cancer stage after the first treatment was applied. It may be defined as three different levels such as “upstage”, “stable” or “downstage”. *Invasion of adjacent organs* represents the presence or absence of adjacent organ invasion for a rectal cancer patient. Pathologic prognostic factors are grouped in three categories: lymph invasion, perineural invasion and vascular invasion. *Lymph invasion* represents the presence or absence of lymph invasion for a rectal cancer patient. The option of non-assessable lymph invasion is also available. *Perineural invasion* represents the presence or absence of perineural invasion for a rectal cancer patient. The option of non-assessable perineural invasion is also available. *Vascular invasion* represents the positive or negative vascular invasion for a rectal cancer patient. The option of non-assessable vascular invasion is also available. *Patient’s age* defines the age of the patient' and it is classified as “0-80” or “above 80”.

Table 4.5 Criteria used in the second decision step.

1) Stage of disease (TNM)*
- T1 N0 M0
- T2 N0 M0
- T3 N0 M0
- T4 N0 M0
- T1 N1 M0
- T2 N1 M0
- T3 N1 M0
- T4 N1 M0
- T1 N2 M0
- T2 N2 M0
- T3 N2 M0
- T4 N2 M0
- T1 N0 M1
- T2 N0 M1
- T3 N0 M1
- T4 N0 M1
- T1 N1 M1
- T2 N1 M1
- T3 N1 M1
- T4 N2 M1
- T1 N2 M1
- T2 N2 M1
- T3 N2 M1
- T4 N2 M1

2) Location of the tumor
- Lower
- Middle
- Upper

3) Patient's age
- 0-80
- Above 80

4) Patient's performance level (Karnovsky)
- Appropriate
- Not appropriate

5) Efficacy level of treatment
- Low
- Middle
- High

6) Presence of obstruction
- Present
- Absent

7) Patient's attitude
- Appropriate
- Not appropriate

8) Coexisting disease or pathology
- Present
  - CVS**
  - Others
    - >One
    - More
- Absent

9) Availability of treatment
- Accessible
- Not accessible

10) Presence of perforation
- Present
- Absent

11) Invasion of adjacent organs
- Present
  - One
  - More
- Absent

12) Surgeon's experience
- Lower than 20
- Equal or upper than 20

13) Pathologic prognostic factors
- Lymph invasion
  - Present
  - Absent
- Vascular invasion
  - Present
  - Absent
- PNI***
  - Positive
  - Negative
- Characteristic of tumour invasion
  - Infiltrative
  - Bound of non-infiltrative

14) Resection margin status
- R0
- R1
- R2

***TNM** is an international staging system for cancer. The grade of T expresses tumor size and extensions, N stands for the level of nodal invasion, M stands for the presence or absence of metastases.

****CVS:** Cardiovascular disease

*****PNI:** Perineural invasion

The *resection margin status* defines the patient's resection margin status. The letter R represents the presence or absence of residual tumor following resection. In the operative report of the patient, while the level of resection margin status R0 indicates the complete tumor resection with all margins histologically negative, R1 designates the incomplete tumor resection with microscopic surgical resection margin involvement. If there is an incomplete tumor resection with gross residual tumor that was not resected, it can be represented by R2 the resection margin status should be considered. *Presence of perforation* represents the presence or absence of perforation regarding a rectal cancer patient. *Presence of obstruction* represents the presence or absence of obstruction regarding a rectal cancer patient. *Availability of*

treatment represents the ability of the patient or the physician to obtain or perform the respective treatment. It may be defined as “accessible” or “not accessible”.

After determining decision process to choose the most appropriate treatment method regarding rectum cancer and criteria that had influence on treatment decision by experts, AHP structure was created to get priorities of the criteria.

4.2 Taking Expert Opinions by Using AHP Method to Determine the Priorities of Criteria

First of all, it was aimed at obtaining priorities of the criteria that determined by using AHP method. The AHP structures that were created for this purpose are shown in Figure 4.2 and Figure 4.3. AHP structures for the two decision steps are nearly the same. There are three levels in both hierarchies. The first level is the goal of the specific treatment, the second level contains the treatment criteria, and the last level contains sub-criteria. The criteria set was organized into two main categories, i.e. tumor-related criteria and patient-surgeon related criteria.

A Web-based application was developed to guide experts in making comparisons. The expert opinions were obtained from five rectal cancer specialists from the Department of General Surgery, Dokuz Eylül University. The results were collected in an electronic environment. The user compares the two options and selects the relatively more significant one, as shown in Figure 4.4. When the user believes there is no priority between criteria pairs, he selects the “both are equal” option. After selecting criteria, the scale developed by Saaty (2008a) appears at the bottom of the user interface. A detailed description of numerical values is shown on the right corner of the interface. When the user wishes to know details about a criterion, he may refer to the corresponding explanation of the criterion on a different page.

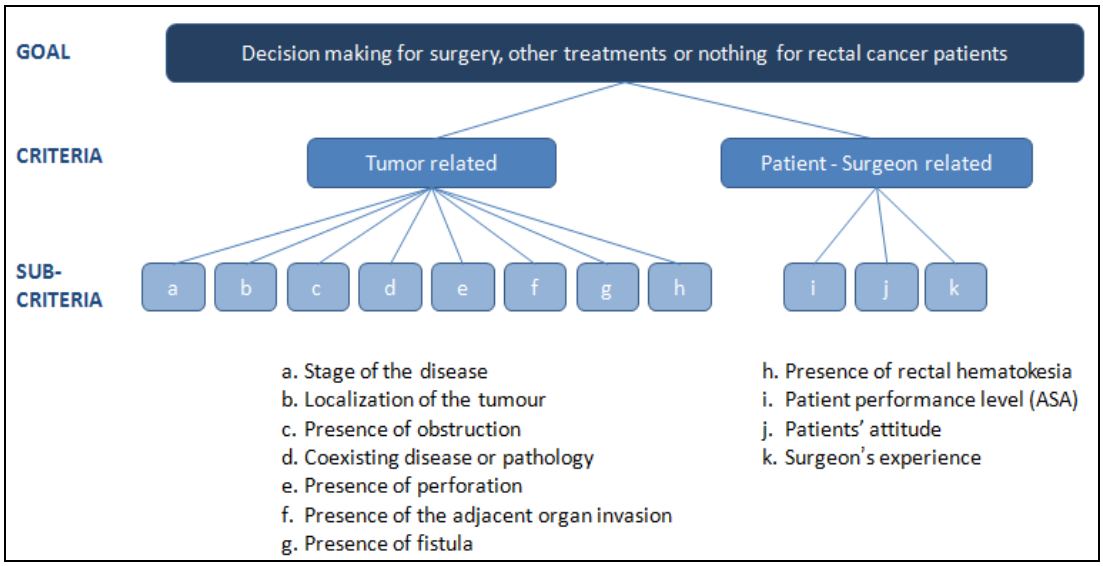

Figure 4.2 AHP structure for the first decision step in designed model.

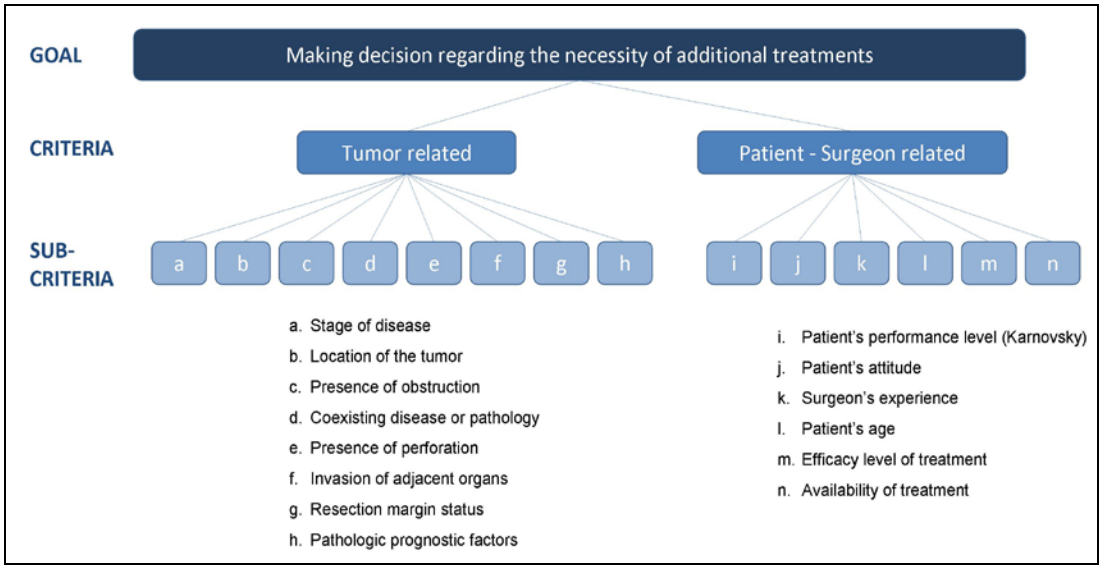

Figure 4.3 AHP structure for the second decision step in designed model.

The collected data were analyzed with "Expert Choice" software developed specifically for AHP applications. After all pairwise comparisons had been completed by each participant; the results were combined and analyzed. Each participant's answers had equal weight.

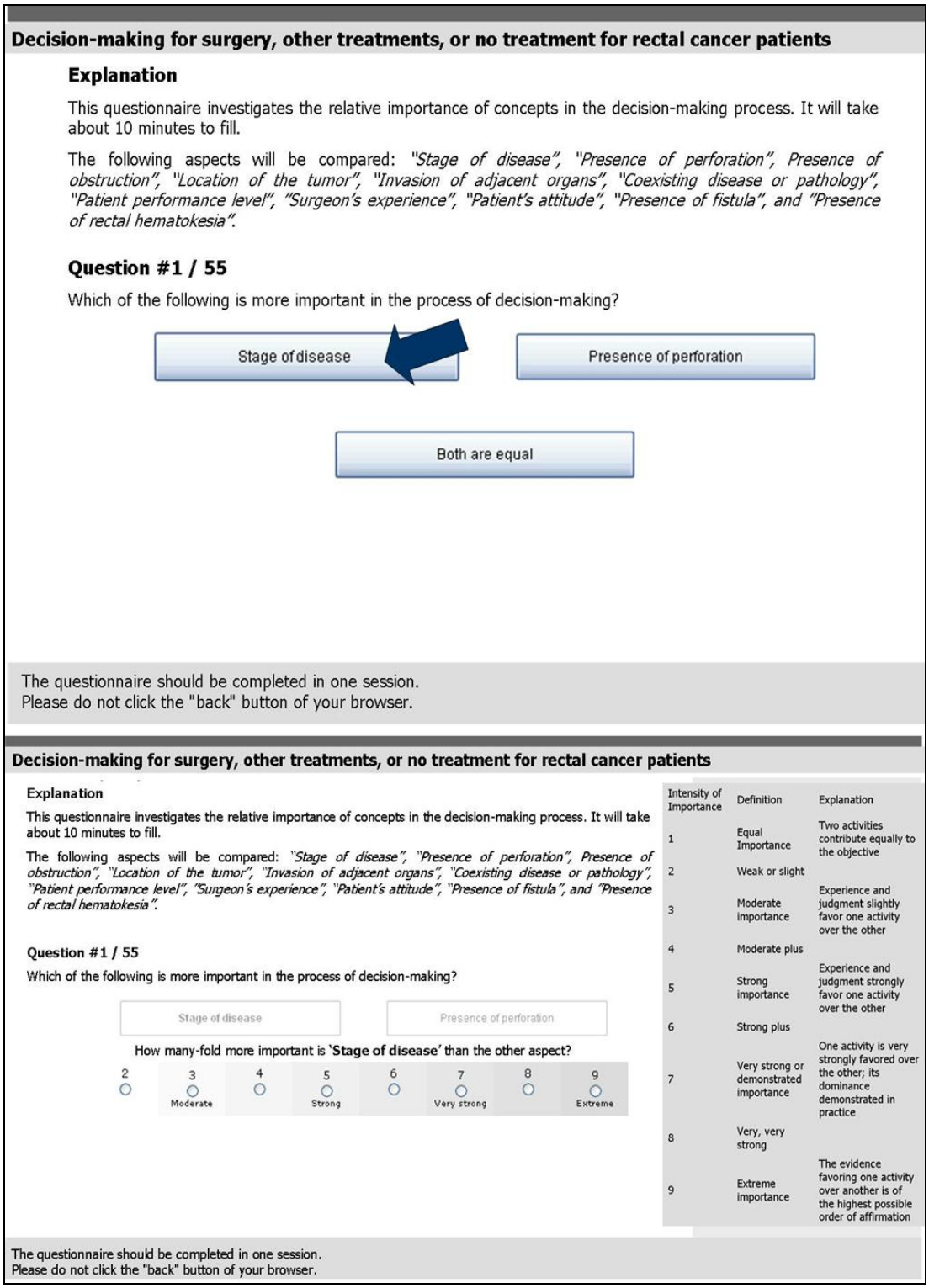

Figure 4.4 Screenshot of the web interface prepared for the first AHP structure.

After the analysis, the Expert Choice software demonstrated criteria weights in the form of a graphic diagram. Finally, the consistencies of results for both decision steps were measured using the *CI*, and the results were interpreted.

In the first AHP structure the decision-makers performed 28 pairwise comparisons among eight tumor-related sub-criteria, and three pairwise comparisons among three patient-surgeon related sub-criteria. Similarly, in the second AHP structure the decision makers performed 28 and 15 pairwise comparisons, respectively.

The *CI* for tumor-related criteria of the first AHP structure was computed as follows:

$$CI = (\lambda_{\max} - n)/(n-1) = (8.573 - 8)/(8-1) = 0.082$$

The *CI* for patient-surgeon related criteria of the first AHP structure was calculated as 0.000. The other *CIs* for tumor-related and patient-surgeon related criteria of the second AHP structure were 0.079 and 0.046, respectively.

After using Table 2.3 to select an appropriate value of *RI* for a matrix size of eight, the *CR* for the tumor-related criteria of the first AHP structure was calculated as follows:

$$CR = CI / RI = 0.082 / 1.41 = 0.058$$

As the *CR* value is equal or lower than 0.10, the matrix is consistent and the expert's judgments are acceptable (Saaty, 2008b). *CR's* for the other criteria and the priorities obtained from pairwise comparisons are shown in Table 4.6. In the first decision step, the most important attribute for tumor-related criteria was "the presence of perforation", achieving a relative priority of 0.331. For patient- and surgeon-related criteria, the "surgeon's experience" had the highest relative priority (0.630). In the second decision step, "stage of the disease" had the highest relative priority for tumor-related criteria, achieving a value of 0.230.

Table 4.6 Combined priorities for the both AHP structures in designed model.

First AHP structure	
Tumor information	**Combined priority vector**
Presence of perforation	0.331
Presence of obstruction	0.183
Presence of fistula	0.142
Invasion of adjacent organ	0.102
Presence of rectal hematokesia	0.081
Stage of disease	0.062
Location of tumor	0.054
Coexisting disease or pathology	0.045
	Σ=1.00
λ_{max} = 8.573, CI = 0.082, RI = 1.41, CR = 0.058 < 0.1 OK	
Decision to perform surgery	**Combined priority vector**
Surgeon's experience	0.630
Patient's performance level (ASA)	0.282
Patient's attitude	0.088
	Σ=1.00
λ_{max} = 3.000, CI = 0.000, RI = 0.58, CR = 0.000 < 0.1 OK	
Second AHP structure	
Tumor information	**Combined priority vector**
Stage of disease	0.230
Resection margin status	0.212
Invasion of adjacent organ	0.145
Pathologic prognostic factors	0.137
Presence of perforation	0.109
Presence of obstruction	0.064
Location of tumor	0.060
Coexisting disease or pathology	0.043
	Σ=1.00
λ_{max} = 8.552, CI = 0.079, RI = 1.41, CR = 0.056 < 0.1 OK	
Decision to perform surgery	**Combined priority vector**
Surgeon's experience	0.281
Efficacy level of treatment	0.260
Patient's performance level (Kamovsky)	0.159
Patient's age	0.105
Patient's attitude	0.099
Availability of treatment	0.096
	Σ=1.00
λ_{max} = 6.230, CI = 0.046, RI = 1.24, CR = 0.037 < 0.1 OK	

For patient- and surgeon-related criteria "the surgeon's experience" again had the highest relative priority, this time with a value of 0.281. The results showed that there were some variations in the ranking of criteria between the two decision: "the presence of perforation" had the highest priority in the first decision step, but ranked fifth in the second step.

4. 3 Building Sequential Decision Tree with the Help of Priorities of Criteria

A sequential decision tree was constructed using the priorities determined by the AHP method. Criteria were sorted according to their priorities, after which the decision steps of the decision process were defined. Both decision trees have the same structure; the first and the second decision trees were shown in Figure 4.5 and Figure 4.6. For reasons of brevity, only one branch of each criterion is shown. Details were omitted.

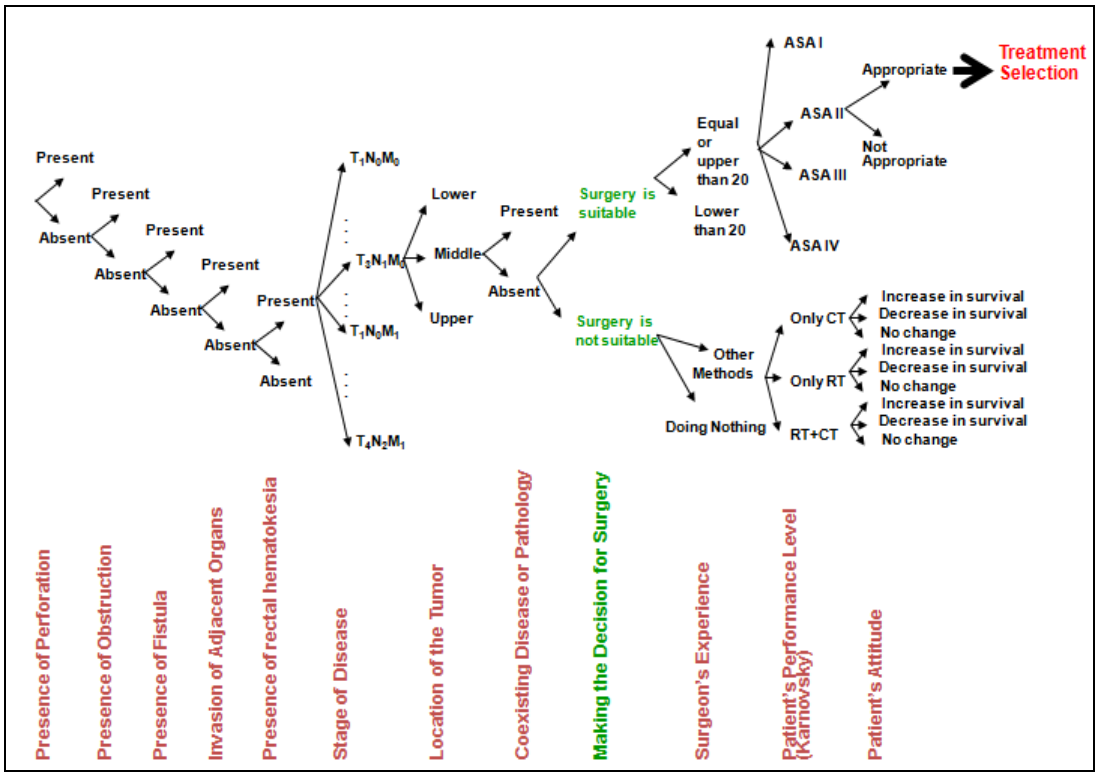

Figure 4.5 The decision tree structure constructed for the first decision step.

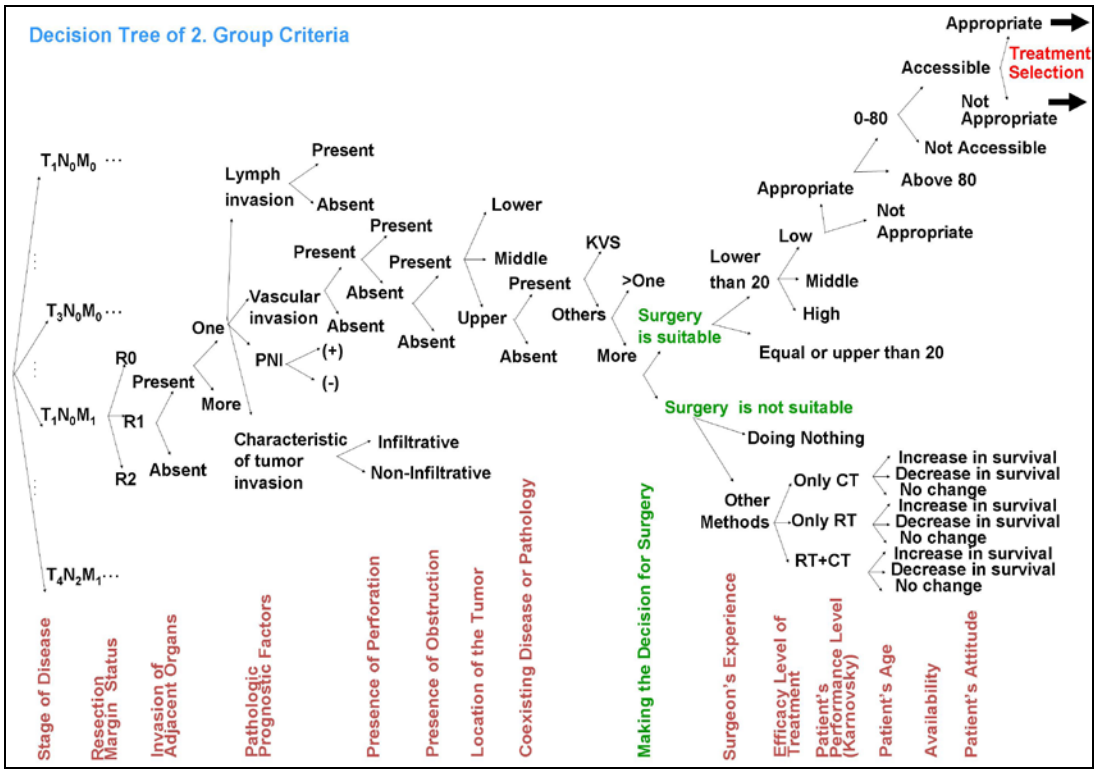

Figure 4.6 The decision tree structure constructed for the second decision step.

The criteria used in the sequential decision tree were sorted according to priorities determined by the AHP structures. Let us consider the construction process of the decision tree for the first decision step: the decision to perform surgery, other treatments, or no treatment. Tumor-related issues were sorted first and a decision node was created for each decision concerning surgical options. In case surgery was deemed appropriate, other relevant criteria were evaluated and the most appropriate surgical method was chosen. In case surgical options were considered unsuitable, either one of the other methods might be selected without other criteria being examined, or one may decide to perform no treatment.

The combined sequential decision tree used to determine the most appropriate treatment method for rectal cancer patients is shown in Figure 4.7. The results of treatment after this decision process are evaluated in terms of increased or decreased survival chances, or no changes.

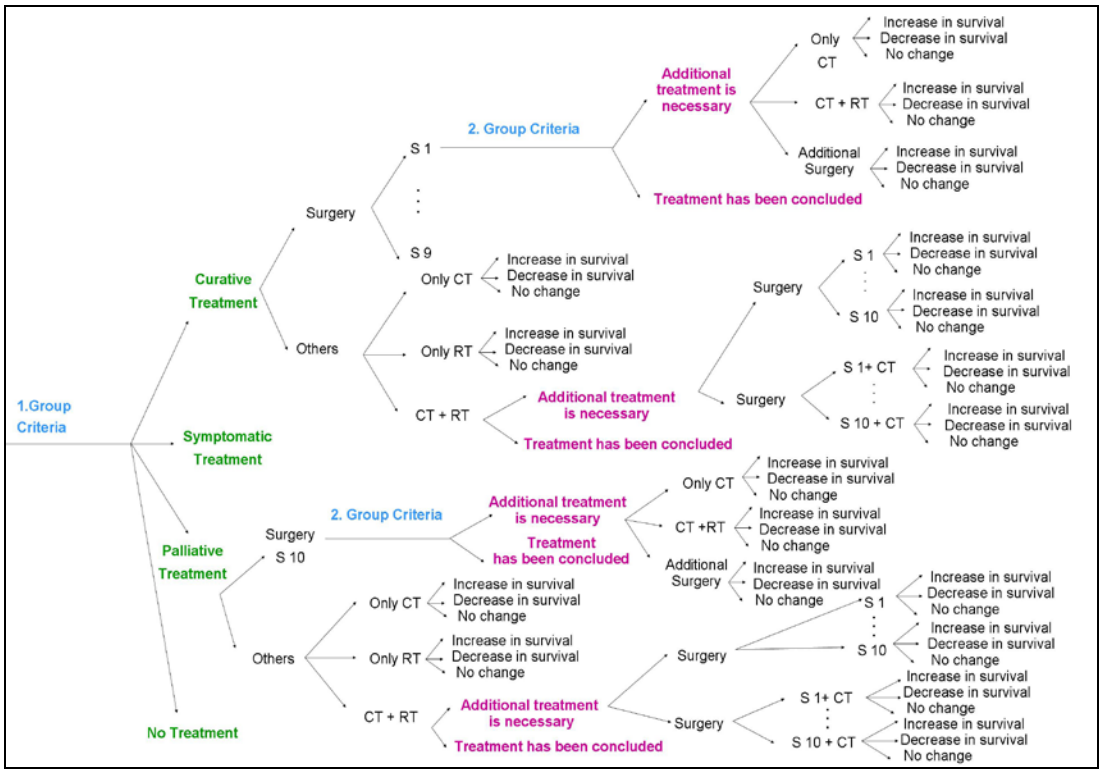

Figure 4.7 The decision process used to determine the most appropriate treatment method for rectal cancer patients.

The sample branch of a decision tree for the most frequently seen case was drawn by SmartDraw Software (Figure 4.8). Because the number of the patient data was not enough to analyze the decision tree with the help of decision theory, the sample branch of a decision tree may be improved if the user reaches the sufficient number of patient data. Therefore, the most appropriate treatment method according to avearge survival time may be shown to the decision maker by using decision theory. CDSS application make use of not only the real patient data, but also expert opinions and literature review. In addition to this application, the model was developed by means of decision theory. If there were a huge patient data set, the developed model might be incorporated in the CDSS.

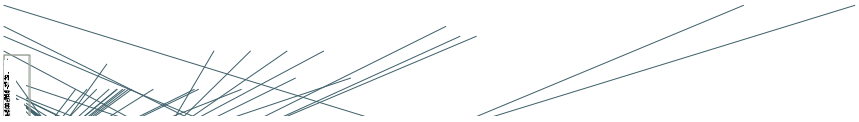

Figure 4.8 The sample branch of a decision tree that drawn by SmartDraw Software.

4.4 Assesment of Patient Data that Obtained from the Hospital

The application of the model that was created for the purpose of determining the most appropriate treatment method for rectum cancer patients was done by real patient data. The data and the previous treatment decisons for rectal cancer patients were achieved from rectal cancer patient data obtained from the Department of General Surgery, Dokuz Eylül University including the years 1988–2010 for 565 cases. After the data set was manually examined and missing values were cleaned or filled, there were totally 388 patient records to use. All rectal cancer cases used to design CDSS were collected retrospectively. Ethical Committee Report regarding patient data is also available in Appendix–1.

The model determined by expert opinions was used in the application of the real rectal cancer patient data. But it was seen that all the criteria determined in the model were not available in the data set. For example, since there was no perforation and obstruction at rectal cancer patients in real data, the criteria levels for presence of obstruction and presence of perforation were selected “absent” in both decision steps. Also criteria level for presence of fistula was selected “absent” in the first decision step, and availability of all the treatment options for data were assumed “accessible”. In the real data application of the model, some criteria such as patient’s performance level (in both decision steps), patient’s attitute (in the first decision step), presence of rectal hematokesia (in the first decision step), location of the tumor (in the second decision step), surgeon’s experience (in the second decision step), efficacy level of treatment (in the second decision step) and coexisting disease and pathology (in the second decision step) was excluded. The levels of coexisting disease or pathology criteria (in the first decision step) and pathologic prognostic factors criteria (in the second decision step) were updated. Additionally levels for stage of the disease criteria in the second decision step were redefined as upstage, stable and downstage.

The criteria levels that used in both the first and second decision steps for data application can be seen in Table 4.7 and Table 4.8.

Table 4.7 Sub-criteria used in the first decision step of the real patient data.

1) Stage of the disease (TNM)*
- T1 N0 M0
- T2 N0 M0
- T3 N0 M0
- T4 N0 M0
- T1 N1 M0
- T2 N1 M0
- T3 N1 M0
- T4 N1 M0
- T1 N2 M0
- T2 N2 M0
- T3 N2 M0
- T4 N2 M0
- T1 N0 M1
- T2 N0 M1
- T3 N0 M1
- T4 N0 M1
- T1 N1 M1
- T2 N1 M1
- T3 N1 M1
- T4 N2 M1
- T1 N2 M1
- T2 N2 M1
- T3 N2 M1
- T4 N2 M1

2) Location of the tumor
- Lower
- Middle
- Upper

3) Coexisting disease or pathology
- Present
  - DM[a]
  - DM+HT[b]
  - DM+CAD[c]
  - DM+CAD+HT+Other
  - DM+COPD[d]
  - DM+COPD+HT
  - HT
  - HT+Other
  - HT+CLF[e]
  - CAD
  - CAD +HT
  - CKF[f]
  - COPD
  - COPD+HT
  - COPD+CAD
  - CLF
  - Other
- Absent

4) Invasion of adjacent organs
- Present
- Absent

5) Surgeon's experience
- Lower than 20
- Equal or upper than 20

6) Presence of perforation
- Absent

7) Presence of obstruction
- Absent

8) Presence of fistula
- Absent

TNM* is an international staging system for cancer. The grade of T expresses tumor size and extensions, N stands for the level of nodal invasion, M stands for the presence or absence of metastases.

DM[a]: Diabetes mellitus

HT[b]: Hypertension

CAD[c]: Coronary artery disease

COPD[d]: Chronic obstructive pulmonary disease

CLF[e]: Chronic liver failure

CKF[f]: Chronic kidney failure

Table 4.8 Sub-criteria used in the second decision step of the real patient data.

1) Stage of disease
- Upstage
- Stable
- Downstage

2) Invasion of adjacent organs
- Present
- Absent

3) Pathologic prognostic factors
- Lymph invasion
  - Present
  - Absent
  - Nonassessable
- Perineural invasion
  - Positive
  - Negative
  - Nonassessable
- Vascular invasion
  - Present
  - Absent
  - Nonassessable

4) Patient's age
- 0–80
- Above 80

5) Resection margin status
- R0
- R1
- R2

6) Presence of perforation
- Absent

7) Presence of obstruction
- Absent

8) Availability of treatment
- Accessible

The criteria and frequencies of rectum cancer patients' data for both decision steps are shown in Table 4.9 and in Table 4.10. It can be seen from Table 4.9 that the most frequent stage of the rectal cancer for the first decision step was T3N1M0 (17.5%).

Table 4.9 Frequencies of rectum cancer patients' data for the first decision step.

Criteria	Frequency	Percent
Stage of disease		
T1N0M0	11	2,8
T1N2M0	1	,3
T2N0M0	28	7,2
T2N0M1	2	,5
T2N1M0	11	2,8
T2N2M0	3	,8
T3N0M0	58	14,9
T3N0M1	7	1,8
T3N1M0	68	17,5
T3N1M1	11	2,8
T3N2M0	52	13,4
T3N2M1	8	2,1
T3N3M1	1	,3
T4N0M0	28	7,2
T4N0M1	1	,3
T4N1M0	39	10,1
T4N1M1	2	,5
T4N2M0	42	10,8
T4N2M1	13	3,4
T4N3M0	1	,3
T4N3M1	1	,3
Location of the tumor		
Lower	153	39,4
Middle	153	39,4
Upper	82	21,1
Coexisting disease or pathology		
Present	121	31,2
DM[a]	17	4,4
DM+HT[b]	13	3,4
DM+CAD[c]	4	1,0
DM+CAD+HT+Other	1	,3
DM+COPD[d]	1	,3
DM+COPD+HT	1	,3
HT	44	11,3
HT+Other	2	,5
HT+CKF[e]	2	,5
CAD	9	2,3
CAD +HT	3	,8
CKF	4	1,0
COPD	12	3,1
COPD+HT	2	,5
COPD+CAD	1	,3
CLF[f]	1	,3
Other	4	1,0
Absent	267	68,8
Invasion of adjacent organs		
Present	46	11,9

Table 4.9 (continues) Frequencies of rectum cancer patients' data for the first decision step.

Criteria	Frequency	Percent
Absent	342	88,1
Surgeon's experience		
Lower than 20	43	11,1
Equal or upper than 20	345	88,9
Presence of perforation		
Present	0	0
Absent	388	100,0
Presence of obstruction		
Present	0	0
Absent	388	100,0
Presence of fistula		
Present	0	0
Absent	388	100,0

DM[a]: Diabetes mellitus
HT[b]: Hypertension
CAD[c]: Coronary artery disease
COPD[d]: Chronic obstructive pulmonary disease
CKF[e]: Chronic kidney failure
CLF[f]: Chronic liver failure

Tumor mostly located at lower (39.4%) and middle (39.4%) parts of the rectum. 31,2% of rectal cancer patients had at least one coexisting disease or pathology and the most common type of the coexisting disease was hypertension (11.3%). Only 11.9% of the patients had invasion of adjacent organs. 88.9% of the surgeons had surgical experience of minimum 20 interventions in a year. Presence of perforation, presence of obstruction and presence of fistula were absent for all cases.

Table 4.10 shows that the stage of the rectal cancer for the second decision step was mostly downstage (57.0%). 3.6% of the patients had invasion of adjacent organs. While 27.3% of these patients had lymph invasion, 24.2% of them had perineural invasion. Vascular invasion was present 77.3% of the rectal cancer patients. Generally 93.8% of all cases were younger than 80. R0 level of the resection margin status (94.8%) was more common than R1 and R2. Presence of perforation and presence of obstruction were absent for all cases. All the treatment availability was accessible.

Table 4.10 Frequencies of rectum cancer patients' data for the second decision step.

Criteria	Frequency	Percent
Stage of disease		
Upstage	36	9,3
Stable	131	33,8
Downstage	221	57,0
Invasion of adjacent organs		
Present	14	3,6
Absent	374	96,4
Pathologic prognostic factors		
Lymph invasion		
Present	106	27,3
Absent	208	53,6
Nonassessable	74	19,1
Perineural invasion		
Present	94	24,2
Absent	218	56,2
Nonassessable	76	19,6
Vascular invasion		
Present	67	17,3
Absent	245	63,1
Nonassessable	76	19,6
Patient's age		
0-80	364	93,8
Above 80	24	6,2
Resection margin status		
R0	368	94,8
R1	18	4,6
R2	2	0,5
Presence of perforation		
Present	0	0
Absent	388	100,0
Presence of obstruction		
Present	0	0
Absent	388	100,0
Availability of treatment		
Accessible	388	100,0
Not accessible	0	0

The frequencies of previous treatment decisions that obtained from patient data set and their respective levels were shown in Table 4.11. Preoperative treatment options, types of surgical operation techniques and adjuvant treatment options can be seen in this table. There was only one surgical option in the data set and the additional surgery option was not available for these patients. For this reason, the criteria for *location of the tumor* and *surgeon's experience* were excluded for the second step in the real data application of the model.

Table 4.11 Frequencies of treatment options for rectum cancer patients' data.

Criteria	Frequency	Percent
Preoperative CRT[a]		
Present	231	59,5
Absent	129	33,2
Preoperative RT[b]	28	7,2
Operation Technique		
APR[c]	113	29,1
AR[d]	19	4,9
Hartmann operation	10	2,6
LAR[e]	146	37,6
Palliative treatment	3	,8
TEM[f]	1	,3
VLAR[g]	94	24,2
ISRx[h]	1	,3
CAA[ı]	1	,3
Adjuvant CT [j]		
Present	287	74,0
Absent	101	26,0
Adjuvant RT[k]		
Present	52	13,4
Absent	336	86,6
Treatment combination for the first decision step		
Preoperative RT+APR	12	3,1
Preoperative RT+AR	8	2,1
Preoperative RT+Hartmann operation	1	,3
Preoperative RT+LAR	6	1,5
Preoperative RT+VLAR	1	,3
Preoperative CRT+APR	82	21,1
Preoperative CRT +Hartmann operation	3	,8
Preoperative CRT +ISRx	1	,3
Preoperative CRT +LAR	68	17,5
Preoperative CRT + CAA	1	,3
Preoperative CRT +VLAR	76	19,6
APR+without preoperative CRT	19	4,9
AR+without preoperative CRT	11	2,8
Hartmann operation+without preoperative CRT	6	1,5
LAR+without preoperative CRT	72	18,6
Palliative treatment+without preoperative CRT	3	,8
TEM+without preoperative CRT	1	,3
VLAR+without preoperative CRT	17	4,4
Treatment combination for the second decision step		
Adjuvant CT+adjuvant RT	48	12,4
Only adjuvant CT	239	61,6
Only adjuvant RT	4	1,0
No adjuvant treatment	97	25,0

CRT[a] : Chemoradiotherapy
RT[b]: Radiotherapy
APR[c]: Abdominal perineal resection
AR[d]: Anterior resection
LAR[e]: Low anterior resection
TEM[f]: Transanal endoscopic microsurgery
VLAR[g]: Very low anterior resection
ISRx[h]: Intersphincteric resection
CAA[ı]: Colo-anal anastomosis
CT [j]: Chemotherapy
RT[k]: Radiotherapy

After determining *i)* the criteria affecting both decision steps, *ii)* levels of these criteria, *iii)* treatment methods and *iv)* treatment results; a decision tree structure was constructed to make a decision regarding the choice of treatment.

In constructing the sequential decision tree, the AHP method was used to determine the new priorities of updated criteria used in the decision making process. Since some criteria in the designed model were excluded in real data application, the expert opinions for updated criteria were obtained as below in Figure 4.9 and Figure 4.10.

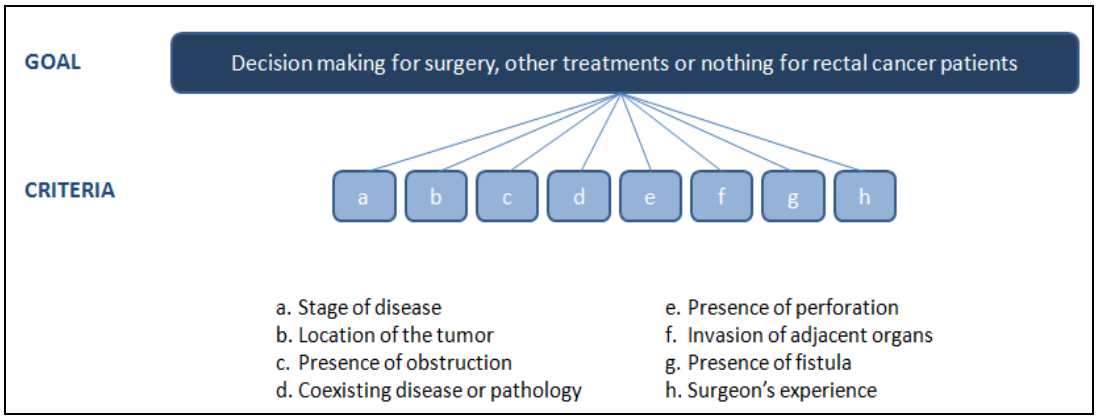

Figure 4.9 AHP structure for the first decision step in real data application model.

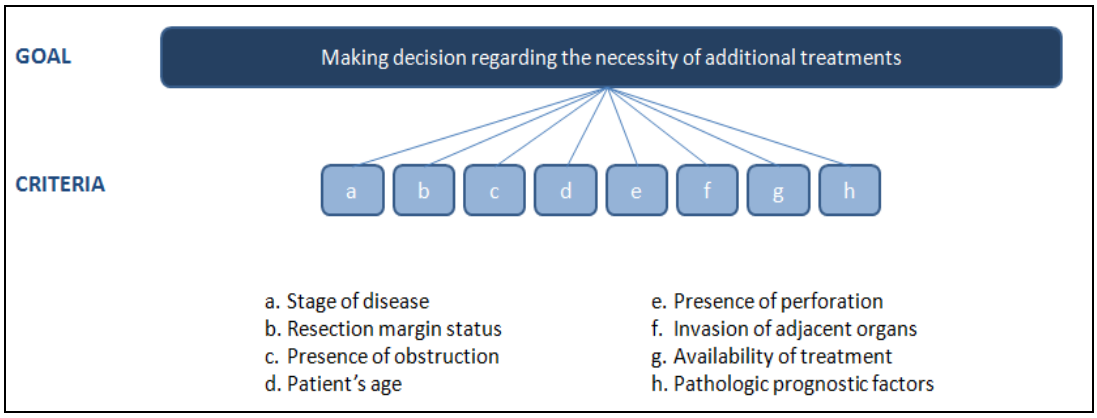

Figure 4.10 AHP structure for the second decision step in real data application model.

As some criteria were excluded from the updated model, the results of combined priorities for the both new AHP structures in real data application model can be seen in Table 4.12.

Table 4.12 Combined priorities for the both new AHP structures in real data application model.

First AHP structure	
Criteria of the first AHP structure	**Combined priority vector**
Presence of perforation	0.331
Presence of obstruction	0.283
Invasion of adjacent organ	0.158
Presence of fistula	0.073
Surgeon's experience	0.053
Stage of disease	0.050
Location of tumor	0.028
Coexisting disease or pathology	0.024
	Σ=1.00
CR = 0.03 < 0.1 OK.	
Second AHP structure	
Criteria of the second AHP structure	**Combined priority vector**
Resection margin status	0.214
Stage of disease	0.210
Invasion of adjacent organ	0.191
Pathologic prognostic factors	0.144
Presence of perforation	0.087
Presence of obstruction	0.063
Availability of treatment	0.054
Patient's age	0.037
	Σ=1.00
CR = 0.01 < 0.1 OK.	

In addition to results of Table 4.12, also Expert Choice results for combined AHP structures in real data application model are shown in Figure 4.11.

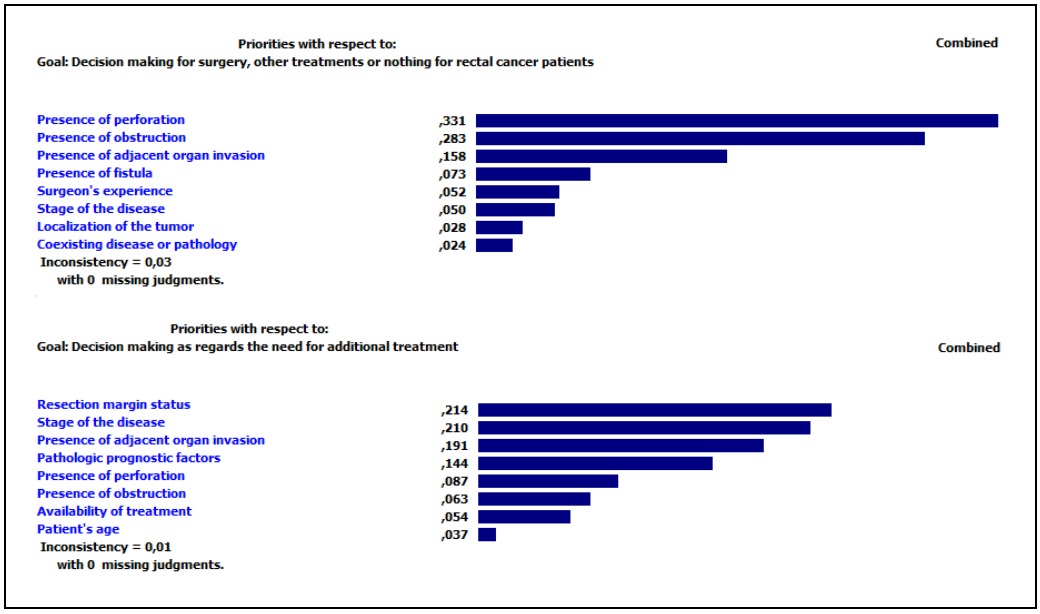

Figure 4.11 Expert Choice results for combined AHP structures.

Results showed that while the most important attribute for the first decision step was “the presence of perforation” with a relative priority of 0.331, “resection margin status” had the highest relative priority (0.214) for the second decision step. Additionally “coexisting disease or pathology” criteria for the first decision step was the lowest with a value of 0.024 and “patient’s age” for the second decision step had the minimum relative priority (0.037). While the first decision step for previous results and new results had the same the highest prior criteria called “the presence of perforation”, results were not similar for the second decision step. The results showed that “the surgeon’s experience” had the highest relative priority for the previous results, but new results showed that “resection margin status” had the highest relative priority for the second decision step.

4.5 Construction of the CDSS

Three basic components of the CDSS are retrospective data, expert opinions and literature review. The rectal cancer patient data were obtained from the Department of General Surgery, Dokuz Eylül University including the years 1988-2010 for cases. The expert opinions were derived from rectal cancer specialists who work in the Department of General Surgery in Dokuz Eylül University. Publications from literature review of PubMed database with the help of MeSH terms were achieved without any restriction of search.

The decision rules to develop decision tree were created with the aid of previous rectal cancer cases and then used for constructing CDSS. The CDSS may help physician’s treatment decisions selecting the most appropriate treatment option for each particular patient. The physician may use avarage survival times of every treatment option to make a decision for each case and receive help from the literature regarding a selected treatment method.

Publications regarding the most appropriate treatment method obtained from the patient data were achieved from PubMed database by using MeSH terms. Frequencies of search terms results about the literature review regarding colorectal cancer and treatment options can be seen in Table 4.13. The number of publications

was achieved at May 2013 without any restriction of search such as publication year, article type, language of the publication. While the user makes the appropriate treatment decision for a particular patient, the link for relevant literature can support user's decision easily.

Because of the presence of the some missing values in patient records, the data set was manually examined to seek out ones which had missing values. 388 patient records remained after filtering out the collected patient data. Then, the records were inserted into the patient record database which was constructed using Mysql version 5.5.31 on Ubuntu Linux server 12.04.1. The user interfaces were created in HTML combined with PHP version 5.3.10 to allow the potential users access the database.

Table 4.13 Frequencies of search terms results about literature regarding colorectal cancer and treatment options.

Search terms	**# of papers**
Colorectal Neoplasms[Mesh] AND "transanal local excision"	46
Colorectal Neoplasms[Mesh] AND "transanal endoscopic microsurgery"	362
Colorectal Neoplasms[Mesh] AND "anterior resection"	2064
Colorectal Neoplasms[Mesh] AND "low anterior resection"	1093
Colorectal Neoplasms[Mesh] AND "very low anterior resection"	15
Colorectal Neoplasms[Mesh] AND ("colo-anal anastomasis" OR "colo anal anastomasis")	0
Colorectal Neoplasms[Mesh] AND "intersphincteric resection"	118
Colorectal Neoplasms[Mesh] AND "abdominal perineal resection"	103
Colorectal Neoplasms[Mesh] AND "hartmann"	276
Colorectal Neoplasms[Mesh] AND ("stoma" OR "stent" OR "internal by-pass" OR "endoscopic cauterization" OR "palliative")	3885
Colorectal Neoplasms[Mesh] AND "chemotherapy"	16841
Colorectal Neoplasms[Mesh] AND "radiotherapy"	8959
Colorectal Neoplasms[Mesh] AND "chemoradiotherapy"	1086
Colorectal Neoplasms[Mesh] AND "transanal local excision" AND "chemotherapy"	6
Colorectal Neoplasms[Mesh] AND "transanal endoscopic microsurgery" AND "chemotherapy"	19
Colorectal Neoplasms[Mesh] AND "anterior resection" AND "chemotherapy"	334
Colorectal Neoplasms[Mesh] AND "low anterior resection" AND "chemotherapy"	200
Colorectal Neoplasms[Mesh] AND "very low anterior resection" AND "chemotherapy"	3
Colorectal Neoplasms[Mesh] AND ("stoma" OR "stent" OR "internal by-pass" OR "endoscopic cauterization" OR "palliative")	3885
Colorectal Neoplasms[Mesh] AND "chemotherapy"	16841
Colorectal Neoplasms[Mesh] AND "radiotherapy"	8959
Colorectal Neoplasms[Mesh] AND "chemoradiotherapy"	1086

Table 4.13 (continues) Frequencies of search terms results about literature regarding colorectal cancer and treatment options.

Search terms	# of papers
Colorectal Neoplasms[Mesh] AND "transanal local excision" AND "chemotherapy"	6
Colorectal Neoplasms[Mesh] AND "transanal endoscopic microsurgery" AND "chemotherapy"	19
Colorectal Neoplasms[Mesh] AND "anterior resection" AND "chemotherapy"	334
Colorectal Neoplasms[Mesh] AND "low anterior resection" AND "chemotherapy"	200
Colorectal Neoplasms[Mesh] AND "very low anterior resection" AND "chemotherapy"	3
Colorectal Neoplasms[Mesh] AND ("colo-anal anastomasis" OR "colo anal anastomasis") AND "chemotherapy"	0
Colorectal Neoplasms[Mesh] AND "intersphincteric resection" AND "chemotherapy"	13
Colorectal Neoplasms[Mesh] AND "abdominal perineal resection" AND "chemotherapy"	31
Colorectal Neoplasms[Mesh] AND "hartmann" AND "chemotherapy"	47
Colorectal Neoplasms[Mesh] AND ("stoma" OR "stent" OR "internal by-pass" OR "endoscopic cauterization" OR "palliative") AND "chemotherapy"	1041
Colorectal Neoplasms[Mesh] AND "transanal local excision" AND "radiotherapy"	16
Colorectal Neoplasms[Mesh] AND "transanal endoscopic microsurgery" AND "radiotherapy"	44
Colorectal Neoplasms[Mesh] AND "anterior resection" AND "radiotherapy"	407
Colorectal Neoplasms[Mesh] AND "intersphincteric resection" AND "radiotherapy"	30
Colorectal Neoplasms[Mesh] AND "low anterior resection" AND "radiotherapy"	223
Colorectal Neoplasms[Mesh] AND "very low anterior resection" AND "radiotherapy"	4
Colorectal Neoplasms[Mesh] AND ("colo-anal anastomasis" OR "colo anal anastomasis") AND "radiotherapy"	0
Colorectal Neoplasms[Mesh] AND "abdominal perineal resection" AND "radiotherapy"	43
Colorectal Neoplasms[Mesh] AND "hartmann" AND "radiotherapy"	34
Colorectal Neoplasms[Mesh] AND ("stoma" OR "stent" OR "internal by-pass" OR "endoscopic cauterization" OR "palliative") AND "radiotherapy"	688
Colorectal Neoplasms[Mesh] AND "transanal local excision" AND "chemoradiotherapy"	1
Colorectal Neoplasms[Mesh] AND "transanal endoscopic microsurgery" AND "chemoradiotherapy"	13
Colorectal Neoplasms[Mesh] AND "anterior resection" AND "chemoradiotherapy"	73
Colorectal Neoplasms[Mesh] AND "low anterior resection" AND "chemoradiotherapy"	50
Colorectal Neoplasms[Mesh] AND "very low anterior resection" AND "chemoradiotherapy"	0
Colorectal Neoplasms[Mesh] AND ("colo-anal anastomasis" OR "colo anal anastomasis") AND "chemoradiotherapy"	0
Colorectal Neoplasms[Mesh] AND "intersphincteric resection" AND "chemoradiotherapy"	10
Colorectal Neoplasms[Mesh] AND "abdominal perineal resection" AND "chemoradiotherapy"	6
Colorectal Neoplasms[Mesh] AND "hartmann" AND "chemoradiotherapy"	5
Colorectal Neoplasms[Mesh] AND ("stoma" OR "stent" OR "internal by-pass" OR "endoscopic cauterization" OR "palliative") AND "chemoradiotherapy"	54

The created interfaces of the database enables retrievement of treatment recommendations and the associated average survival time for each recommendation based on user defined selection criteria. In the first decision step, there are 8 distinct selection criteria, previously as defined in the section of variable determination process. Based on the user specified parameters, recommended treatment options regarding the first decision step appear on the same page where selection criteria are listed. Decision steps and criteria have a question mark icon next to them, so users may easily find explanations about decision steps and criteria. For instance, Figure 4.12 shows recommendations for a particular patient from the demo set. Arbitrarily, users may continue their queries to retrieve average survival time and treatment recommendations associated with the second decision step by clicking the link that appears in the first page.

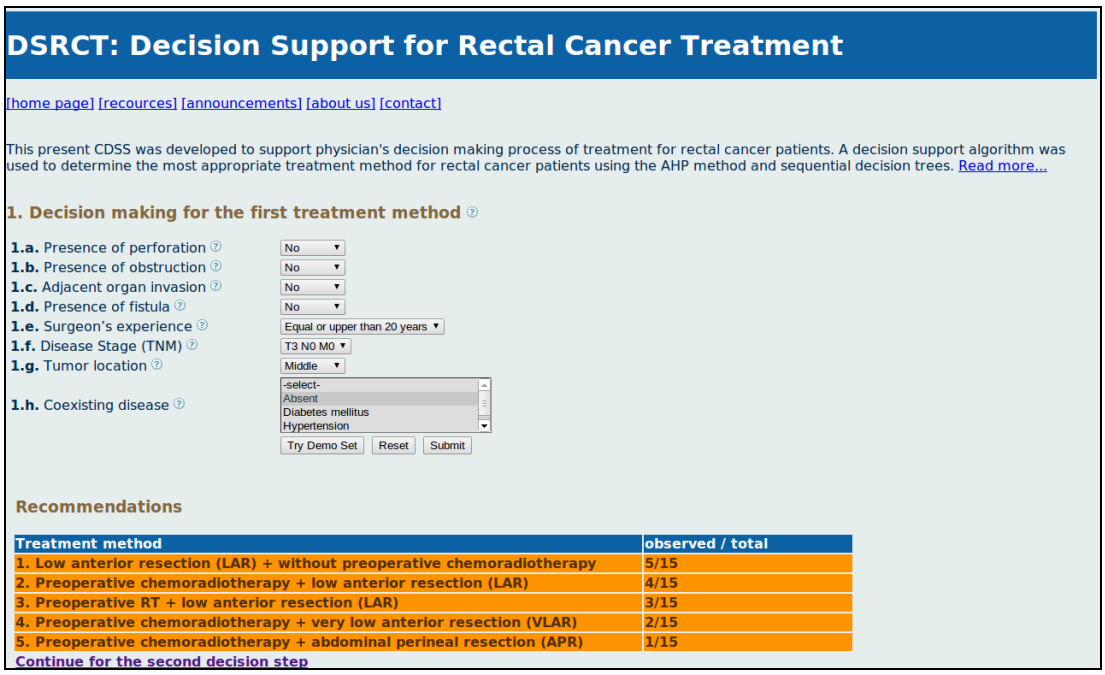

Figure 4.12 The screenshot for the main page of the CDSS application to determine the most appropriate treatment method for rectal cancer patients.

10 distinct parameters are available for selection in the second decision step. After selecting the mandatory form fields, the combination of both the first and the second treatment recommendations and associated average survival times are listed in a table form (Figure 4.13). Average survivals concerning each treatment option for patients

who have same criteria levels were calculated by last visit date minus operation date of individual patient. In addition, average survivals for patients who have the same criteria levels regarding the different treatment method were shown on the screen from maximum to minimum value. The currently available publications regarding the recommended treatment from PubMed search results may be seen at the bottom of the page.

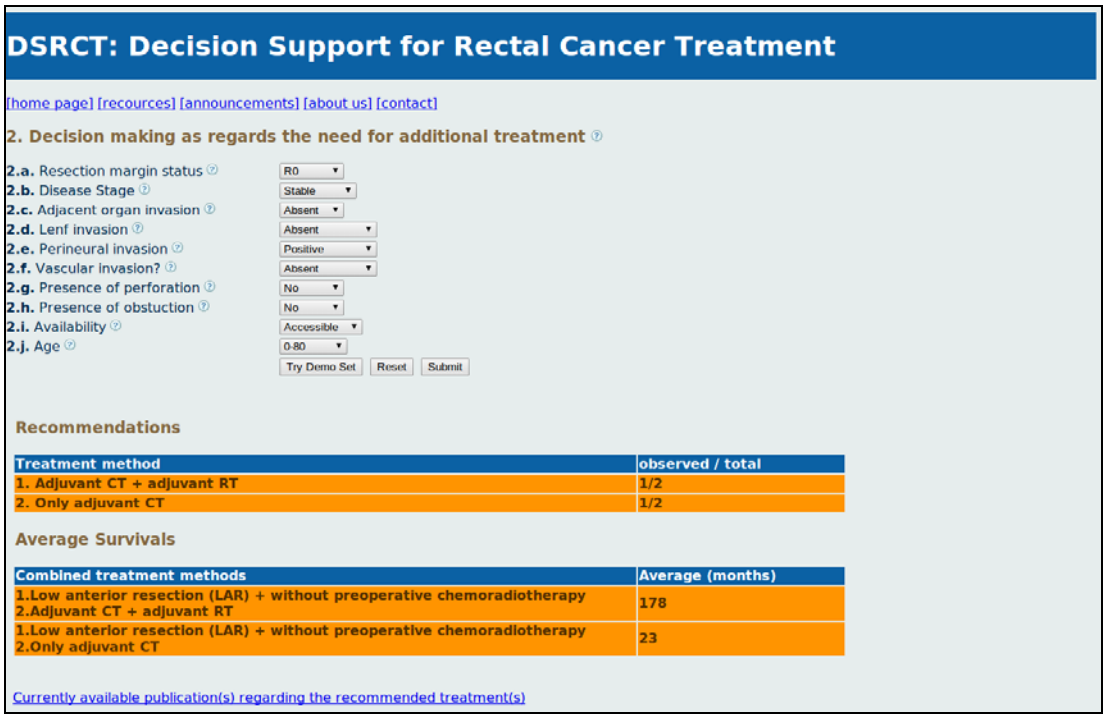

Figure 4.13 The screenshot for the second page of the CDSS application to determine the most appropriate treatment method for rectal cancer patients.

Due to the presence of limited number of patient data, either the first or the second decision step users are noticed in case there is no available patient record to meet the user defined parameters. The web page of the CDSS named DSRCT: Decision Support for Rectal Cancer Treatment was defined as https://sites.google.com/site/cdstool4crc/.

4.6 Assessing Consistency of the System by Experts

Two experts who were not involved in the expert opinion part of the study and did not give any treatment decisions according to patient data from the hospital, gave their opinions for the purpose of consistency check of the data. Expert opinions of general surgeons who work in the Department of General Surgery, Dokuz Eylül University were obtained by using two similar forms of case studies in Appendix–2 and Appendix–3. Treatment options for filling the form were shown in Appendix–4. While the suggested treatment options from both the system and experts for the most frequently seen cases were shown in Appendix–5, the same values for the least seen cases were shown in Appendix–6. The experts filled the case study forms for *the most frequently seen cases* and *the least seen cases.* The experts were asked to choose as a treatment option from Appendix-4 while taking the determined criteria levels in case studies into account.

The expert decisions and real patient data for the rectal cancer treatment were compared for ten cases, it was found that the consistency of *the most frequently seen cases* was 8/10, for the first decision step and 10/10, for the second decision step. Similarly, the consistency of *the least seen cases* was 5/10, for the first decision step and 8/10, for the second decision step. The results regarding the consistency of both steps were satisfactory and acceptable for the model.

CHAPTER FIVE
DISCUSSION

In the present study, a CDSS was developed to determine the most appropriate treatment method for rectal cancer patients using the AHP method and decision trees. The decision for the most appropriate treatment of rectal cancer is a complex problem involving several decision criteria and a variety of treatment options.

5.1 Concluding Remarks

A Web-based application to collect data for the AHP method was created. Althought there were some studies that weighted each decision-maker inequally, experts in our study have equal contribution (Pecchia, Bath, Pendleton & Bracale, 2011). The AHP has been used as a decision support tool in medical decision making, but has been scarcely employed for treatment studies of colorectal cancer. In the review performed by Liberatore and Nydick (Liberatore & Nydick, 2008), eight of 50 studies were focused on the evaluation and selection of medical treatments; none of these concerned colorectal cancer. In the few studies focused on AHP applications for colorectal cancer, the method was used for the diagnosis of colorectal cancer - such as screening methods - but not for treatment (Katsumura, Yasunaga, Imamura, Ohe & Oyama, 2008; Dolan & Frisina. 2002; Dolan, 2000; Dolan, 2005). Our study is distinct from other studies owing to the use of AHP method by combining sequential decision trees for rectal cancer treatment.

Classification and regression tree (C&RT or CART) and C5.0 classification algorithms which are the most prominent data mining methods was also used for building statistical model from real patient data. But results of the analysis by SPSS Clementine 12.0 showed that the results of offered treatment options from models and results of cross-validation were not acceptable, therefore the analysis of these methods were excluded from our study. We also tried to use multivariate statistical methods to develop a model for rectum cancer treatment. But none of these methods was suitable for our data set.

When the AHP and decision tree methods were used in the past, resulting systems such as expert systems were expected to automatically make decisions on their own. This situation does not permit the expert to monitor the patient and the disease in a stepwise manner. Our study supports a stepwise decision making process using patient data and disease criteria as well as expert knowledge.

There were some differences between designed model and real patient data model. Because the patient data set from hospital includes not all of the criteria that determined in the model, real patient data model has fewer criteria than designed model. Also the criteria rankings of both models have insignificant changes. For example; while the first decision step for designed model and real patient data model had the same the highest prior criteria called “the presence of perforation”, results were not similar for the second decision step. The results showed that “the surgeon’s experience” had the highest relative priority for the designed model, but real patient data model showed that “resection margin status” had the highest relative priority for the second decision step. Real patient data model is valid and useful for the application of clinical decision support system.

The study of Bates et al (2003) can be seen as the ‘ten commandments’ to build an effective CDSS. When the CDSS that was built in our study was assessed in accordance with these ten important features, the properties of our CDSS was fairly satisfactory.

In the current study we focused on the algorithmic structure of the decision making process. The limitation of the method is that although the algorithm has been developed so far; numerical application of the method has not been fully performed yet due to the lack of enough number of patient data. Besides, as the study was planned to be conducted in Dokuz Eylül University Hospital, expert opinions were taken from general surgeons working at this hospital. Although decisions for additional treatment after surgery are made by expert teams including oncologists, radiologists and surgeons, the primary decision-makers are surgeons. For data collection in the AHP method, five experts gave their opinions separately and

independently. If more specialists in colorectal cancer surgery - both locally and abroad - would collaborate, one may well achieve a better consensus on treatment choices in more diverse patients. We believe the present model could be improved once the feasibility of our method has been established and its validation completed.

5.2 Future Research

Our next task will consist of using CDSS for the treatment of rectal cancer patients in the hospital. With utilizing a comprehensive database collected for this purpose, probabilistic results could be examined for every condition and interpretations can be made for the corresponding patient. If our CDSS can be fed by integrating and linking to the corresponding data from hospital information system, the decision tree may be analyzed with the help of decision theory and may be improved with the help of comprehensive patient data.

While there are studies of cost effectiveness analysis for different aims such as estimating lifetime cost for colorectal cancer care, comparing cost effectiveness of diagnostic and screening methods; the cost effectiveness of different treatment options for rectal cancer was not evaluated in details before. Therefore the cost effectiveness of different treatment options from health care payer's perspective, patient's perspective and physician's perspective can also be considered as a future research. Also, analytic network process (ANP) method and Bayesian approach may be used in addition to AHP method.

At the project that was conducted during the research process in Medical University of Vienna, it was seen that it is important to use genetic markers and genetic tests to optimize treatment selection in colorectal cancer therapy. In the study that completed in the aforementioned university (Karakülah, Suner, Addlasnig & Samwald, 2012), colorectal cancer was classified according to the genetical factors, and a living review was created for colorectal cancer pharmacotherapy. Owing to the fact that the use of genetic markers and genetic tests are not so common in colorectal cancer treatment in our country, these criteria were omitted from our decision model.

If these criteria are added to the CDSS in future, the doctor’s decision to choose the most approprite treatment method for personalized treatment will also be supported.

In conclusion, the consistency of decision support systems largely depends on the quality of the underlying decision trees. When several choices and criteria have to be taken into account when making a decision, the determination of priorities is of great importance. The AHP method seems to be effective in the preparation of sequential decision trees. The decision algorithm developed by this method will be more robust and will improve the quality of the decision tree. Data obtained from similar studies will also facilitate the use of the method.

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APPENDIX

Appendix 1: Ethical Committee Report Regarding Patient Data.

DOKUZ EYLÜL ÜNİVERSİTESİ
GİRİŞİMSEL OLMAYAN ARAŞTIRMALAR ETİK KURULU

Konu: Karar hk.- 152 29.02.2013

Sayın Prof.Dr.Can Cengiz ÇELİKOĞLU

Kurulumuz tarafından 28.02.2013 tarih ve 877-GOA protokol numaralı 2013/07-22 karar numarası ile görüşülen **"Rektum Kanseri Tedavisinde Analitik Hiyerarşi Süreci ve Karar Ağacı Temelli Bir Klinik Karar Destek Sisteminin Geliştirilmesi"** konulu araştırmanıza ilişkin Kurulumuz kararı ekte sunulmuştur.

Bilgilerinizi ve gereğini rica ederim.

Prof.Dr.Banu ÖNVURAL
Başkan

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Appendix 1(continues): Ethical Committee Report Regarding Patient Data.

DOKUZ EYLÜL ÜNİVERSİTESİ
GİRİŞİMSEL OLMAYAN ARAŞTIRMALAR ETİK KURUL KARARI

ETİK KOMİSYONUN ADI	**DOKUZ EYLÜL ÜNİVERSİTESİ GİRİŞİMSEL OLMAYAN ARAŞTIRMALAR ETİK KURULU**
AÇIK ADRES	**Dokuz Eylül Üniversitesi Tıp Fakültesi Dekanlığı 2. Kat İnciraltı-İZMİR**
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BAŞVURU BİLGİLERİ	DOSYA NO:	877-GOA	
	ARAŞTIRMA	UZMANLIK TEZİ ☐	AKADEMİK AMAÇLI ☐
	ARAŞTIRMANIN AÇIK ADI	Rektum Kanseri Tedavisinde Analitik Hiyerarşi Süreci ve Karar Ağacı Temelli Bir Klinik Karar Destek Sisteminin Geliştirilmesi	
	ARAŞTIRMA PROTOKOL KODU	-	
	SORUMLU ARAŞTIRMACI ÜNVANI/ADI/SOYADI ve UZMANLIK ALANI	Prof.Dr.Can Cengiz ÇELİKOĞLU Fen Fakültesi İstatistik Bölümü	
	DESTEKLEYİCİ VE AÇIK ADRESİ	-	
	DESTEKLEYİCİNİN YASAL TEMSİLCİSİ VE ADRESİ	-	
	ARAŞTIRMAYA KATILAN MERKEZLER	TEK MERKEZ ☒	ÇOK MERKEZLİ☐

	Belge Adı	Tarihi	Versiyon Numarası	Dili
DEĞERLENDİRİLEN BELGELER	ARAŞTIRMA PROTOKOLÜ	Mevcut		Türkçe ☒ İngilizce ☐ Diğer ☐
	ARAŞTIRMA İLE İLGİLİ LİTERATÜR	Mevcut		Türkçe ☐ İngilizce ☒ Diğer ☐
	BİLGİLENDİRİLMİŞ GÖNÜLLÜ OLUR FORMU	Mevcut		Türkçe ☒ İngilizce ☐ Diğer ☐
	OLGU RAPOR FORMU	Mevcut		Türkçe ☒ İngilizce ☐ Diğer ☐

Dokuz Eylül Üniversitesi Girişimsel Olmayan Araştırmalar Etik Kurulu Karar Formu

Appendix 1(continues): Ethical Committee Report Regarding Patient Data.

KARAR BİLGİLERİ	**Karar No:2013/07-22**	**Tarih: 28.02.2013**
	Prof.Dr.Can Cengiz ÇELİKOĞLU'nun sorumlusu olduğu **"Rektum Kanseri Tedavisinde Analitik Hiyerarşi Süreci ve Karar Ağacı Temelli Bir Klinik Karar Destek Sisteminin Geliştirilmesi"** isimli klinik araştırmaya ait başvuru dosyası ve ilgili belgeler araştırmanın gerekçe, amaç, yaklaşım ve yöntemleri dikkate alınarak incelenmiş, etik açıdan çalışmanın gerçekleştirilmesinin uygun olduğuna oy birliği ile karar verilmiştir.	
ETİK KURUL BİLGİLERİ		
ÇALIŞMA ESASI	Dokuz Eylül Üniversitesi Girişimsel Olmayan Araştırmalar Etik Kurulu İşleyiş Yönergesi İyi Klinik Uygulamaları Kılavuzu	
ETİK KURUL ÜYELERİ		

Unvanı/Adı/Soyadı	Uzmanlık Alanı	Kurumu	Cinsiyet	Araştırma ile İlişkili mi?		İmza
Prof.Dr.Banu ÖNVURAL (Başkan)	Tıbbi Biyokimya	DEU Tıp Fakültesi Tıbbi Biyokimya Anabilim Dalı	Kadın	E ☐	H ☒	
Prof.Dr..Besti ÜSTÜN (Başkan Yardımcısı)	Ph.D.Yüksek Hemşire	DEU Hemşirelik Fakültesi	Kadın	E ☐	H ☒	
Prof.Dr.Kemal Kürşad GENÇ	Fizyoloji	DEU Tıp Fakültesi Sağlık Hizmetleri Meslek Yüksekokulu	Erkek	E ☐	H ☒	
Prof.Dr.Ş.Reyhan UÇKU	Halk Sağlığı	DEU Tıp Fakültesi Halk Sağlığı A.D.	Kadın	E ☐	H ☒	
Prof.Dr.Nejat SARIOSMANOĞLU	Kalp Damar Cerrahisi	DEU Tıp Fakültesi Kalp Damar Cerrahisi Anabilim Dalı	Kadın	E ☐	H ☒	
Prof.Dr.Ece BÖBER	Pediatrik Endokrinoloji	DEU Tıp Fakültesi Çocuk Sağlığı ve Hastalıkları Anabilim Dalı	Erkek	E ☐	H ☒	
Prof.Dr.Hüseyin BASKIN	Mikrobiyoloji	DEU Tıp Fakültesi Mikrobiyoloji Anabilim Dalı	Erkek	E ☐	H ☒	
Prof.Dr.Vesile ÖZTÜRK	Nöroloji	DEU Tıp Fakültesi Nöroloji Anabilim Dalı	Kadın	E ☐	H ☒	
Prof.Dr.Bilgin CÖMERT	İç Hastalıkları (Yoğun Bakım B.D)	DEU Tıp Fakültesi İç Hastalıkları Anabilim Dalı	Erkek	E ☐	H ☒	
Prof.Dr.Mukaddes GÜNELİ	Tıbbi Farmakoloji	DEU Tıp Fakültesi Tıbbi Farmakoloji Anabilim Dalı	Kadın	E ☐	H ☒	
Prof.Dr.Ayşe Aydan ÖZKÜTÜK	Mikrobiyoloji	DEU Tıp Fakültesi Mikrobiyoloji Anabilim Dalı	Kadın	E ☐	H ☒	
Doç.Dr.Nihal GELECEK	Fizik Tedavi ve Rehabilitasyon	DEU Fizik Tedavi ve Rehabilitasyon Yüksek Okulu	Kadın	E ☐	H ☒	
Doç.Dr.Işıl TEKMEN	Histoloji ve Embriyoloji	DEU Tıp Fakültesi Histoloji ve Embriyoloji Anabilim Dalı	Kadın	E ☐	H ☒	
Uzm.Dr.Ahmet Can BİLGİN	Hukuk	DEU Tıp Tarihi ve Etik A.D	Erkek	E ☐	H ☒	
İhsan ÇELİKDEMİR	Sağlık mensubu olmayan üye	75. Yıl Özel İlköğretim Okulu Müdür Yrd.	Erkek	E ☐	H ☒	

Dokuz Eylül Üniversitesi Girişimsel Olmayan Araştırmalar Etik Kurulu Karar Formu

Appendix 2: Case Studies Regarding the Most Frequently Seen Cases.

Case Study 1: A surgeon wants to determine the most appropriate treatment method for a particular patient who has these criteria levels: no perforation, no obstruction, no adjacent organ invasion, no fistula, T3N1M0 stage, middle tumor location, no coexisting disease or pathology, and at least 20 surgical operation experiences in a year.
1) What is your decision concerning the required type of treatment? (Please choose your decision from the table below).....
After the first treatment was applied to this patient, some criteria were assessed for making a decision regarding the additional treatments that should be provided. Patient has R0 resection margin status, decrease at the stage of the disease after the first treatment applied, no adjacent organ invasion, no lymph invasion, no perinoral invasion and no vascular invasion. It was determined that patient has neither perforation nor obstruction after the first treatment was applied. Availability of treatment is accessible and the patient's age is below 80.
2) If you think that additional treatment is neccessery for this patient, what is your decision concerning the required type of treatment? (Please choose your decision from the table below).....
3) How many months do you expect for the survival of this patient after the treatment combination was applied?.....

Case Study 2: A surgeon wants to determine the most appropriate treatment method for a particular patient who has these criteria levels: no perforation, no obstruction, no adjacent organ invasion, no fistula, T4N1M0 stage, lower tumor location, no coexisting disease or pathology, and at least 20 surgical operation experiences in a year.
1) What is your decision concerning the required type of treatment? (Please choose your decision from the table below).....
After the first treatment was applied to this patient, some criteria were assessed for making a decision regarding the additional treatments that should be provided. Patient has R0 resection margin status, decrease at the stage of the disease after the first treatment applied, no adjacent organ invasion, no lymph invasion, no perinoral invasion and no vascular invasion. It was determined that patient has neither perforation nor obstruction after the first treatment was applied. Availability of treatment is accessible and the patient's age is below 80.
2) If you think that additional treatment is neccessery for this patient, what is your decision concerning the required type of treatment? (Please choose your decision from the table below).....
3) How many months do you expect for the survival of this patient after the treatment combination was applied? .....

Case Study 3: A surgeon wants to determine the most appropriate treatment method for a particular patient who has these criteria levels: no perforation, no obstruction, no adjacent organ invasion, no fistula, T3N1M0 stage, lower tumor location, no coexisting disease or pathology, and at least 20 surgical operation experiences in a year.
1) What is your decision concerning the required type of treatment? (Please choose your decision from the table below).....
After the first treatment was applied to this patient, some criteria were assessed for making a decision regarding the additional treatments that should be provided. Patient has R0 resection margin status, decrease at the stage of the disease after the first treatment applied, no adjacent organ invasion, no lymph invasion, no perinoral invasion and no vascular invasion. It was determined that patient has neither perforation nor obstruction after the first treatment was applied. Availability of treatment is accessible and the patient's age is below 80.
2) If you think that additional treatment is neccessery for this patient, what is your decision concerning the required type of treatment? (Please choose your decision from the table below).....
3) How many months do you expect for the survival of this patient after the treatment combination was applied?.....

Case Study 4: A surgeon wants to determine the most appropriate treatment method for a particular patient who has these criteria levels: no perforation, no obstruction, no adjacent organ invasion, no fistula, T4N2M0 stage, lower tumor location, no coexisting disease or pathology, and at least 20 surgical operation experiences in a year.
1) What is your decision concerning the required type of treatment? (Please choose your decision from the table below).....
After the first treatment was applied to this patient, some criteria were assessed for making a decision regarding the additional treatments that should be provided. Patient has R0 resection margin status, decrease at the stage of the disease after the first treatment applied, no adjacent organ invasion, no lymph invasion, no perinoral invasion and no vascular invasion. It was determined that patient has neither perforation nor obstruction after the first treatment was applied. Availability of treatment is accessible and the patient's age is below 80.
2) If you think that additional treatment is neccessery for this patient, what is your decision concerning the required type of treatment? (Please choose your decision from the table below).....
3) How many months do you expect for the survival of this patient after the treatment combination was applied?.....

Case Study 5: A surgeon wants to determine the most appropriate treatment method for a particular patient who has these criteria levels: no perforation, no obstruction, no adjacent organ invasion, no fistula, T3N0M0 stage, lower tumor location, no coexisting disease or pathology, and at least 20 surgical operation experiences in a year.
1) What is your decision concerning the required type of treatment? (Please choose your decision from the table below).....
After the first treatment was applied to this patient, some criteria were assessed for making a decision regarding the additional treatments that should be provided. Patient has R0 resection margin status, decrease at the stage of the disease after the first treatment applied, no adjacent organ, nonassessable lymph, perinoral and vascular invasions. It was determined that patient has neither perforation nor obstruction after the first treatment was applied. Availability of treatment is accessible and the patient's age is below 80.
2) If you think that additional treatment is neccessery for this patient, what is your decision concerning the required type of treatment? (Please choose your decision from the table below).....
3) How many months do you expect for the survival of this patient after the treatment combination was applied?.....

Appendix 2: Case Studies Regarding the Most Frequently Seen Cases (continues).

Case Study 6: A surgeon wants to determine the most appropriate treatment method for a particular patient who has these criteria levels: no perforation, no obstruction, no adjacent organ invasion, no fistula, T3N2M0 stage, lower tumor location, no coexisting disease or pathology, and at least 20 surgical operation experiences in a year.
1) What is your decision concerning the required type of treatment? (Please choose your decision from the table below)……
After the first treatment was applied to this patient, some criteria were assessed for making a decision regarding the additional treatments that should be provided. Patient has R0 resection margin status, decrease at the stage of the disease after the first treatment applied, no adjacent organ, no lymph invasion, perinoral invasion and vascular invasion. It was determined that patient has neither perforation nor obstruction after the first treatment was applied. Availability of treatment is accessible and the patient's age is below 80.
2) If you think that additional treatment is neccessery for this patient, what is your decision concerning the required type of treatment? (Please choose your decision from the table below)……
3) How many months do you expect for the survival of this patient after the treatment combination was applied?.....

Case Study 7: A surgeon wants to determine the most appropriate treatment method for a particular patient who has these criteria levels: no perforation, no obstruction, no adjacent organ invasion, no fistula, T1N0M0 stage, middle tumor location, no coexisting disease or pathology, and at least 20 surgical operation experiences in a year.
1) What is your decision concerning the required type of treatment? (Please choose your decision from the table below)……
After the first treatment was applied to this patient, some criteria were assessed for making a decision regarding the additional treatments that should be provided. Patient has R0 resection margin status, stable stage of the disease after the first treatment applied, no adjacent organ, nonassessable lymph, perinoral and vascular invasions. It was determined that patient has neither perforation nor obstruction after the first treatment was applied. Availability of treatment is accessible and the patient's age is below 80.
2) If you think that additional treatment is neccessery for this patient, what is your decision concerning the required type of treatment? (Please choose your decision from the table below)……
3) How many months do you expect for the survival of this patient after the treatment combination was applied?.....

Case Study 8: A surgeon wants to determine the most appropriate treatment method for a particular patient who has these criteria levels: no perforation, no obstruction, no adjacent organ invasion, no fistula, T2N0M0 stage, middle tumor location, no coexisting disease or pathology, and at least 20 surgical operation experiences in a year.
1) What is your decision concerning the required type of treatment? (Please choose your decision from the table below)……
After the first treatment was applied to this patient, some criteria were assessed for making a decision regarding the additional treatments that should be provided. Patient has R0 resection margin status, stable stage of the disease after the first treatment applied, no adjacent organ invasion, no lymph invasion, no perinoral invasion and no vascular invasion. It was determined that patient has neither perforation nor obstruction after the first treatment was applied. Availability of treatment is accessible and the patient's age is below 80.
2) If you think that additional treatment is neccessery for this patient, what is your decision concerning the required type of treatment? (Please choose your decision from the table below)……
3) How many months do you expect for the survival of this patient after the treatment combination was applied?.....

Case Study 9: A surgeon wants to determine the most appropriate treatment method for a particular patient who has these criteria levels: no perforation, no obstruction, no adjacent organ invasion, no fistula, T3N2M0 stage, upper tumor location, no coexisting disease or pathology, and at least 20 surgical operation experiences in a year.
1) What is your decision concerning the required type of treatment? (Please choose your decision from the table below)……
After the first treatment was applied to this patient, some criteria were assessed for making a decision regarding the additional treatments that should be provided. Patient has R0 resection margin status, decrease at the stage of the disease after the first treatment applied, no adjacent organ invasion, no lymph invasion, no perinoral invasion and no vascular invasion. It was determined that patient has neither perforation nor obstruction after the first treatment was applied. Availability of treatment is accessible and the patient's age is below 80.
2) If you think that additional treatment is neccessery for this patient, what is your decision concerning the required type of treatment? (Please choose your decision from the table below)……
3) How many months do you expect for the survival of this patient after the treatment combination was applied?.....

Case Study 10: A surgeon wants to determine the most appropriate treatment method for a particular patient who has these criteria levels: no perforation, no obstruction, no adjacent organ invasion, no fistula, T4N2M0 stage, middle tumor location, no coexisting disease or pathology, and at least 20 surgical operation experiences in a year.
1) What is your decision concerning the required type of treatment? (Please choose your decision from the table below)……
After the first treatment was applied to this patient, some criteria were assessed for making a decision regarding the additional treatments that should be provided. Patient has R0 resection margin status, decrease at the stage of the disease after the first treatment applied, no adjacent organ invasion, no lymph invasion, no perinoral invasion and no vascular invasion. It was determined that patient has neither perforation nor obstruction after the first treatment was applied. Availability of treatment is accessible and the patient's age is below 80.
2) If you think that additional treatment is neccessery for this patient, what is your decision concerning the required type of treatment? (Please choose your decision from the table below)……
3) How many months do you expect for the survival of this patient after the treatment combination was applied?.....

Appendix 3: Case Studies Regarding the Least Seen Cases.

Case Study 1: A surgeon wants to determine the most appropriate treatment method for a particular patient who has these criteria levels: no perforation, no obstruction, adjacent organ invasion, no fistula, T4N2M0 stage, upper tumor location, no coexisting disease or pathology, and at least 20 surgical operation experiences in a year.
1) What is your decision concerning the required type of treatment? (Please choose your decision from the table below)……
After the first treatment was applied to this patient, some criteria were assessed for making a decision regarding the additional treatments that should be provided. Patient has R0 resection margin status, increase at the stage of the disease after the first treatment applied, adjacent organ invasion, lymph invasion, positive perinoral invasion and no vascular invasion. It was determined that patient has neither perforation nor obstruction after the first treatment was applied. Availability of treatment is accessible and the patient's age is below 80.
2) If you think that additional treatment is neccessery for this patient, what is your decision concerning the required type of treatment? (Please choose your decision from the table below)……..
3) How many months do you expect for the survival of this patient after the treatment combination was applied?.....

Case Study 2: A surgeon wants to determine the most appropriate treatment method for a particular patient who has these criteria levels: no perforation, no obstruction, adjacent organ invasion, no fistula, T3N1M1 stage, middle tumor location, diabetes, hypertansion and coronary artery diseases, and at least 20 surgical operation experiences in a year.
1) What is your decision concerning the required type of treatment? (Please choose your decision from the table below)……
After the first treatment was applied to this patient, some criteria were assessed for making a decision regarding the additional treatments that should be provided. Patient has R0 resection margin status, stable stage of the disease after the first treatment applied, adjacent organ invasion, lymph invasion, nonassessable perinoral invasion and no vascular invasion. It was determined that patient has neither perforation nor obstruction after the first treatment was applied. Availability of treatment is accessible and the patient's age is below 80.
2) If you think that additional treatment is neccessery for this patient, what is your decision concerning the required type of treatment? (Please choose your decision from the table below)……..
3) How many months do you expect for the survival of this patient after the treatment combination was applied?.....

Case Study 3: A surgeon wants to determine the most appropriate treatment method for a particular patient who has these criteria levels: no perforation, no obstruction, adjacent organ invasion, no fistula, T3N1M1 stage, middle tumor location, no coexisting disease or pathology, and at least 20 surgical operation experiences in a year.
1) What is your decision concerning the required type of treatment? (Please choose your decision from the table below)……
After the first treatment was applied to this patient, some criteria were assessed for making a decision regarding the additional treatments that should be provided. Patient has R0 resection margin status, increase at the stage of the disease after the first treatment applied, no adjacent organ invasion, lymph invasion, positive perinoral invasion and vascular invasion. It was determined that patient has neither perforation nor obstruction after the first treatment was applied. Availability of treatment is accessible and the patient's age is below 80.
2) If you think that additional treatment is neccessery for this patient, what is your decision concerning the required type of treatment? (Please choose your decision from the table below)……..
3) How many months do you expect for the survival of this patient after the treatment combination was applied?.....

Case Study 4: A surgeon wants to determine the most appropriate treatment method for a particular patient who has these criteria levels: no perforation, no obstruction, adjacent organ invasion, no fistula, T4N2M1 stage, middle tumor location, no coexisting disease or pathology, and at least 20 surgical operation experiences in a year.
1) What is your decision concerning the required type of treatment? (Please choose your decision from the table below)……
After the first treatment was applied to this patient, some criteria were assessed for making a decision regarding the additional treatments that should be provided. Patient has R0 resection margin status, decrease at the stage of the disease after the first treatment applied, no adjacent organ invasion, lymph invasion, positive perinoral invasion and vascular invasion. It was determined that patient has neither perforation nor obstruction after the first treatment was applied. Availability of treatment is accessible and the patient's age is upper than 80.
2) If you think that additional treatment is neccessery for this patient, what is your decision concerning the required type of treatment? (Please choose your decision from the table below)……..
3) How many months do you expect for the survival of this patient after the treatment combination was applied?.....

Case Study 5: A surgeon wants to determine the most appropriate treatment method for a particular patient who has these criteria levels: no perforation, no obstruction, no adjacent organ invasion, no fistula, T1N0M0 stage, upper tumor location, no coexisting disease or pathology, and at least 20 surgical operation experiences in a year.
1) What is your decision concerning the required type of treatment? (Please choose your decision from the table below)……
After the first treatment was applied to this patient, some criteria were assessed for making a decision regarding the additional treatments that should be provided. Patient has R0 resection margin status, stabel stage of the disease after the first treatment applied, no adjacent organ invasion, nonassessable lymph invasion, nonassessable perinoral invasion and nonassessable vascular invasion. It was determined that patient has neither perforation nor obstruction after the first treatment was applied. Availability of treatment is accessible and the patient's age is upper than 80.
2) If you think that additional treatment is neccessery for this patient, what is your decision concerning the required type of treatment? (Please choose your decision from the table below)……..
3) How many months do you expect for the survival of this patient after the treatment combination was applied?.....

Appendix 3: Case Studies Regarding the Least Seen Cases (continues).

Case Study 6: A surgeon wants to determine the most appropriate treatment method for a particular patient who has these criteria levels: no perforation, no obstruction, no adjacent organ invasion, no fistula, T4N0M0 stage, lower tumor location, diabetes and hypertansion diseases, and at least 20 surgical operation experiences in a year.
1) What is your decision concerning the required type of treatment? (Please choose your decision from the table below)……
After the first treatment was applied to this patient, some criteria were assessed for making a decision regarding the additional treatments that should be provided. Patient has R1 resection margin status, decrease at the stage of the disease after the first treatment applied, no adjacent organ invasion, lymph invasion, positive perinoral invasion and no vascular invasion. It was determined that patient has neither perforation nor obstruction after the first treatment was applied. Availability of treatment is accessible and the patient's age is below 80.
2) If you think that additional treatment is neccessery for this patient, what is your decision concerning the required type of treatment? (Please choose your decision from the table below)……..
3) How many months do you expect for the survival of this patient after the treatment combination was applied?.....

Case Study 7: A surgeon wants to determine the most appropriate treatment method for a particular patient who has these criteria levels: no perforation, no obstruction, no adjacent organ invasion, no fistula, T4N1M0 stage, upper tumor location, chronic liver disease, and at least 20 surgical operation experiences in a year.
1) What is your decision concerning the required type of treatment? (Please choose your decision from the table below)……
After the first treatment was applied to this patient, some criteria were assessed for making a decision regarding the additional treatments that should be provided. Patient has R0 resection margin status, stable stage of the disease after the first treatment applied, no adjacent organ invasion, no lymph invasion, no perinoral invasion, and a vascular invasion. It was determined that patient has neither perforation nor obstruction after the first treatment was applied. Availability of treatment is accessible and the patient's age is below 80.
2) If you think that additional treatment is neccessery for this patient, what is your decision concerning the required type of treatment? (Please choose your decision from the table below)……
3) How many months do you expect for the survival of this patient after the treatment combination was applied?.....

Case Study 8: A surgeon wants to determine the most appropriate treatment method for a particular patient who has these criteria levels: no perforation, no obstruction, no adjacent organ invasion, no fistula, T4N2M0 stage, middle tumor location, hypertansion and chronic obstructive pulmonary diseases, and at least 20 surgical operation experiences in a year.
1) What is your decision concerning the required type of treatment? (Please choose your decision from the table below)……
After the first treatment was applied to this patient, some criteria were assessed for making a decision regarding the additional treatments that should be provided. Patient has R1 resection margin status, stable stage of the disease after the first treatment applied, no adjacent organ invasion, a lymph invasion, positive perinoral invasion, and a vascular invasion. It was determined that patient has neither perforation nor obstruction after the first treatment was applied. Availability of treatment is accessible and the patient's age is below 80.
2) If you think that additional treatment is neccessery for this patient, what is your decision concerning the required type of treatment? (Please choose your decision from the table below)……..
3) How many months do you expect for the survival of this patient after the treatment combination was applied?.....

Case Study 9: A surgeon wants to determine the most appropriate treatment method for a particular patient who has these criteria levels: no perforation, no obstruction, no adjacent organ invasion, no fistula, T4N2M0 stage, middle tumor location, no coexisting disease or pathology, and at least 20 surgical operation experiences in a year.
1) What is your decision concerning the required type of treatment? (Please choose your decision from the table below)……
After the first treatment was applied to this patient, some criteria were assessed for making a decision regarding the additional treatments that should be provided. Patient has R1 resection margin status, stable stage of the disease after the first treatment applied, no adjacent organ invasion, a lymph invasion, positive perinoral invasion, and a vascular invasion. It was determined that patient has neither perforation nor obstruction after the first treatment was applied. Availability of treatment is accessible and the patient's age is below 80.
2) If you think that additional treatment is neccessery for this patient, what is your decision concerning the required type of treatment? (Please choose your decision from the table below)……..
3) How many months do you expect for the survival of this patient after the treatment combination was applied?.....

Case Study 10: A surgeon wants to determine the most appropriate treatment method for a particular patient who has these criteria levels: no perforation, no obstruction, no adjacent organ invasion, no fistula, T2N2M0 stage, lower tumor location, hypertansion disease, and maksimum 20 surgical operation experiences in a year.
1) What is your decision concerning the required type of treatment? (Please choose your decision from the table below)……
After the first treatment was applied to this patient, some criteria were assessed for making a decision regarding the additional treatments that should be provided. Patient has R0 resection margin status, decrease at the stage of the disease after the first treatment applied, no adjacent organ invasion, a lymph invasion, positive perinoral invasion, and a vascular invasion. It was determined that patient has neither perforation nor obstruction after the first treatment was applied. Availability of treatment is accessible and the patient's age is upper than 80.
2) If you think that additional treatment is neccessery for this patient, what is your decision concerning the required type of treatment? (Please choose your decision from the table below)……
3) How many months do you expect for the survival of this patient after the treatment combination was applied?.....

Appendix 4: Treatment Options in Order to Fill the Form.

TREATMENT OPTIONS FOR THE FIRST TREATMENT METHOD

1. Curative Treatment
    1.1. Surgery
        1.1.1. Transanal local excision
        1.1.2. Transanal endoscopic microsurgery
        1.1.3. Anterior resection of rectum
        1.1.4. Low anterior resection
        1.1.5. Very low anterior resection
        1.1.6. Colo-anal anastomosis
        1.1.7. Intersphincteric resection
        1.1.8. Abdominal perineal resection
        1.1.9. Hartmann operation
    1.2. Preoperative chemoradiotherapy+Surgery
        1.2.1. Preoperative chemoradiotherapy+Transanal local excision
        1.2.2. Preoperative chemoradiotherapy+Transanal endoscopic microsurgery
        1.2.3. Preoperative chemoradiotherapy+Anterior resection of rectum
        1.2.4. Preoperative chemoradiotherapy+Low anterior resection
        1.2.5. Preoperative chemoradiotherapy+Very low anterior resection
        1.2.6. Preoperative chemoradiotherapy+Colo-anal anastomosis
        1.2.7. Preoperative chemoradiotherapy+Intersphincteric resection
        1.2.8. Preoperative chemoradiotherapy+Abdominal perineal resection
        1.2.9. Preoperative chemoradiotherapy+Hartmann operation
    1.3. Preoperative radiotherapy+Cerrahi
        1.3.1. Preoperative radiotherapy+Transanal local excision
        1.3.2. Preoperative radiotherapy+Transanal endoscopic microsurgery
        1.3.3. Preoperative radiotherapy+Anterior resection of rectum
        1.3.4. Preoperative radiotherapy+Low anterior resection
        1.3.5. Preoperative radiotherapy+Very low anterior resection
        1.3.6. Preoperative radiotherapy+Colo-anal anastomosis
        1.3.7. Preoperative radiotherapy+Intersphincteric resection
        1.3.8. Preoperative radiotherapy+Abdominal perineal resection
        1.3.9. Preoperative radiotherapy+Hartmann operation
    1.4. Others
        1.4.1. Only Chemotherapy
        1.4.2. Only Radiotherapy
        1.4.3. Chemoradiotherapy
2. Palliative treatment
    2.1. Palliative operations (stoma, stent, internal by-pass, endoscopic cauterization)
    2.2. Others
        2.2.1. Only Chemotherapy
        2.2.2. Only Radiotherapy
        2.2.3. Chemoradiotherapy
3. Symptomatic treatment
4. No treatment
5. Chemotherapy for liver metastases+Radiotherapy for rectum+Surgery

Appendix 4: Treatment Options in Order to Fill the Form (continues).

TREATMENT OPTIONS FOR ADDITIONAL TREATMENT

1. Additional treatment is necessary
    1.1. Only Chemotherapy
    1.2. Only Radiotherapy
    1.3. Chemoradiotherapy
    1.4. Additional surgery
        1.4.1. Transanal local excision
        1.4.2. Transanal endoscopic microsurgery
        1.4.3. Anterior resection of rectum
        1.4.4. Low anterior resection
        1.4.5. Very low anterior resection
        1.4.6. Colo-anal anastomosis
        1.4.7. Intersphincteric resection
        1.4.8. Abdominal perineal resection
        1.4.9. Hartmann operation
    1.5. Additional surgery+Chemotherapy
        1.5.1. Transanal local excision+Chemotherapy
        1.5.2. Transanal endoscopic microsurgery+Chemotherapy
        1.5.3. Anterior resection of rectum+Chemotherapy
        1.5.4. Low anterior resection+Chemotherapy
        1.5.5. Very low anterior resection+Chemotherapy
        1.5.6. Colo-anal anastomoz+Chemotherapy
        1.5.7. Intersphincteric resection+Chemotherapy
        1.5.8. Abdominal perineal resection+Chemotherapy
        1.5.9. Hartmann operation+Chemotherapy
2. Treatment is concluded

Appendix 5: The Suggested Treatment Options from Both the System and Experts for the Most Frequently Seen Cases.

Variable Name	**Levels of Criteria for the First Decision Step**									
Presence of perf.	None	None	None	None	None	None	None	None	None	None
Presence of obst.	None	None	None	None	None	None	None	None	None	None
Coex. Disea./Path.	None	None	None	None	None	None	None	None	None	None
Presence of fistula	None	None	None	None	None	None	None	None	None	None
Surgeon's exp.	Exp. ≥ 20	Exp. ≥ 20	Exp. ≥ 20	Exp. ≥ 20	Exp. ≥ 20	Exp. ≥ 20	Exp. ≥ 20	Exp. ≥ 20	Exp. ≥ 20	Exp. ≥ 20
Stage of dis. (TNM)	T3N1M0	T4N1M0	T3N1M0	T4N2M0	T3N0M0	T3N2M0	T1N0M0	T2N0M0	T3N2M0	T4N2M0
Loc. of tumor	Middle	Lower	Lower	Lower	Lower	Lower	Middle	Middle	Upper	Middle
Adj. organ inv.	None	None	None	None	None	None	None	None	None	None
Suggested by	**Treatment option 1**									
Data 1	1.2.8	1.2.8	1.2.8	1.2.8	1.1.8	1.2.8	1.1.2	1.1.4	1.2.4	1.1.4
Data 2	1.2.4	1.2.4	1.2.5	1.2.5	1.3.8	1.2.4	1.1.4	1.1.5	1.2.5	1.2.5
Data 3	1.2.5	1.2.5	-	-	-	1.2.5	1.3.4	-	-	-
Expert 1 (T.Ü)	1.2.4	1.2.4	1.2.5	1.2.5	1.2.5	1.2.5	1.1.4	1.1.4	1.2.3	1.2.4
Expert 2 (T.E)	1.2.4	1.2.5	1.2.5	1.2.5	1.2.5	1.2.5	1.1.4	1.1.4	1.2.3	1.2.5
Variable Name	**Levels of Criteria for the Second Decision Step**									
Resec. Marg. Status	R0	R0	R0	R0	R0	R0	R0	R0	R0	R0
Stage of dis.	Downstage	Downstage	Downstage	Downstage	Stable	Downstage	Stable	Stable	Downstage	Downstage
Adj. organ inv.	None	None	None	None	None	None	None	None	None	None
Lymph inv.	None	None	None	None	Nonassessable	None	Nonassessable	None	None	None
Per. inv.	Negative	Negative	Negative	Negative	Nonassessable	Negative	Nonassessable	Negative	Negative	Negative
Vasc. Inv.	None	None	None	None	Nonassessable	None	Nonassessable	None	None	None
Presence of perf.	None	None	None	None	None	None	None	None	None	None
Presence of obst.	None	None	None	None	None	None	None	None	None	None
Availability	Accessible	Accessible	Accessible	Accessible	Accessible	Accessible	Accessible	Accessible	Accessible	Accessible
Patient's age	0-80	0-80	0-80	0-80	0-80	0-80	0-80	0-80	0-80	0-80
Suggested by	**Treatment option 2**									
Data 1	2	2 / 1.1	2/1.3/1.1	1.1	2/1.3	2/1.1	2	2	1.1	2
Data 2	2 / 1.1	1.1	1.1	2/1.1	1.1/1.3	1.1	2	2	1.1	1.1
Data 3	2 / 1.1	1.1	-	-	-	1.1	2	-	-	-
Expert 1 (T.Ü)	1.1	1.1	1.1	1.1	1.1	1.1	2	2	1.1	1.1
Expert 2 (T.E)	1.1	1.1	1.1	1.1	1.1	1.1	1.2	1.1	1.1	1.1
Suggested by	**Survival (months)**									
Data 1	45	2 / 30.66	35/53/73.33	61.25	22/94	36/116	93	146.5	3	120
Data 2	25 / 104.5	43	68	25/32	135/46	57	155	236	67	64.5
Data 3	23 / 97.5	43	-	-	-	46	123	-	-	-
Expert 1 (T.Ü)	36-72	24-48	36-72	24-48	60-84	36-72	96 +	84 +	48 +	24-48
Expert 2 (T.E)	72	48	36	24	24	36	72	72	48	36

Appendix 6: The Suggested Treatment Options from Both the System and Experts for the Least Seen Cases.

Variable Name	**Levels of Criteria for the First Decision Step**									
Presence of perf.	None	None	None	None	None	None	None	None	None	None
Presence of obst.	None	None	None	None	None	None	None	None	None	None
Coex. Disea./Path.	Present	Present	Present	Present	None	None	None	None	None	None
Presence of fistula	None	None	None	None	None	None	None	None	None	None
Surgeon's exp.	Exp. ≥ 20	Exp. ≥ 20	Exp. ≥ 20	Exp. ≥ 20	Exp. ≥ 20	Exp. ≥ 20	Exp. ≥ 20	Exp. ≥ 20	Exp. ≥ 20	Exp. < 20
Stage of dis. (TNM)	T2N0M1	T3N1M1	T3N1M1	T4N2M1	T1N0M0	T4N0M0	T4N1M0	T4N2M0	T4N2M0	T2N2M0
Loc. of tumor	Upper	Middle	Middle	Middle	Upper	Lower	Upper	Middle	Middle	Lower
Adj. organ inv.	None	(DM+COPD+HT)	None	None	None	(DM+HT)	(CLF)	(HT+COPD)	None	(HT)
Suggested by	**Treatment option 1**									
Data 1	1.2.4	1.1.4	1.2.5	1.1.4	1.3.3	1.2.5	1.1.3	1.2.8	1.2.8	1.3.4
Expert 1 (T.Ü)	5	5	5	5	1.1.3	1.2.5	1.2.3	1.2.4	1.2.4	1.2.5
Expert 2 (T.E)	1.1.3	1.3.3	1.3.3	1.3.3	1.1.3	1.2.5	1.2.3	1.2.4	1.2.4	1.2.5
Variable Name	**Levels of Criteria for the Second Decision Step**									
Resec. Marg. status	R0	R0	R0	R0	R0	R1	R0	R1	R1	R0
Stage of dis.	Upstage	Stable	Upstage	Downstage	Stable	Downstage	Stable	Stable	Stable	Downstage
Adj. organ inv.	Present	Present	None	None	None	None	None	None	None	None
Lymph inv.	Present	Present	Present	Present	Nonassessable	Present	None	Present	Present	Present
Per. inv.	Positive	Nonassessable	Positive	Positive	Nonassessable	Positive	Negative	Positive	Positive	Positive
Vasc. Inv.	None	None	Present	Present	Nonassessable	None	Present	Present	Present	Present
Presence of perf.	None	None	None	None	None	None	None	None	None	None
Presence of obst.	None	None	None	None	None	None	None	None	None	None
Availability	Accessible	Accessible	Accessible	Accessible	Accessible	Accessible	Accessible	Accessible	Accessible	Accessible
Patient's age	0-80	0-80	0-80	80+	80+	0-80	0-80	0-80	0-80	80+
Suggested by	**Treatment option 2**									
Data 1	2	1.1	1.1	1.1	2	1.1	1.3	1.1	1.3	2
Expert 1 (T.Ü)	1.1	1.1	1.1	1.1	2.1	1.1	1.1	1.1	1.3	1.1
Expert 2 (T.E)	1.3	1.3	1.3	1.3	1.3.1	1.4.8	1.3	1.4.5	1.4.5	1.3
Suggested by	**Survival (months)**									
Data 1	1	28	44	43	178	58	11	16	1	183
Expert 1 (T.Ü)	60 +	48	48	36	120	48-60	24-36	24-36	18-24	36-48
Expert 2 (T.E)	24	18	18	16	96	48	24	18	18	48