NEAR EAST UNIVERSITY

INSTITUTE OF GRADUATE STUDIES

DEPARTMENT OF COMPUTER ENGINEERING

FUZZY SYSTEM FOR DIAGNOSING ESOPHAGEAL CANCER

MSC THESIS

Mohammed Jameel SADEQ

Nicosia

September, 2023

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Approval

We certify that we have read the thesis submitted by Mohammed Jameel Sadeq **"fuzzy system for diagnosing esophageal cancer"** and that in our combined opinion it is fully adequate, in scope and in quality, as a thesis for the degree of masters of Computer Engineering.

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Declaration

I hereby declare that all information, documents, analysis and results in this thesis have been collected and presented according to the academic rules and ethical guidelines of Institute of Graduate Studies, Near East University. I also declare that as required by these rules and conduct, I have fully cited and referenced information and data that are not original to this study.

Mohammed Jameel Sadeq

08/09/2023

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Abstract

Fuzzy System for Diagnosing Esophageal Cancer

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Due to global changes, the incidence and mortality rate of esophagus cancer has skyrocketed in the last decades, with about 500,000 new cases. Esophageal cancer is a real life problem that has uncertain data and human error, giving room for possible misdiagnosis. This study developed a fuzzy intelligent system (FIS) to screen and provide predictive diagnosis of esophageal cancer. Fuzzy IF THEN rules were generated from a combination of esophageal symptoms, general risk factors, and diagnostic tests, under expert considerations. MATLAB software was used to design and run the FIS. The data was retrieved from a hospital in Erbil for 7 patients. The system provides recommendations with each predictive diagnosis, whether a patient is positive or negative for esophageal cancer or something suspicious is wrong with the esophagus. After implementing the data on FIS, the system shows an overall system accuracy of 95.24%, with an even higher accuracy (98%) for each patient’s prediction. For future studies, it is highly recommended that the fuzzy rules be expanded to include more variables and dataset.

Keywords: Esophageal cancer, Artificial intelligence, Fuzzy Logic, FIS, MATLAB

Özet

Özofagus Kanseri Teşhisi için Yapay Zeka Bulanık Sistem

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Küresel değişiklikler nedeniyle, özofagus kanseri insidansı ve ölüm oranı son on yıllarda yaklaşık 500.000 yeni vaka ile hızla arttı. Özofagus kanseri, kesin olmayan verileri ve insan hatası olan, olası yanlış teşhislere yer veren gerçek bir yaşam sorunudur. Bu çalışma, özofagus kanserini taramak ve tahmine dayalı tanı sağlamak için bir bulanık akıllı sistem (FIS) geliştirdi. Bulanık IF THEN kuralları, uzman değerlendirmeleri altında yemek borusu semptomları, genel risk faktörleri ve teşhis testlerinin bir kombinasyonundan oluşturulmuştur. FIS'i tasarlamak ve çalıştırmak için MATLAB yazılımı kullanılmıştır. Veriler Erbil'deki bir hastaneden 7 hasta için alındı. Sistem, bir hasta özofagus kanseri için pozitif veya negatif veya yemek borusunda şüpheli bir sorun olup olmadığına bakılmaksızın, her öngörü tanısında öneriler sunar. FIS'deki verileri uyguladıktan sonra sistem, her hastanın tahmini için daha da yüksek bir doğruluk (%98) ile %95,24'lük bir genel sistem doğruluğu gösterir. Gelecekteki çalışmalar için, bulanık kuralların daha fazla değişken ve veri seti içerecek şekilde genişletilmesi şiddetle tavsiye edilir.

Anahtar Kelimeler: Özofagus kanseri, Yapay zeka, Bulanık Mantık, FIS, MATLAB

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List of Abbreviations

ACDC	Australian center for disease control
AHP	Analytical Hierarchal Process
ANP	Analytical Network Process
BMJ	British Medical Journal
CDC	Center for Disease Control
DEA	Data Envelopment Analysis
ECDC	European Center for Disease Control
EDS	Electronic Data Systems
EIU	Economist Intelligence Unit
FMCDM	Fuzzy Multi-Criteria Decision Making
GDP	Growth Domestic Product
GHS	Global Health Security
H. Beds/1k	Hospital Beds per 1000

CHAPTER I

Introduction

In this chapter, the background of the thesis are discussed with detailed information about the plans, objectives, and aims of the study.

1.1 Background of the Study

When the cells and tissues in the inside lining of the esophagus begin to uncontrollably differentiate (multiply) or die (apoptosis), this leads to cancer of the esophagus. The esophagus is an important organ in the human body. It is a hallow tube that connects the throat to the stomach, where ingestion from the mouth is passed through to the stomach for digestion. This type of cancer can develop in any part of the organ and can occur in stages. Just like other cancer types, esophageal cancer can start in the organ lining, but can become malignant and spread to nearby organs.

Esophageal cancer is an aggressive malignancy and a major health burden (Bray et al., 2018; Corona et al., 2021). Clinical reports have shown several factors to be related to esophageal cancer such as age, gender, ethnicity, region, and individual lifestyle (like smoking, drinking, and obesity) etc. (Huang and Yu, 2016; Geoffrey et al., 2022). Among all cancer deaths, esophagus cancer is ranked the 6^{th} most common cause of cancer deaths globally (Bray et al., 2018), making it a fatal medical condition. The annual cancer mortality rate for esophageal cancer in 2018 was above 500,000 (Thakkar and Kaul, 2020).

Due to global changes, the incidence rate of esophagus cancer has skyrocketed in the last decades, with about 500,000 new cases (Ferlay et al., 2015; Huang et al., 2021). Unlike the mortality, the incidence rate of the cancer varies from region to region in relation to ethnicity and other factors mentioned previously. Among all malignancy, esophageal cancer is the most variably distributed cross nationalities, with a reported sixty-fold rates from country to country (Salek et al., 2009). In general, developing countries have the highest incidence and mortality rate of esophageal cancer compared to developed countries, especially in the continents of Africa and Asia (incidence rates reported in Asia and the African ESCC corridor (Abnet et al., 2017; McCormack et al., 2017; Bray et al., 2018).

Esophageal cancer is of different types, but the adenocarcinoma and squamous are the two most common esophageal cancer diagnosed in about 95% of patients (Thakkar and Kaul, 2020). The squamous sub variant of esophageal cancer occurs more in developing countries (like Tanzania), while adenocarcinoma is more prevalent in developed countries (like USA) (Arnold et al., 2018; Simba et al., 2022).

Earlier references show that the squamous sub variant of esophageal cancer is mostly prevalent in eastern Asia, Africa, and southern Europe and Africa (Pickens and Orringer, 2003; Bosetti et al., 2008), it however have a low prevalence in northern America (. Jemal et al., 2011). In fact, the United States is reported to have the highest prevalence of adenocarcinoma compared to any part of the world (Thakkar and Kaul, 2020). Generally, there is an increased incidence of esophageal cancer in developed countries in the past few decades compared to developing countries (Huang and Yu, 2018).

Whatever the variant is, it is important to determine the prognosis as well as survival rates of esophageal cancer patients include early screening/diagnosis and accurate staging (Corona et al., 2021). There are several ways to screen and reach an acceptable diagnosis. For effective and efficient diagnosis, as well as staging, imaging techniques such as Endoscopy, computed tomography, whole-body positron emission tomography with 18-fluorodeoxyglucose, and endoscopic ultrasound (EUS) are paramount (Thakkar and Kaul, 2020).

Unfortunately, despite the many advances in medicine in recent times, esophageal cancer still remain an aggressive malignancy with poor prognosis (Corona et al., 2021) and poor early diagnosis. It is usually detected at a later or malignant stage, which can attributed to some factors include lac of early manifestation of clinical symptoms. According to Hopkins Medicine, to improve the clinical outlook of esophageal cancer is to devise means of improving accuracy in diagnosis as well as the effective staging of the cancer (Hopkins Medicine, 2022) to decide on the most useful medical intervention.

The success of any cancer types mostly depends on early diagnosis. Cancer types like esophageal cancer that have tendency to undetected (early), to be malignant, and aggressive at the same, thus there is a dare requirement of different screening and diagnostic approaches and procedures that can improve early detection. In fact, the survival rate of esophageal greatly depends on the early detection. Once detected early, there are plethoras of treatment options like surgery, radiotherapy, chemotherapy, targeted therapy, including minimally invasive procedures that can effectively defeat the cancer. Although the mean five-year survival rate of esophageal cancer is 20%, however this rate for some patients can be as low as 5% (especially when diagnosed late) and can be higher than 47%, when detected early) (Huang and Yu, 2018; National Cancer Institute, 2022). In the wake of poor prognosis of esophageal cancer, it increased incidence recorded in recent decades, there is need for developing novel methods of early detection and prognosis (Huang and Yu, 2016; Huang and Yu, 2018).

This study aims to develop an intelligent AI system for diagnosing esophageal cancer. The most widely popular fuzzy logic principle, which is a part of machine learning, is used to achieve the set out aims and objectives of the study. The developed system functions to screen and provide assisted diagnosis of esophageal cancer. Several symptoms are used as indicators for diagnosing esophageal cancer that can be vital in predicting the status of any form of cancer that can assist medical decision making on proper diagnosis, treatment, and prognosis. Of contributing importance is the role of risk factors in screening individuals for esophageal cancer. It has the ability of revealing the susceptibility or vulnerability of individual to the occurrence of esophageal cancer.

With this given information, it is possible to develop an AI system that can combine the symptoms, risk factors, demography and other important indicators to diagnose esophageal cancer especially in the early stage. This will prevent ignorance or misdiagnosis (due to uncertainty and human error) of the cancer before it reaches advance stage. Several studies have developed AI models for diagnosing different types of cancer and several other types of diseases. Among the models used, Fuzzy Inference System (FIS), MATLAB (Matrix laboratory) software function and Graphics users Interface (GUI) have been utilized to create AI systems that assist doctors to make effective diagnosis. Fuzzy expert systems are capable of solving and preventing ambiguity that can affect diagnosis

1.2 Statement of Problem

The annual incidence and mortality of esophageal cancer has increased over the past decades. Despite technological advancement, the cancer is not easily detected until late or metastatic stage. This significantly reduces the survival rate, making esophageal cancer one of the fatal cancer and diseases. Cancer types like esophageal cancer that have tendency to be undetected (early), to be malignant, and aggressive at the same time; thus there is a dare requirement of different screening and diagnostic approaches and procedures that can improve early detection.

Esophageal cancer is a real life problem that has uncertainty and human error, giving room for possible misdiagnosis. Artificial intelligence have been attempting to reduce and eliminate possibility of misdiagnosis of the cancer before it reaches advance stage. In fact, the survival rate of esophageal greatly depends on the early detection. Once detected early, there are plethoras of treatment options that can effectively defeat the cancer. Although the mean five-year survival rate of esophageal cancer is 20%, however this rate for some patients can be as low as 5% (especially when diagnosed late) and can be higher than 47%, when detected early) (Huang and Yu, 2018; National Cancer Institute, 2022). In the wake of poor prognosis of esophageal cancer, it increased incidence recorded in recent decades, there is need for developing novel methods of early detection and prognosis (Huang and Yu, 2016; Huang and Yu, 2018).

1.3 Aims and Objectives

The aim of this study to construct an intelligent AI diagnostic system that works with dynamic flow to detect esophageal cancer, especially in early stage. The objective of the study is to utilize clinical symptoms, risk factors and other vital data to come up with a useful detection of the diseases. Other objectives include

- To explore the many indicators that may lead to an early diagnosis of the cancer
- To construct an AI fuzzy logic system, from the MATLAB (Matrix laboratory) software.

- To establish fuzzy rules from real life specialist consultation, extensive dataset research, and other indicators for use in our created AI system and for future works in esophageal and other cancer types.

1.4 Significance of the Study

The significance of this study cannot be overestimated. In a time when both the incidence and mortality rate of esophageal cancer is skyrocketing, there is need for novel approaches to diagnosis. This is especially because esophageal cancer is mostly not detected early but later, and can become aggressive/metastatic. Our study contribute to the limited but growing literature on automated diagnosis of esophageal cancer. Fuzzy logic that has been growing in its application in the medical has also been used in this study. Additionally, research is very limited on the implementation of intelligent systems in esophageal cancer; hence developing such systems is very significant and relevant.

1.5 Limitation of the Study

The major limitation of this study is readily available data for analysis. This is because there is very little academic articles that has been peer-review in journals, making it difficult to obtain the much-needed insight. Just like any AI diagnostic system, there may be tendency for bias; hence, more improvement is needed in future works.

CHAPTER II

Literature Review

This chapter focuses on previous works related to artificial intelligence in cancer diagnosis, particularly the role of intelligent fuzzy systems in esophageal cancer predictive diagnosis.

2.1 Overview

There have been several academic articles on AI in medical diagnosis that were published. These studies have developed and applied different AI systems to diverse medical conditions such as cancers, communicable diseases, pandemics, and liver disorders, to mention but a few. Some of the AI systems that have attracted interest in the past decades are mostly based on algorithms for automation in genetics, fuzzy, as well as ANN/ML (artificial neural networks/machine learning) (Adeli and Neshat, 2010). Of important major importance in the last decade is algorithms related to fuzzy logic, which has caught the attraction of researchers.

Some of the fuzzy logic based computational intelligent and mathematical systems are mentioned as follows; fuzzy expert system (FES) (Seritas et al., 2013), cubic hesitant fuzzy set (CHFS) (Fu et al., 2018), and adaptive network-based fuzzy inference system (ANFIS) (Rajabi et al., 2019) etc. These systems can be designed as rule based fuzzy logic to beat the traditional logic of reasoning. The essence of AI in general is to help improve the limitation of human intelligence whether in the form of accuracy, sensitivity, or specificity of reasoning. This study focuses on the principle and capacity of fuzzy logic to predict and diagnose esophageal cancer.

The traditional logic otherwise called the Aristotelian logic works on both extreme of data without, taking in to consideration data in between these extremes. The Aristotelean system only provides the option of two logic options. For example, it provides option of hot or cold, good or bad, and small or big etc., which coded as 1 or 0. Hence, the traditional logic system cannot be reliable, precise, certain, especially when every detail in dataset is significant for decision (Gorgulu and Akilli, 2016). Because of the limitations of the traditional logic, a new method of reasoning was required to take in to consideration virtually all significant attributes of a dataset. This gave birth to fuzzy logic in 1965.

Fuzzy logic is classified under conventional logic in operational research. Fuzzy logic is also referred to as fuzzy sets in the field of mathematics and system theory where the rules becomes more complicated to solve problems that are more complex. The novel role of fuzzy logic as mentioned earlier seeks to expand the dichotomy of true or false to be inclusive of a wide range of truth and falsehood in degrees between the two extremes (Scrobotă et al., 2017). With the evolution of fuzzy logic in to virtually all aspect of human life, the application has been widely accepted in medicine and healthcare. Fuzzy logic in medicine involves the use of more complicated datasets of real world problem, which are usually uncertain and imprecise (Latha et al., 2013).

2.2 The Concept of Fuzzy Logic

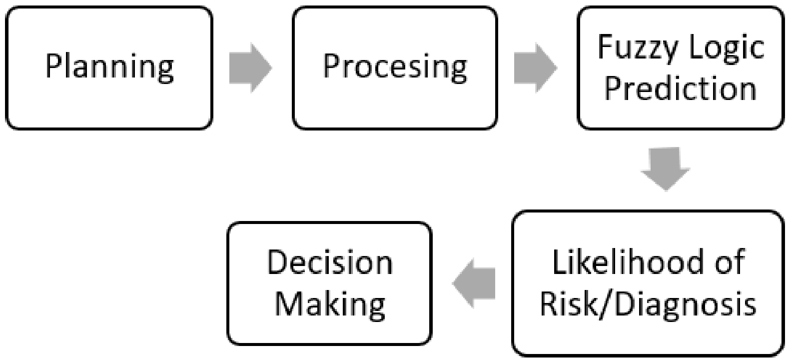
Fuzzy logic is classified under AI, consisting of linguistic terms that directly are directly used to match a machine language in mathematical models (Gorgulu and Akilli, 2016). These models are established for uncertain and imprecise data associated to real life issues. The concept tof fuzzy logic taps in to multi-valued logic (Mahanta and Panda, 2018), where there is proper representation of values in imprecise real world problems. This multi-valued logic that is used by fuzzy logic convert all data in a dataset and convert them to machine logic or language in values ranging from 0 to 1, which is unlike the Aristotelian logic where values are either 1 or 0.

There are unique characterizes to fuzzy logic that have attracted researchers to implement it in real life problems including medicine. Its ability to consider a wide range of values in a given dataset, it is cost effective, precise and accurate. It is also very user friendly, in the sense that both novice and experts can use it for diverse objectives. This is because there are no complex processes attached to it compared to other techniques like deep leaning. There are three major areas that fuzzy logic have been implemented for medical purposes; they include of risk prediction, decision-making, and automated diagnosis. In diagnosis and prediction, it has been used to automate diagnosis of breast cancer, prostate cancer, brain cancer, and liver cancer among many other diseases. In decision making, fuzzy logic have been applied by

Unfortunately, there are very limited research on fuzzy logic in improving prediction, diagnosis, and decision making in the matter of esophageal cancer. This is troubling considering esophageal cancer is one of the major disease causing mortality globally.

Figure 2.1.

Simplified steps for automating cancer diagnosis using AI (Gorgulu and Akilli, 2016).



2.3 Related Literature Review

For different applications, AI has been used for solving several real life issues affecting esophageal cancer. Wang, et al. (2012) created an AI system on the principles of fuzzy logic. The system was developed with the aim of predicting the esophageal cancer risk associated with each individual in the study. The input considers several factors, while the output predict the risk score of esophageal cancer. The dataset utilized in the study are numerical values from serum concentrations of C-reactive protein (CRP) and albumin. This dataset was cultivated from 271 patients who had been confirmed to have esophageal cancer, but were not treated with radiotherapy yet. The result shows that applying fuzzy logic to datasets improved esophageal cancer prediction for complete one year survival (area under curve (AUC) = 0.773). The study also found fuzzy logic to perform better than Glasgow prognostic score (AUC = 0.745). The study concluded that fuzzy logic I a useful tool that can help analyze and predict the result of esophageal cancer patients.

Hamed (2015) developed a fuzzy logic algorithm to tackle issues of esophageal cancer. The algorithm is called adaptive fuzzy Petri net (AFPN), which is a system that shows the prognosis of the diseases, and it uses if then rules to achieve the predictive outcome for esophageal cancer. The input variables are e serum concentrations of C-reactive protein and albumin. Simulations and experimental results demonstrate the effectiveness and performance of the proposed algorithms.

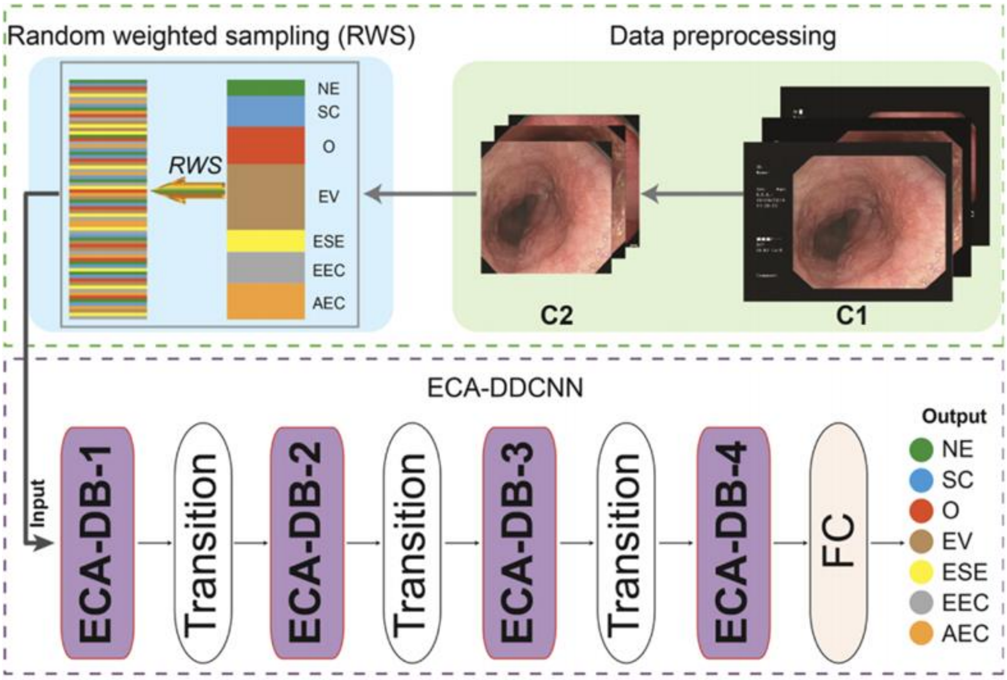
Scrobotă et al. (2017) applied the principles of fuzzy logic to assess all cancer affecting the mouth, among which esophageal cancer was the focus. The main of the study was to use fuzzy logic to estimate the oral cancer risks, to improve early detection, and better management. They used clinical data and data from histopathological exam of 16 patients who were already diagnosed with oral potentially malignant disorders. Additionally, the study utilized fuzzy logic to interpret the values in the input numerical data (MDA and DONORS_PROTONS) and, based on a set of rules, to assign values to the output (ILLNESS RISK). The result found the highest MDA value associated with the lowest DONORS_PROTONS value in the variation fields corresponds to the highest value of ILLNESS RISK, and vice versa.

Li et al. (2018) identified the implication of manual segmentation of medical images especially in esophageal cancer. Therefore, they utilized semantic to automatically segment the pathological sections of esophageal cancer images. The main contribution of their study was establishing a comprehensively labeled dataset containing 1388 patches that were marked with cancer cells. Thee patches were divided in to Normal (958), and Abnormal (430). The study proceeded to test the dataset on DeeplabV3, FCN+ResNet, Unet etc. The result reveal FCN+ResNet as the best performing among all. Huang, et al. (2021) attempted to diagnose esophageal cancer in it early stage, using AI.

A new AI system was developed by Du et al. (2021) to solve esophageal issues. The study was the first of it kind and it is referred to as an efficient channel deep dense convolution neural network (ECA-DDCNN). The ECA-DDCNN is capable of classifying gastroscopic images of the esophagus. In the classification, the system is able to group them in to healthy, pre-cancer, early cancer, and advanced esophageal cancer. The participants of the study included 4,077 patients. From these patients, 20,965 gastroscopic images were gathered for training and testing the system. After system was run through the implementation of the collected data, the system achieved an overall accuracy of 90.63%, which when compared with other similar AI models; the proposed ECA-DDCNN performs better. Figure 2.2 shows diagram illustrating the proposed AI system by Du et al. (2021).

Figure 2.2

Diagrammatic illustration of the proposed model of Du et al. (2021).



Fang et al. (2022) developed a semantic segmentation model with the aim to diagnose esophageal cancer in early stage. The segmentation model predicts and label esophageal cancer using some of the early factors that are helpful in screening the cancer. a total of 165 esophagus images (75 white-light images (WLI) and 90 narrow-band images (NBI)). These images included images of normal or healthy esophagus. The image dataset also included two other categories, which are esophageal dysplasia and squamous cell carcinoma of the esophagus. Result shows that within a mean time of 111 milliseconds, the AI system was able to predict the state of the esophagus whether it is normal or healthy, dysplasia, or squamous cell carcinoma, with an overall accuracy of 84.724% and 82.377% respectfully for NBI and WLI respectively.

CHAPTER III

Biology and Morbidity of Esophageal Cancer

The basic biology and morbidity of esophageal cancer is presented in this chapter so we can better understand the esophagus, and how cancer affects its functions. In order to develop an intelligent system for diagnosing esophageal cancer, the researcher must understand the basic biology and morbidity of the esophagus, as well as the cancer that develops in inside it. This chapter provides basic information on the anatomy of esophageal cancer, its symptoms and risk factors, traditional diagnosis, and the types and stages of esophageal cancer

3.1 Anatomy of the Esophagus

Anatomy of the esophagus organ includes the structure, location, and function of the esophagus. The esophagus is a muscular tube that connect the mouth to the stomach, thus it is part of the complex digestive system. Regarding it structure, the esophagus does not have a specific structure, rather it is long (reaching up to 9 inches) and hallow. There is slight difference between the structure of esophagus in men and women, which affect the incidence of cancer according to gender. In centimeters, the esophagus in 25 in males, while it is 23cm in females (Enzinger, 2019). The esophagus is located from the back of the mouth, through the throat/neck, the chest and the abdomen, where it connects to the stomach. It functions to transport food from the mouth to the stomach. The secreted mucous in the esophagus also helps in primary digestion of food before reaching the stomach. The mucous membrane also serves as lubricant to allow hitch free swallowing of food and to protect the esophagus.

3.2 Esophageal Cancer

A cancer in the esophagus normally starts from the cells in the walls of the organ. The cancer gradually multiply uncontrollably to form a tumor in the esophagus, which may obstruct the normal transport of food from the mouth to the stomach (dysphagia and later odynophagia). As the cancer/tumor grows in size and malignancy in the early stage of growth, individuals may begin to experience partial blockage of the esophagus; however, as the cancer progress to a much later stage, the esophagus goes from partial to total blockage, which obstruct the flow of food to the stomach from the mouth (Enzinger, 2019).

3.2.1 Types of esophageal cancer

There are about six types of esophageal cancer including lymphoma, melanoma, carcinoid tumors, leiomyosarcoma, or sarcoma, squamous cell carcinoma (SCC) and adenocarcinoma (AC). However most of esophageal cancer types rarely occur. SCC and AC are the dominant esophageal cancer types that occurs in more than 95% of esophageal cancer patients. The types of esophageal cancer is affected by several factors such as ethnicity, region, and gender etc. for example, more Caucasians have more AC than African Americans, while the incidence of SCC is more prevalent in African American population compared to other ethnicity (Stabellini et al., 2020). It is important to note that cancer primarily originating from other parts of the body can metastasize and spread to the esophagus via blood stream, however this is rare cases (Enzinger, 2019).

3.2.2 Symptoms and risk factors of esophageal cancer

Esophageal cancer is associated with genetic, environmental, and behavioral risk factors (Huang et al., 2018; Abnet et al., 2018). The risk factors and symptoms excited by an individual is usually the first step to screen for esophageal cancer. In this case, screening for esophageal cancer entails that medical physicians conduct clinical tests to check the presence of esophageal cancer, based on the symptoms and the risk factors of the patients. In fact, screening is observed even when an individual does not exhibit any symptoms of esophageal cancer. The risk factor associated with esophageal cancer are those factors that may increase an individual's chances of getting the cancer (Castro et al., 2018). However, it is possible that an individual has one or two risk factors but does not develop any type of esophageal cancer, and vice versa.

Esophageal cancer is associated with several risk factors, but the most important is smoking and drinking (Chen et al., 2019). Smokers are liable to get SCC while alcoholics are liable to develop AC. Individuals with prolonged or chronic condition of gastroesophageal reflux have a risk of developing Barrett esophagus;

Barrett esophagus has higher risk of developing AC compared to individuals who don't. Other risks of AC include obesity, being in Western Europe, North America, and Australia, and being a Caucasian (Kou et al., 2019). There is a higher risk of developing SCC if the following risk factors are present; A high starch diet, low in fruits and vegetables, habit of drinking extremely hot liquids (149^0F, or 65^0C), being from East Asia and the Middle East, African-American (Wong et al., 2018).

Furthermore, more males develop esophageal cancer compared to females at a three times higher rate (ratio of about 3 to 1). Age is also a factor as most cases of the cancer is reported in individual within the age range of 55 and above (Huang et al., 2018; Enzinger, 2019). Early on esophageal cancer is asymptomatic or shows signs of common esophageal disorders; however, as it grows to advance stage, some symptoms become eminent like unintended weight loss, dyspepsia, chest pain, and heartburn to mention but a few (Cui et al., 2020). Symptoms such as dysphagia and odynophagia can tell a distinguishing difference between esophageal cancers and esophageal disorders.

3.3 Diagnosis and Staging of Esophageal Cancer

Just like other cancers, esophageal cancer is traditionally diagnosed using a combination of factors. It involves the analysis of symptoms/risk factors for screening, patient medical history, comprehensive clinical tests/evaluation. Biopsy is important in diagnosis as it confirms the presence or absence of cancer cells in specific region of interest in the esophagus. Other test that may check for cancer in the esophagus or the gastroesophageal junction may include Video-fluoroscopic swallowing studies (VFSS), Endoscopic confocal microscopy (ECM), Esophagogastroduodenoscopy (EGD) Endoscopy with biopsy, and Endoscopic ultrasonography (EUS) etc. Among the things that these tests may reveal include plaques, small swellings otherwise called nodules, and ulceration of the esophagus linings. EUS images the esophagus in details and can show the extent of cancer progression in the esophagus, and its spread to other parts of the body.

Lastly imaging modalities like computerized tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) scan that is used to stage esophageal cancer (Xie et al., 2021), which is useful for treatment. Staging esophageal cancer is not only important to understand the progression of the disease, but also the potential disease course. The general staging system utilized for any type of cancer is the Tumor Node Metastasis (TNM) Staging. It is also used extensively for the staging esophageal cancer. the TNT system on the basis of degree of tumor (T), the spread and its degree to lymph nodes (N), as well as metastization of the cancer and its spread to both distant and proxy parts of the body. According to Thakkar and Kaul (2020), esophageal cancer staging is very crucial for the prognosis and survival of both subtypes of the cancer.

CHAPTER IV

Process Methodology and Software Implementation

This chapter shows how the methodology alongside the dataset were implemented to achieve the goals and objectives of the study. The study utilized the principles of fuzzy logic to develop a fuzzy intelligent system (FIS) that diagnose esophageal cancer. Fuzzy logic is an excellent choice for dealing with real world (uncertain data) medical problems, because it uses natural language (Chen and Bau 2013; Fraccaro 2015). Artificial intelligent models that used fuzzy logic principles have been shown to be highly sensitive, accurate and flexible in dealing with vogue data. It also have ability to resist errors/dynamism in the data set.

In this study, the intelligent system developed utilized certain medical values as input variables to make an automatic diagnosis. These values were obtained from symptoms, general risk factors, and Histopathology test data, biopsy, TNM staging, Gleason score. The MATLAB software was used to design and run the intelligent system for screening and diagnosing esophageal cancer. MATLAB software is a suitable choice because it has favorable characteristics such as its flexibility with data types, and it provides high fuzzy logic simulation efficiency compared to other software. The MATLAB software also has a wide range of operational functions that is optional for researchers to use, depending on the type of data and objective of the research. The MATLAB tools used in this study include Interference fuzzy system (IFS) and Graphics users Interface (GUI) as used by (Farokhzad and Ebrahimi, 2016; Hadi, 2020).

4.1 Data Set

The data set was retrieved from a hospital in Erbil (due to confidentiality request by the hospital, name will not be mentioned in the study). The data set was divided in to these categories of input variables; symptoms, general risk factors, and Histopathology test data, for 7 patients whose identity are not allowed to be published in this study as well. Due to this confidentiality, the 7 patients are presented as patient-1 (P1) to patient-7 (P7). Lastly, radiographic images were not approved for the study, hence were not used for the study. Table 4.1 shows the dataset collected for 7 patients.

Table 4.1.

The dataset collected for 7 patients.

Variables		**P1**	**P 2**	**P3**	**P4**	**P5**	**P 6**	**P7**
Age		50	76	47	33	61	53	45
Gender		M	M	M	F	M	M	F
Biopsy		S	P	S	N	S	P	NIL
Ethnicity		Kurdish	Arab	Kurdish	Kurdish	Kurdish	Arab	Kurdish
Lifestyle	Barrett	✓			✓		✓	
	Bile reflux		✓		✓	✓	✓	
	GERD	✓		✓		✓		
	Indigestion	✓	✓	✓				
	Obese	✓				✓		✓
	Smoke		✓	✓			✓	
Region		AS	AS	AS	AS	AS	AS	AS
Diagnostic Tests	VFSS	YES	Tumor	NO	NO	NO	YES	NO
	ECM	Cancer	Cancer	Tumor	NO	Tumor	Cancer	NIL
	EGD	Imaging	Imaging	Imaging	NO	Imaging	Imaging	NIL
	EUS	Staging	Staging	Staging	NO	NO	Staging	NIL
Diagnosis		Positive AC	Positive AC	Positive SCC	Negative	Suspicious	Positive AC	NIL

Generally, the risk factors of esophageal cancer show the level of vulnerability of an individual to esophageal cancer. They include age, gender, ethnicity, region, and general lifestyle etc. Symptoms are those physical or clinical manifestations on patient that may be related to esophageal cancer. Symptoms of esophageal cancer that may indicate the occurrence of the cancer include dysphagia, weight loss, chest pain, coughing or hoarseness, digestive problems, and the esophageal conditions of GERD and Barrett etc. These symptoms individually or collectively can indicate esophageal cancer. A combination of the symptoms and the general risk factors may provide a better screening of esophageal cancer. The dataset also included data from the following;

4.1.1 Video-fluoroscopic swallowing studies (VFSS)

VFSS is a noninvasive medical procedure that utilizes radiation to provide strategic ad detailed view of the esophagus. It has capacity to image the upper esophageal functions including the mouth and pharyngeal. The main of a VFSS procedure is to examine irregularities with aspiration and the functional status of the oropharyngeal. For aspiration, VFSS checks the presence, time, as well as volume, while in regards to oropharyngeal; VFSS seeks to comprehend the anatomical and pathophysiological swallow function (Morgan and Murphy, 2022). The limitation of VFSS is that it only a general procedure to check the health of the esophagus, hence it is incapable of detecting cancer, particularly in asymptomatic cases. There are three main indication in a VFSS test; potential aspiration, oropharyngeal dysphagia, and odynophagia sensation.

4.1.2 Endoscopic confocal microscopy (ECM)

ECM helps to detect Barrett esophagus and associated neoplasia by detailed visualizing the tissues, which are specialized columnar Barrett epithelium in microscopic level. The visualization also includes glands and each goblet cells in the esophagus organ. EC microscopy is powerful in the sense that it can detects depletion in very small goblet cells of esophagus epithelium, and as well can find areas in the same epithelium where neoplastic epithelial cells have grown pass the basement membrane, and attack the lamina propria (Kiesslich et al., 2006). However, this does not still show cancer, rather disorder in the esophagus. There are four main indication in a ECM test; depleted goblet cells, Barrett esophagus, neoplastic epithelial cells, and cancer.

4.1.3 Esophagogastroduodenoscopy (EGD) Endoscopy with Biopsy

When a patient is at high risk or tumor/cancer is suspected without sufficient evidence, physicians utilize EGD to check for precancerous disorders. An important pre-cancer disorder is Barrett's esophagus, which is a noncancerous rumor with high possibility of morphing into esophageal cancer. The medical procedure helps visualize a combination of the esophagus, stomach and duodenum using a camera inserted through the mouth of the patient. (John Hopkin Medicine, 2022).

4.1.4 Endoscopic ultrasonography (EUS)

EUS is an important imaging technique once esophageal cancer has been detected, because it helps with staging the cancer for appropriate therapy. The powerful medical examination includes a combination of endoscopy camera and high frequency ultrasound technology to provide high-resolution images of any abnormality in the esophagus such as esophageal tumor, wall, cancer, and even surrounding structures. From the EUS procedure, esophageal cancer can be staged according to tumor, node, and metastasis (TNM) staging system that was first established by the Union for International Cancer Control (UICC) and American Joint Committee on Cancer (AJCC) (Rice et al., 2017). One of the powerful capabilities of EUS is that it can shows the in depth condition of tumor as well as esophageal wall. The normal staging includes T1, T2, T3, and T4 tumors (Thakkar and Kaul, 2020).

4.2 Fuzzy Rules for Predictive Diagnosis of Esophageal Cancer

All rules were developed using trapmf membership function. The words very low is represented as (VL), low (L), medium (M), high (H), very high (VH), and normal (N) which are given alongside the fuzzy rule bases used for the diagnosis of esophageal cancer are presented below.

4.2.1 Fuzzy Rules for Predictive Esophageal Cancer Screening by Risk Factors

- **Age as a risk factor**

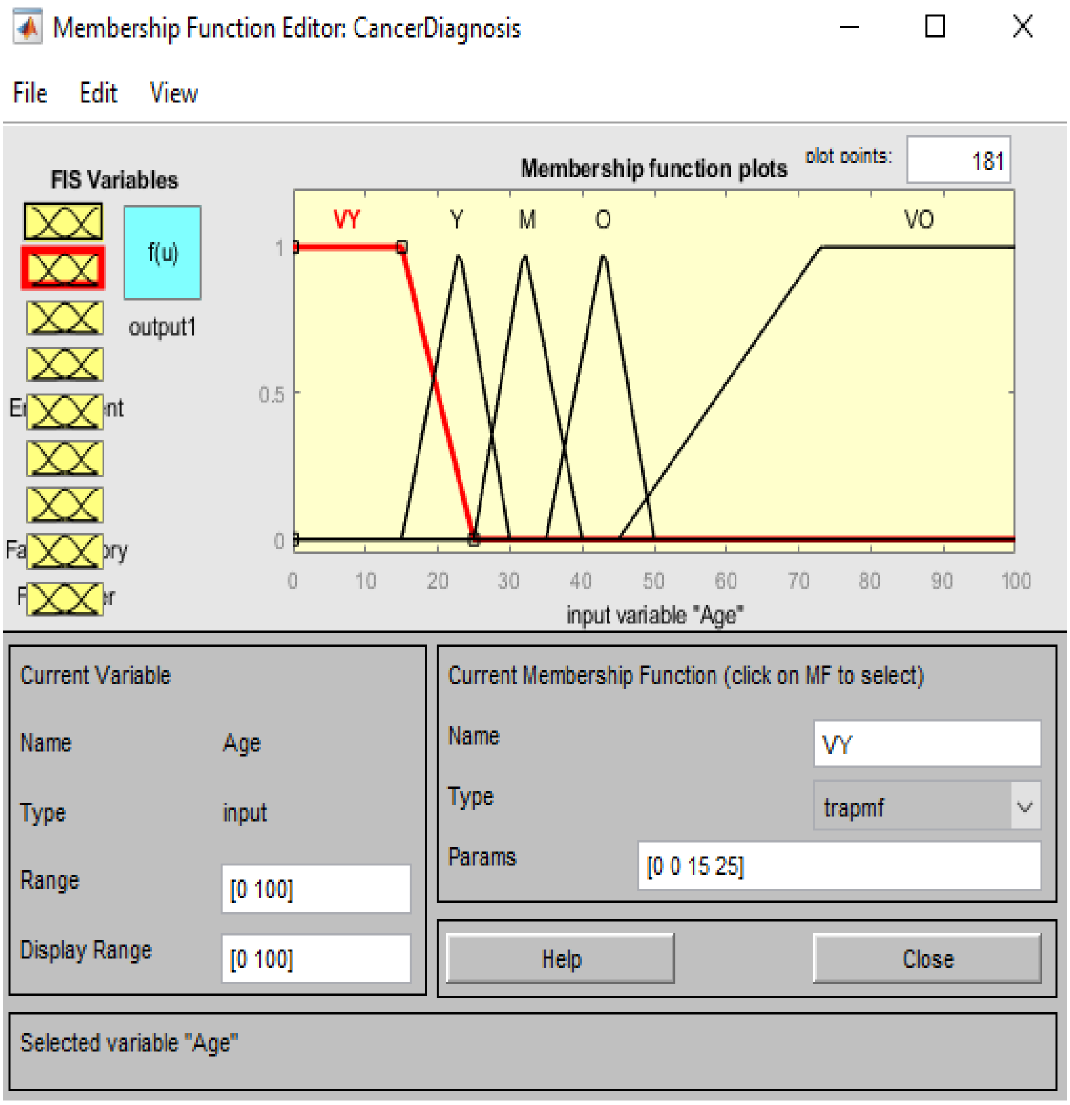
IF age (INDICATE) older than 50 years, high risk

IF age (INDICATE) between 31 to than 49 years, medium risk

IF age (INDICATE) between 20 to 30, low risk

Figure 4.1.

Fuzzy rules membership plots for Age risk



- **Gender as a risk factor**

IF gender (INDICATE) man, 3 to 4 times high risk (75%)

IF gender (INDICATE) female, lower risk (25%)

- **Ethnicity as a risk factor**

IF ethnicity (INDICATE) African American, 2 to 4 times high risk of SCC

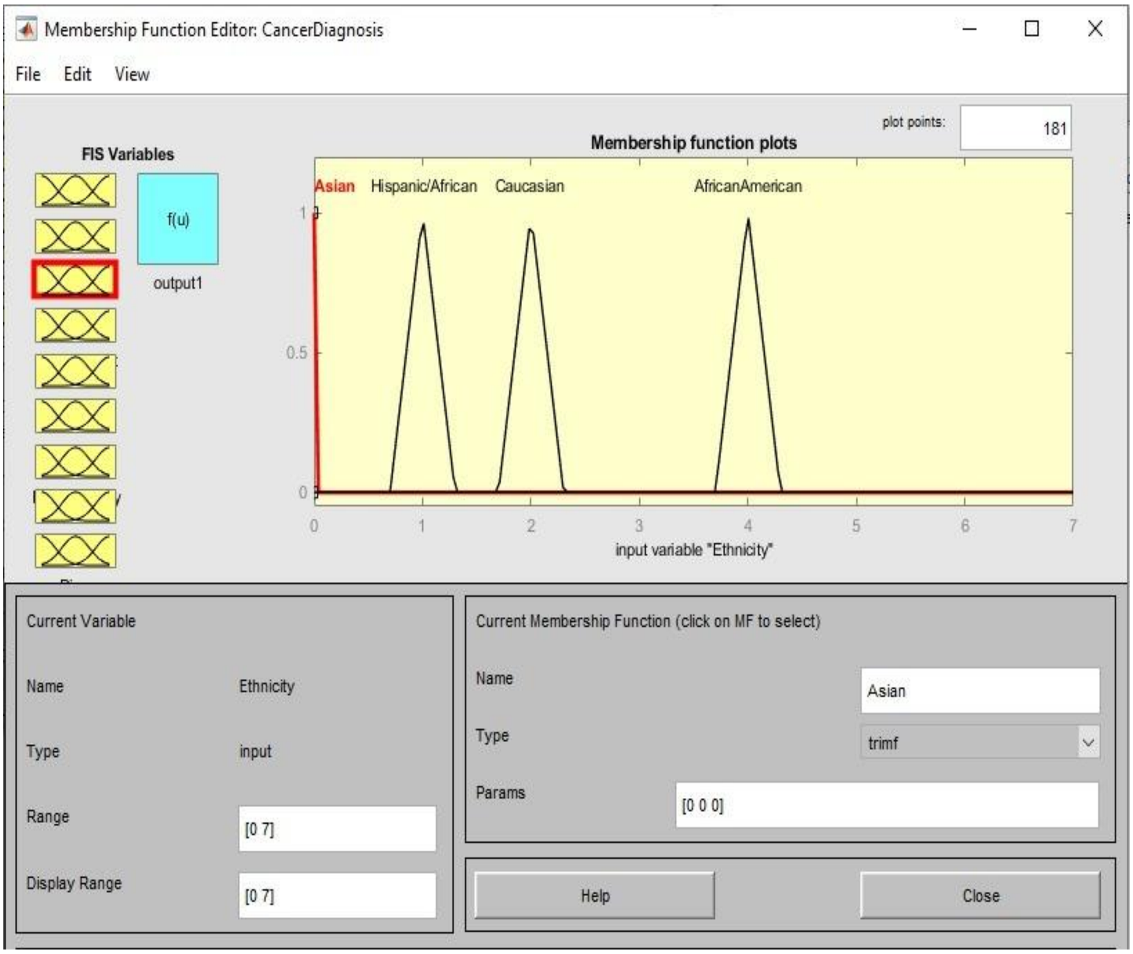
IF ethnicity (INDICATE) Caucasian, lower risk of SCC

IF ethnicity (INDICATE) Caucasian, 2 times high risk of AC

IF ethnicity (INDICATE) African American, lower risk of AC

Figure 4.2

Fuzzy rules membership plots for ethnicity risk



- **Region of Patients as a risk factor**

Based on region of the patients the following rules were established according to expert specifications.

IF region (INDICATE) North America (NA), Europe (E), Australia/New-Zealand (A/NZ), and Caribbean Islands (CI), AC high risk

IF region (INDICATE) Asia (AS), Africa (A), Central America (CA), and South America (SA), high risk of SCC

- **General lifestyle as a risk factor**

IF general lifestyle (INDICATE) bile reflux, high risk of esophageal cancer

IF general lifestyle (INDICATE) achalasia, high risk of esophageal cancer

IF general lifestyle (INDICATE) steady habit of drinking very hot liquids, high risk of cancer

IF general lifestyle (INDICATE) Not eating enough fruits/vegetables, high risk of cancer

IF general lifestyle (INDICATE) Smoking, 2 times risk for AC and 6 times risk for SCC

IF general lifestyle (INDICATE) Obese, high risk of AC

IF general lifestyle (INDICATE) Alcohol, high risk of SCC

- **Video-fluoroscopic swallowing studies (VFSS) as a risk factor**

IF VFSS (INDICATE) potential aspiration, possible esophageal problem, need further screening

IF VFSS (INDICATE) odynophagia sensation, possible esophageal problem, further screening

IF VFSS (INDICATE) oropharyngeal dysphagia, tumor endoscopy and further screening needed

- **Symptoms as a risk factor**

IF symptoms (INDICATE) dysphagia, high risk of esophageal cancer

IF symptoms (INDICATE) Weight loss without trying, low to medium risk of esophageal cancer

IF symptoms (INDICATE) chest pain, pressure, burning, low to medium risk of esophageal cancer

IF symptoms (INDICATE) Worsening indigestion, medium risk of cancer

IF symptoms (INDICATE) Coughing or hoarseness, high risk of esophageal cancer

IF symptoms (INDICATE) Chronic Chest Pain, medium to high risk of esophageal cancer

IF symptoms (INDICATE) Digestive problems, medium risk of cancer

IF symptoms (INDICATE) GERD, 5 times risk of AC

IF symptoms (INDICATE) Barrett, 30 to 40 times risk of AC

4.2.2 Fuzzy Rules for Predictive Esophageal Cancer Screening by Diagnostic Tests

- **Endoscopic confocal microscopy (ECM)**

IF ECM (INDICATE) normal, no further test

IF ECM (INDICATE) depleted goblet cells, esophageal problem, biopsy needed

IF ECM (INDICATE) Barrett, esophageal problem, biopsy and further screening needed

IF ECM (INDICATE) neoplastic epithelial cells, tumor endoscopy, biopsy and further test

IF ECM (INDICATE) cancer, tumor endoscopy, biopsy and further test

- **Biopsy**

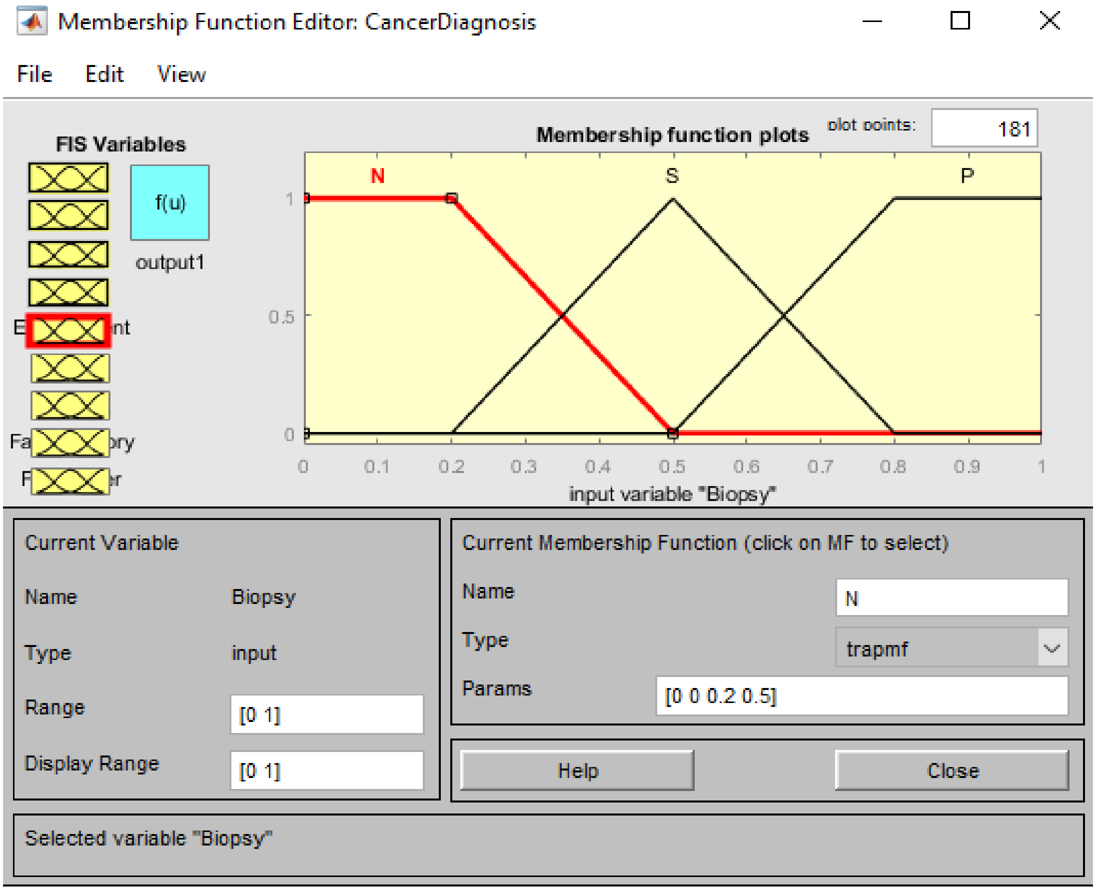
IF biopsy (INDICATE) absence of cancer cells, esophagus is negative for cancer

IF biopsy (INDICATE) abnormal cells, esophagus health status is suspicious

IF biopsy (INDICATE) presence of cancer cells, esophagus is positive for esophageal cancer

Figure 4.3

Fuzzy rules membership plots for biopsy test



- **Esophagogastroduodenoscopy (EGD) Endoscopy with Biopsy**

IF EGD (INDICATE) primary tumor, imaging, staging and Gleason score

IF EGD (INDICATE) ocoregional adenopathy, further confirmation

IF EGD (INDICATE) metastatic loco-regional adenopathy, positive cancer, imaging, staging and Gleason score

IF EGD (INDICATE) normal, no further confirmation

IF EGD (INDICATE) periesophageal lymphadenopathy, further confirmation

IF EGD (INDICATE) metastatic periesophageal lymphadenopathy, positive cancer, imaging, staging and Gleason score

IF EGD (INDICATE) cancer metastases, imaging, staging and Gleason score

4.2.3 Esophageal Cancer Staging

- **Endoscopic ultrasonography (EUS)**

Based on region of the patients the following rules were established according to expert specifications;

- Primary Tumor

IF EUS (INDICATE) TX, Primary tumor cannot be assessed

IF EUS (INDICATE) T0, No evidence of primary tumor

IF EUS (INDICATE) T1, tumor is superficial to the muscularis propria

IF EUS (INDICATE) T2, tumor invades into, but not through, the muscularis propria

IF EUS (INDICATE) T3, tumor invades through the muscularis propria (adventitia)

IF EUS (INDICATE) T4, imaging, tumor invasion into the adjacent structures or organs

- Regional Lymph Nodes

IF EUS (INDICATE) NX, Lymph node status cannot be assessed

IF EUS (INDICATE) N0, No regional lymph node metastases

IF EUS (INDICATE) N1, Metastasis in ≤2 regional lymph nodes

IF EUS (INDICATE) N2, Metastasis in 3-6 regional lymph nodes

IF EUS (INDICATE) N3, Metastasis in ≥7 regional lymph nodes

- Staging Distant Metastases

IF EUS (INDICATE) MX, Distant metastases not found

IF EUS (INDICATE) M0, Negative distant metastases

IF EUS (INDICATE) M1, Positive Distant metastases

4.2.2 Output Variables: Predictive Diagnosis of Esophageal Cancer

After dataset is implemented in the developed AI system, the expected output of the system is positive (P), suspicious (S), and negative (N), which is according to the fuzzy logic IF then rules that were established according to expert consideration. The system provides recommendations with each predictive diagnosis for further procedure. For a positive (P) diagnosis, the system recommends staging of the cancer and other possible recommendation useful for selecting the best therapy options. For suspicious (S) diagnosis, the system recommends a further screening to arrive at a conclusive diagnosis.

Lastly, for a negative (N), there is no need for further evaluation, hence, there is no recommendation. Figure 4.6 a screen shot of input crisp variables and the output of the system. The input variables consisted of various crisp data including the risk factors, symptoms, and diagnostic tests that are fed in to the developed AI system to provide a predictive diagnosis of esophageal cancer of each patient's data through output.

Figure 4.4

A Screen shot of input crisp variables and the output of the system

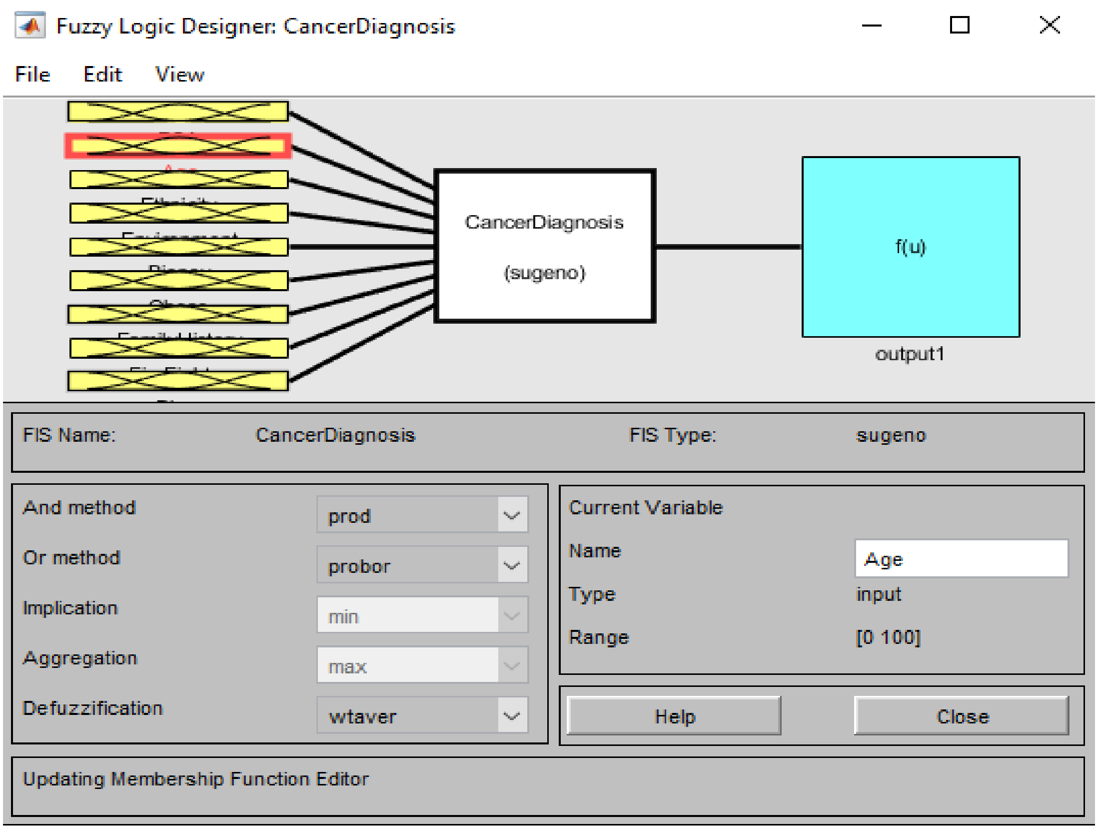


Table 4.2.

Summary of the Multi-input Single-output IF THEN Fuzzy Rule of the Proposed System.

Patients	Multi-input Single-output IF THEN Fuzzy Rules
1	IF age (INDICATE) 50, gender (INDICATE) male, biopsy (INDICATE) S, VFSS (INDICATE) YES, and region of patient (INDICATE) AS/A/CA/SA, THEN test result = positive for AC. As shown in figure 5.2
2	IF age (INDICATE) 76, gender (INDICATE) male, biopsy (INDICATE) P, EGD (INDICATE) imaging, and region of patient (INDICATE) NA, E, A/NZ, CI, THEN test result = positive for AC. As shown in figure 5.3
3	IF age (INDICATE) 47, gender (INDICATE) male, biopsy (INDICATE) S, VFSS (INDICATE) no, and region of patient (INDICATE) AS, A, CA, SA, THEN test result = positive for SCC. As shown in figure 5.4
4	IF age (INDICATE) 33, gender (INDICATE) female, biopsy (INDICATE) N, VFSS (INDICATE) no, and region of patient (INDICATE) AS, A, CA, SA, THEN test result = negative for AC. As shown in figure 5.5
5	IF age (INDICATE) 61, gender (INDICATE) male, biopsy (INDICATE) S, VFSS (INDICATE) no, and region of patient (INDICATE) AS, A, CA, SA, THEN test result = suspecious, requires further screening. As shown in figure 5.6
6	IF age (INDICATE) 53, gender (INDICATE) male, biopsy (INDICATE) P, VFSS (INDICATE) yes, and region of patient (INDICATE) AS, A, CA, SA, THEN test result = positive for AC. As shown in figure 5.7

CHAPTER V

Results and Discussion

Presentation of the result of system implementation is realized here, with a detailed discussion on the implications.

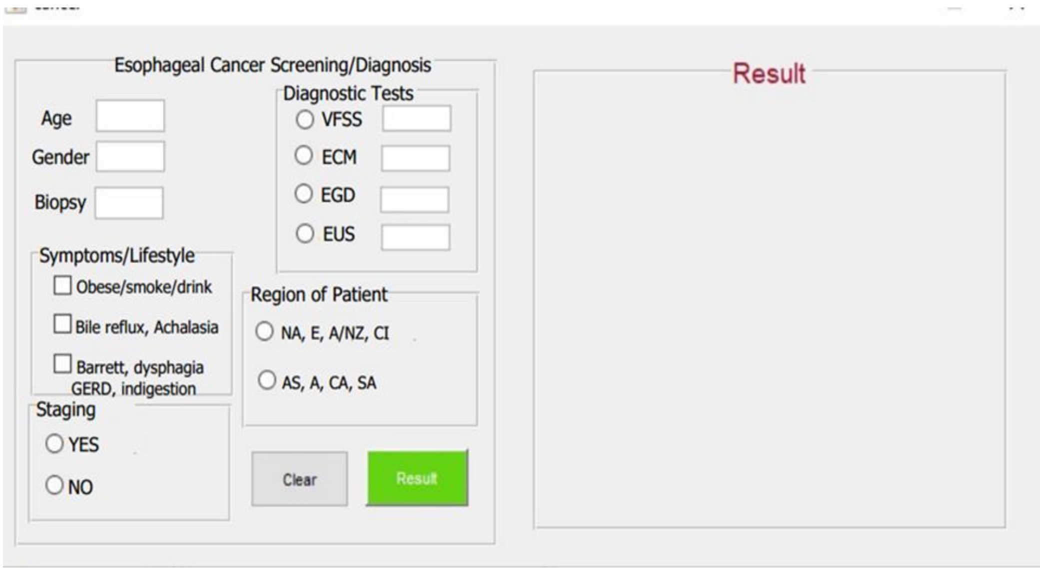
After implementing the dataset on the established fuzzy intelligent system in chapter four, the results of the predictive diagnosis of esophageal cancer is presenter in this chapter (chapter 5). The methodology used in this study included the development of Fuzzy Inference System (FIS) that establishes IF and THEN fuzzy rules. These rules ascertain the range and values of all input variables, were incorporated in to MATLAB (Matrix laboratory) software. Graphics User Interface (GUI) provides an easier technique for inputting esophageal cancer patients. With the help of Graphics User Interface (GUI), the study was able to predict the clinical outcomes of six possible esophageal cancer based on the fuzzy rules presented in Table 4.1 in chapter four.

The dataset used was retrieved from a local hospital in Erbil, Iraq. The dataset (input) take in to consideration several risk factors, including symptoms, and diagnostic tests. The dataset were inputted in to the FIS system, the system provides an output, which is the predictive diagnosis, which is compared to the real result provided by the hospital. Figure 5.1 shows the first main page of the developed FIS system; the left side of the page is where data are inputted, while the right side of the page provides the output (esophageal cancer predictive diagnosis).

As depicted on the UI of the proposed system in Figure 5.1 below, the user can inputs patients' data accordingly to various dialogs in the left side of the main page. When the user clicks on the result button to simulate the input variables to provide a predictive diagnosis (output) in the right side of the main page. The system operates a comparative of patients' risk factors, symptoms, and diagnostic tests. The system provides a diagnosis by utilizing the IF and THEN fuzzy rules (including the range) of each variable that was established through expert guidance.

Figure 5.1

Input and output dialog boxes shown in the Main page of the FIS system



5.1 Predictive Results of Esophageal Cancer by FIS

The predictive diagnosis of esophageal cancer by FIS is presented on the output dialog box either as positive for cancer, with ability to differentiate between AC and SCC esophageal cancer subtypes. For a Positive (P) prediction, the system detects the presence of esophageal cancer cells from a combination of all patient's input variables, and recommends a staging test to determine the stage of the test. The system also provides a Negative (N) prediction of esophageal cancer if comparative simulation of input variable of a patient is outputted as so.

Lastly, the system can also provide an output of Suspicious (S), when the system is indecisive between negative or positive prediction. This means the system's result is ambiguous, and which recommends a repeat of previous clinical screening/tests, or a more advance medical examination to come to reach a more precise diagnosis. Concisely, a Suspicious (S) output indicate that the patient may not have cancer, but a noncancerous tumor or any other esophageal condition (such as GERD and Barrett), that may require further screening. The intelligent predictive result/diagnosis of esophageal cancer for six patients' data implemented in this study is are provided and discussed in the following sections accordingly.

5.1.1 Predictive Diagnosis for Patient 1 Data

The result of Patient 1 is provided in Figure 5.2 which is according to the data retrieved from Erbil hospital, will follow the fuzzy IF and THEN rules. The Patient 1 is a male gender, aged 50 years old falling in the interval [≥ 50]; a high risk age group according to experts which is incorporated in the fuzzy rules. Men are at a 75% higher risk of esophageal cancer compared to females. The patient is obese (high risk of AC), has indigestion issues (medium risk), Barrett (30 to 40 times risk of AC), and GERD (5 times risk of AC).

Furthermore, Patient 1 is in the Asian (AS) region, which has risk of SCC esophageal subtype. Data from the hospital shows that Patient 1 has odynophagia from VFSS test (YES), ECM indicated cancer (cancer), imaging was performed through EGD and staging was recommended by the procedure of EUS. For Patient1, the FIS system predicted the diagnosis to be POSITIVE for esophageal cancer with the AC subtype. The system recommends patient to go for procedure to check Gleason score and stage of the cancer development. Predictive Diagnosis for Patient 2 Data

- **Fuzzy structure for Screening of Esophageal cancer (Risk factors) for Patient 1**

IF age (INDICATE) older than 50 years, high risk

IF gender (INDICATE) man, 3 to 4 times high risk (75%)

IF region (INDICATE) Asia, Africa, Central America, and South America, high risk of SCC

IF general lifestyle (INDICATE) Obese, high risk of AC

IF VFSS (INDICATE) odynophagia sensation, possible esophageal problem, further screening

IF symptoms (INDICATE) GERD, 5 times risk of AC

IF symptoms (INDICATE) Barrett, 30 to 40 times risk of AC

IF ECM (INDICATE) cancer, tumor endoscopy, biopsy and further test

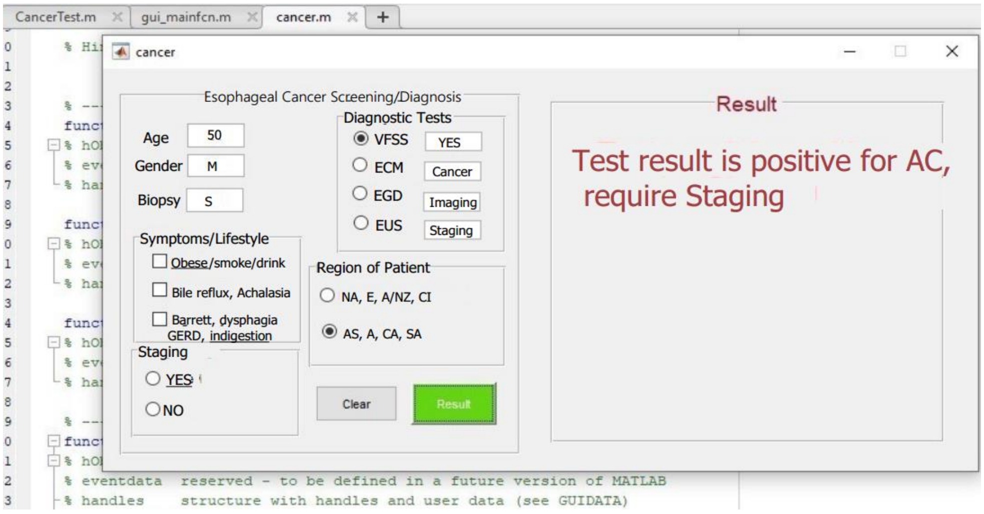
IF biopsy (INDICATE) cancer cells, then patient is positive for esophageal cancer

IF EGD (INDICATE) primary tumor, imaging, staging and Gleason score

This prediction is summarized as: IF age (INDICATE) 50, gender (INDICATE) male, biopsy (INDICATE) S, VFSS (INDICATE) YES, and region of patient (INDICATE) AS/A/CA/SA, THEN test result = positive for AC. As shown in figure 5.2

Figure 5.2

Predictive diagnostic result of patient 1 showing positive cancer (AC)



5.1.2 Predictive Diagnosis for Patient 2 Data

The result of Patient 2 is provided in Figure 5.3 which is according to the data retrieved from Erbil hospital, will follow the fuzzy IF and THEN rules. The Patient 2 is a male gender, aged 76 years old falling in the interval [≥ 50]; a high risk age group according to experts which is incorporated in the fuzzy rules. Men are at a 75% higher risk of esophageal cancer compared to females. The patient smokes (2 times risk for AC and 6 times risk for SCC), has indigestion issues (medium risk), and Bile reflux (high risk).

Furthermore, Patient 2 is in the Asian (AS) region, which has risk of SCC esophageal subtype. Data from the hospital shows that Patient2 has oropharyngeal dysphagia from VFSS test (Tumor), ECM indicated cancer (cancer), imaging was performed through EGD and staging was recommended by the procedure of EUS. For Patient 2, the FIS system predicted the diagnosis to be POSITIVE for esophageal cancer with the AC subtype. The system recommends patient to go for procedure to check Gleason score and stage of the cancer development.

- **Fuzzy structure for Screening of Esophageal cancer (Risk factors) for Patient 2**

IF age (INDICATE) older than 50 years, high risk

IF gender (INDICATE) man, 3 to 4 times high risk (75%)

IF region (INDICATE) Asia, Africa, Central America, and South America, high risk of SCC

IF general lifestyle (INDICATE) Smoking, 2 times risk for AC and 6 times risk for SCC

IF VFSS (INDICATE) oropharyngeal dysphagia, tumor endoscopy and further screening needed

IF symptoms (INDICATE) GERD, 5 times risk of AC

IF ECM (INDICATE) cancer, tumor endoscopy, biopsy and further test

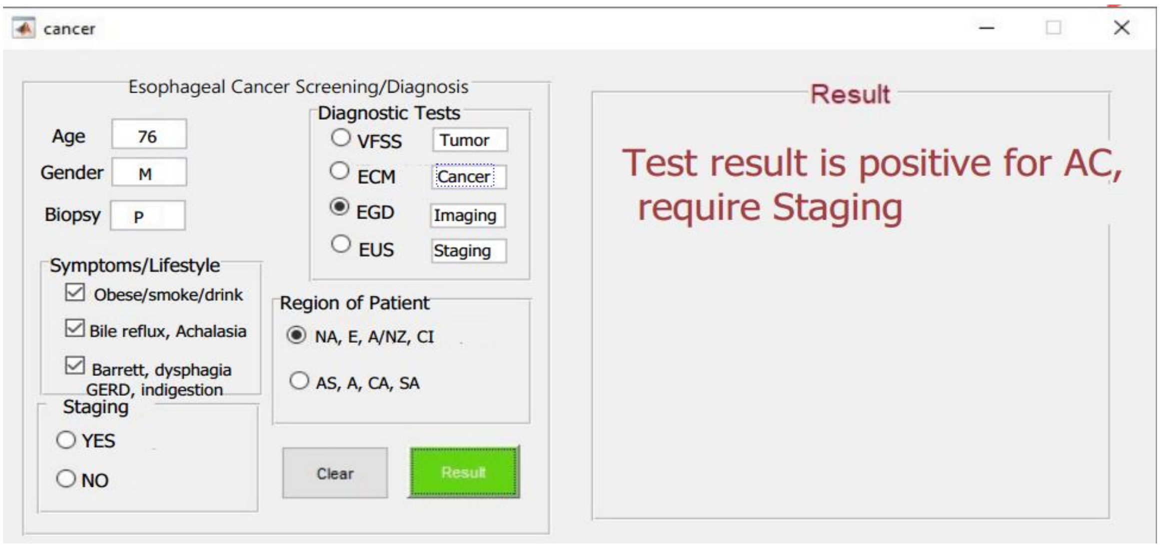
IF biopsy (INDICATE) cancer cells, then patient is positive for esophageal cancer

IF EGD (INDICATE) primary tumor, imaging, staging and Gleason score

This diagnosis is summarized as: IF age (INDICATE) 76, gender (INDICATE) male, biopsy (INDICATE) P, EGD (INDICATE) imaging, and region of patient (INDICATE) NA, E, A/NZ, CI, THEN test result = positive for AC. As shown in figure 5.3

Figure 5.3

Predictive diagnostic result of patient 2 showing positive cancer (AC)



5.1.3 Predictive Diagnosis for Patient 3 Data

The result of Patient 3 is provided in Figure 5.4 which is according to the data retrieved from Erbil hospital, will follow the fuzzy IF and THEN rules. The Patient 3 is a male gender, aged 47 years old falling in the interval [≥31≤49]; a medium risk age group according to experts which is incorporated in the fuzzy rules. Men are at a 75% higher risk of esophageal cancer compared to females. The patient smokes (2 times risk for AC and 6 times risk for SCC), has indigestion issues (medium risk), and GERD (5 times risk of AC).

Furthermore, Patient 3 is in the Asian (AS) region, which has risk of SCC esophageal subtype. Data from the hospital shows that Patient 3 has no issues from VFSS test (NO), ECM indicated tumor (Tumor), imaging was performed through EGD where cancer was found, and staging was recommended by the procedure of EUS. For Patient 3, the FIS system predicted the diagnosis to be POSITIVE for esophageal cancer with the SCC subtype. The system recommends patient to go for procedure to check Gleason score and stage of the cancer development.

- **Fuzzy structure for Screening of Esophageal cancer (Risk factors) for Patient 3**

IF age (INDICATE) between 31 to than 49 years, medium risk

IF gender (INDICATE) man, 3 to 4 times high risk (75%)

IF region (INDICATE) Asia, Africa, Central America, and South America, high risk of SCC

IF general lifestyle (INDICATE) Smoking, 2 times risk for AC and 6 times risk for SCC

IF VFSS (INDICATE) no, then patient is positive

IF symptoms (INDICATE) GERD, 5 times risk of AC

IF ECM (INDICATE) cancer, tumor endoscopy, biopsy and further test

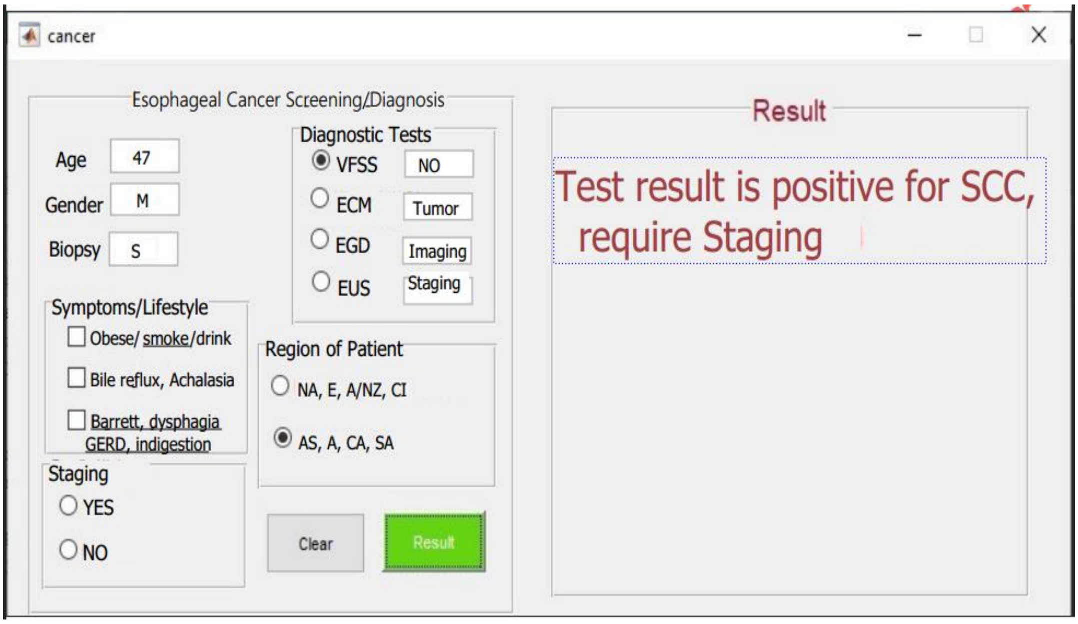
IF biopsy (INDICATE) cancer cells, then patient is positive for esophageal cancer

IF EGD (INDICATE) primary tumor, imaging, staging and Gleason score

This diagnosis is summarized as: IF age (INDICATE) 47, gender (INDICATE) male, biopsy (INDICATE) S, VFSS (INDICATE) no, and region of patient (INDICATE) AS, A, CA, SA, THEN test result = positive for SCC. As shown in figure 5.4

Figure 5.4

Predictive diagnostic result of patient 3 showing positive cancer (SCC)



5.1.4 Predictive Diagnosis for Patient 4 Data

The result of Patient 4 is provided in Figure 5.5 which is according to the data retrieved from Erbil hospital, will follow the fuzzy IF and THEN rules. The Patient 4 is a female gender, aged 33 years old falling in the interval [≥31≤49]; a medium risk age group according to experts which is incorporated in the fuzzy rules. Females have a lower risk of esophageal cancer at only 25% risk compared to males. The patient has Bile reflux (high risk) and Barrett (30 to 40 times risk of AC).

Furthermore, Patient 4 is in the Asian (AS) region, which has risk of SCC esophageal subtype. Data from the hospital shows that Patient 4 has no issues from VFSS test (NO), ECM did not indicate any tumor or cancer (NO), there was no need for EGD (NO) and EUS (NO). For Patient 4, the FIS system predicted the diagnosis to be NEGATIVE for esophageal cancer.

- **Fuzzy structure for Screening of Esophageal cancer (Risk factors) for Patient 4**

IF age (INDICATE) between 31 to than 49 years, medium risk

IF gender (INDICATE) female, lower risk (25%)

IF region (INDICATE) Asia, Africa, Central America, and South America, high risk of SCC

IF general lifestyle (INDICATE) bile reflux, high risk of esophageal cancer

IF VFSS (INDICATE) no test

IF symptoms (INDICATE) Barrett, 30 to 40 times risk of AC

IF ECM (INDICATE) no, then patient is negative

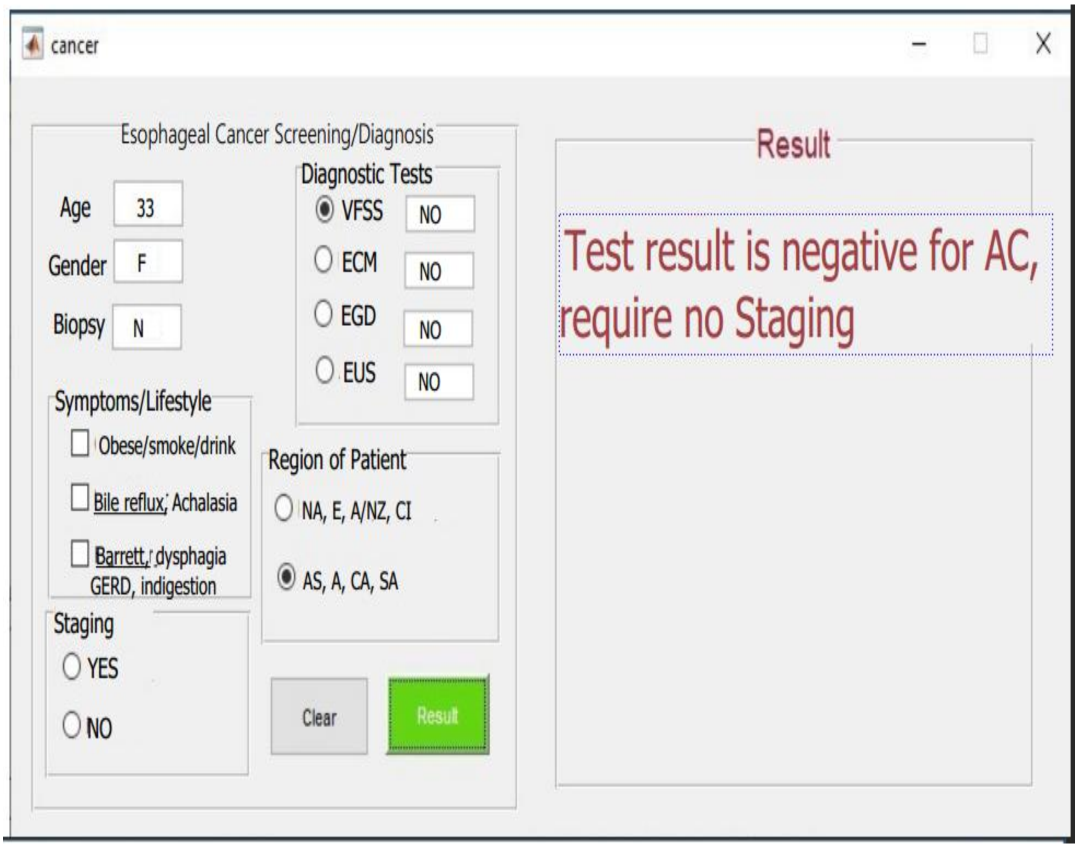
IF biopsy (INDICATE) no, then patient is negative

IF EGD (INDICATE) no, then patient is negative

This diagnosis is summarized as: IF age (INDICATE) 33, gender (INDICATE) female, biopsy (INDICATE) N, VFSS (INDICATE) no, and region of patient (INDICATE) AS, A, CA, SA, THEN test result = negative for AC. As shown in figure 5.5

Figure 5.5

Predictive diagnostic result of patient 4 showing negative cancer



5.1.5 Predictive Diagnosis for Patient 5 Data

The result of Patient 5 is provided in Figure 5.6 which is according to the data retrieved from Erbil hospital, will follow the fuzzy IF and THEN rules. The Patient 5 is a male gender, aged 61 years old falling in the interval [≥50]; a high risk age group according to experts which is incorporated in the fuzzy rules. Men are at a 75% higher risk of esophageal cancer compared to females. The patient is obese (high risk of AC), Bile reflux (high risk), and GERD (5 times risk of AC).

Furthermore, Patient 5 is in the Asian (AS) region, which has risk of SCC esophageal subtype. Data from the hospital shows that Patient 5 has no issues from VFSS test (NO), ECM indicated tumor (Tumor), imaging was performed through EGD where cancer was not found, hence EUS was not recommended. For Patient 5, the FIS system predicted the diagnosis to be SUSPICIOUS, indicating that Patient 5 may not have cancer, but a noncancerous tumor or any other esophageal condition. The system recommends patient to go for further screening.

- **Fuzzy structure for Screening of Esophageal cancer (Risk factors) for Patient 5**

IF age (INDICATE) older than 50 years, high risk

IF gender (INDICATE) man, 3 to 4 times high risk (75%)

IF region (INDICATE) Asia, Africa, Central America, and South America, high risk of SCC

IF general lifestyle (INDICATE) bile reflux, high risk of esophageal cancer

IF general lifestyle (INDICATE) Obese, high risk of AC

IF VFSS (INDICATE) no, then further test required

IF symptoms (INDICATE) GERD, 5 times risk of AC

IF ECM (INDICATE) cancer, tumor endoscopy, biopsy and further test

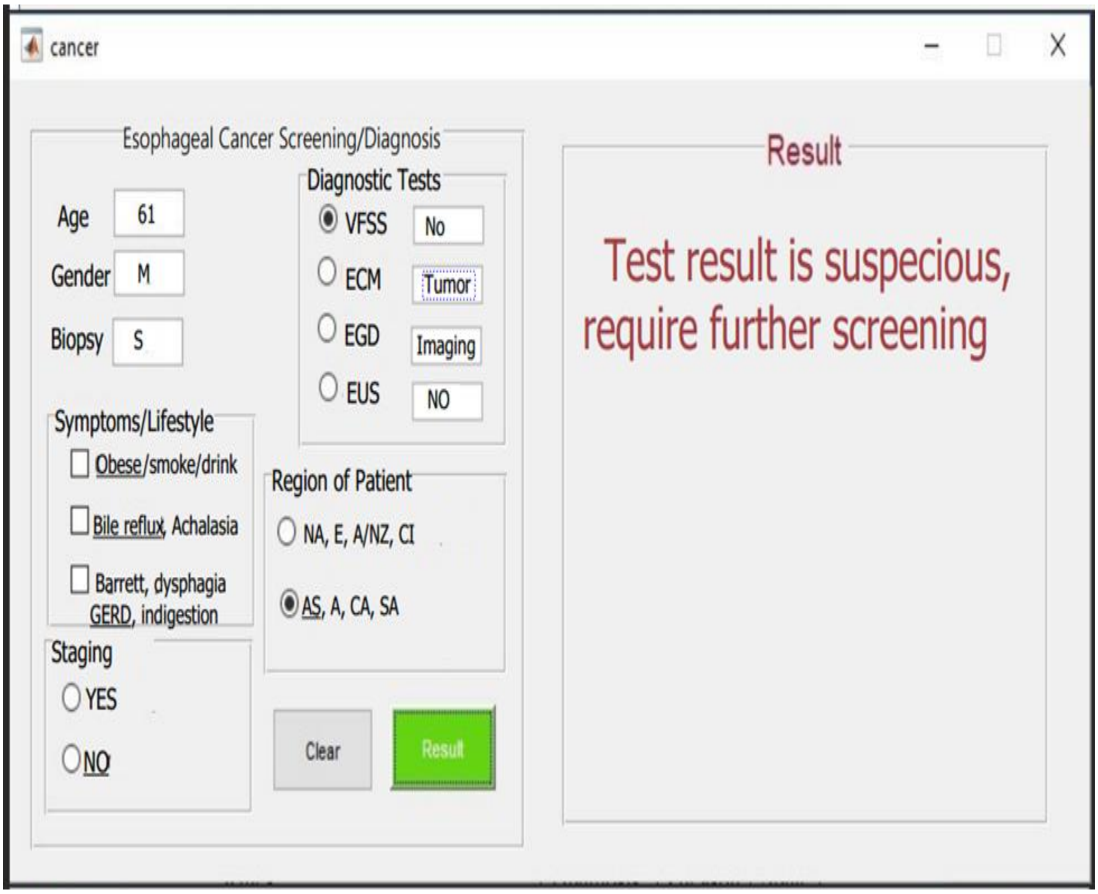
IF biopsy (INDICATE) cancer cells, then patient is positive for esophageal cancer

IF EGD (INDICATE) primary tumor, imaging, staging and Gleason score

IF age (INDICATE) 61, gender (INDICATE) male, biopsy (INDICATE) S, VFSS (INDICATE) no, and region of patient (INDICATE) AS, A, CA, SA, THEN test result = suspecious, requires further screening. As shown in figure 5.6

Figure 5.6

Predictive diagnostic result of patient 5 showing suspicious output



5.1.6 Predictive Diagnosis for Patient 6 Data

The result of Patient 6 is provided in Figure 5.7 which is according to the data retrieved from Erbil hospital, will follow the fuzzy IF and THEN rules. The Patient 6 is a male gender, aged 53 years old falling in the interval [≥ 50]; a high risk age group according to experts which is incorporated in the fuzzy rules. Men are at a 75% higher risk of esophageal cancer compared to females. The patient smokes (2 times risk for AC and 6 times risk for SCC), Bile reflux (high risk), and Barrett (30 to 40 times risk of AC).

Furthermore, Patient 6 is in the Asian (AS) region, which has risk of SCC esophageal subtype. Data from the hospital shows that Patient 6 has odynophagia sensation from VFSS test (YES), ECM indicated cancer (cancer), imaging was performed through EGD and staging was recommended by the procedure of EUS.

For Patient 6, the FIS system predicted the diagnosis to be POSITIVE for esophageal cancer with the AC subtype. The system recommends patient to go for procedure to check Gleason score and stage of the cancer development.

A sum up of patient 1 to patient 6 results shows an overall system accuracy of 95.24% and individual patient accuracy as shown in table 5.1. The overall accuracy is the overall ability of the system to predict the diagnostic outcome of esophageal cancer according to the fuzzy rules and patent data retrieved from Erbil hospital, while the individual accuracy is the individual prediction of the system, to provide diagnosis of each patient that match the diagnosis provided by the Erbil hospital. The FIS system developed in this study have performed considerably well with an overall accuracy of 95.24% which in comparison with DU et al. (2021)'s accuracy of 90.63% and Fang et al. (2022)'s 84.724%, is an improvement.

- **Fuzzy structure for Screening of Esophageal cancer (Risk factors) for Patient 6**

IF age (INDICATE) older than 50 years, high risk

IF gender (INDICATE) man, 3 to 4 times high risk (75%)

IF region (INDICATE) Asia, Africa, Central America, and South America, high risk of SCC

IF general lifestyle (INDICATE) Smoking, 2 times risk for AC and 6 times risk for SCC

IF VFSS (INDICATE) odynophagia sensation, possible esophageal problem, further screening

IF symptoms (INDICATE) GERD, 5 times risk of AC

IF ECM (INDICATE) cancer, tumor endoscopy, biopsy and further test

IF biopsy (INDICATE) cancer cells, then patient is positive for esophageal cancer

IF EGD (INDICATE) primary tumor, imaging, staging and Gleason score

IF symptoms (INDICATE) Barrett, 30 to 40 times risk of AC

IF general lifestyle (INDICATE) bile reflux, high risk of esophageal cancer

This diagnosis as summarized as: IF age (INDICATE) 53, gender (INDICATE) male, biopsy (INDICATE) P, VFSS (INDICATE) yes, and region of patient (INDICATE) AS, A, CA, SA, THEN test result = positive for AC. As shown in figure 5.7

Figure 5.7

Predictive diagnostic result of patient 6 showing positive cancer (AC)

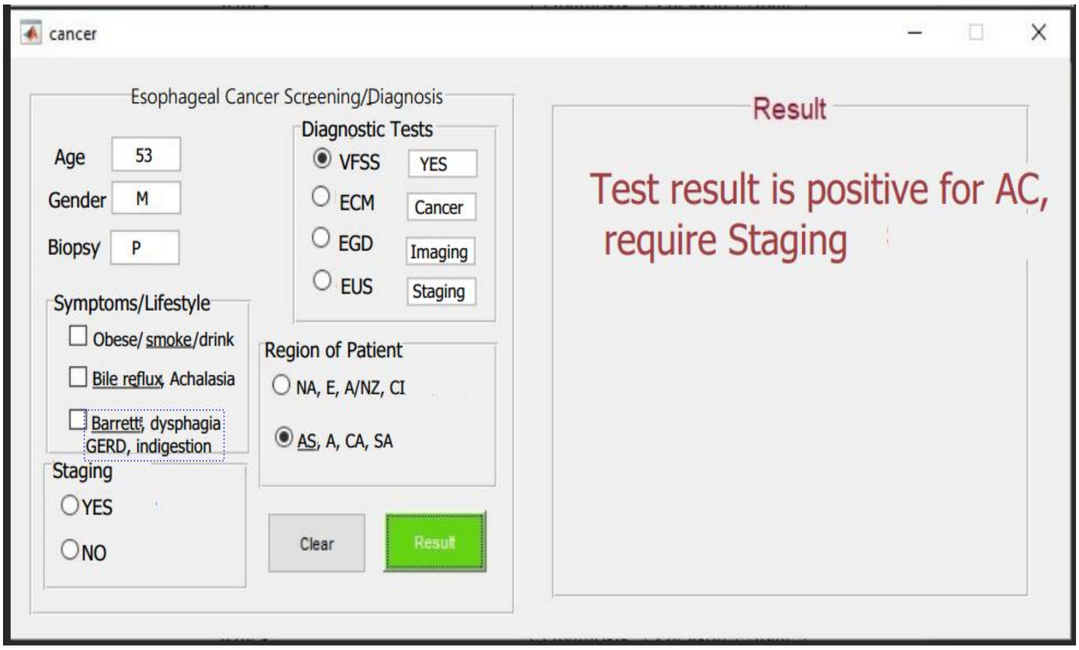


Table 5.1

Summary of all patient predictive diagnostic results for esophageal cancer.

Patients	**Diagnosis (output)**	**Recommendation**	**Accuracy**
Patient 1	Positive AC	Staging	93.91
Patient 2	Positive AC	Staging	94.24
Patient 3	Positive SCC	Staging	94.01
Patient 4	Negative	No need for staging	98.2
Patient 5	Suspicious	Further screening	92.53
Patient 6	Positive AC	Staging	98.52

CHAPTER VI

Conclusion and Recommendation

The study have successfully collected data, developed an AI system and fuzzy IF THEN rule, and implemented the system for predictive diagnosis of esophageal cancer. Among the tools used for the actualization of the objectives of this study, include MATLAB (Matrix laboratory) software, which contains the Graphics users Interface (GUI) function tool. Data was collected for a total of 7 patients from a hospital in Erbil. After the fuzzy logic rules were established and implemented in the AI system, the dataset were inputted to run the system. It is of vital importance to note that the predictive result was according to the established fuzzy IF THEN rules which was attained through expert consideration. Our result obtained a high accuracy of up to 98% for each patient's predictive diagnosis, and an overall accuracy of 95.24% for all patients'. This give our study a competitive advantage compared to studies of DU et al. (2021)'s accuracy of 90.63% and Fang et al. (2022)'s 84.724%. Above all, this study reveals the capabilities of fuzzy logic in assistive diagnosis of not only cancer, but of other ailment that have uncertain data. The result of the developed system was successful due to the system linking of all vital input variables (symptoms, risk factors, and diagnostic tests) to reach a predictive diagnosis of esophageal cancer.

For future studies, it is highly recommended that the fuzzy logic rule should be expanded to include more variables and scenarios, so that esophageal cancer can be detected early on time before it reaches advanced or late stage. In addition, it is important to point out the limitation in the dataset, which is only a collection of 7 patients' data. From this 7 patients, only 6 patients' data was complete. Hence only 6 patients' data were used in this study, which is very limited. Therefore, future studies should collect as much data as possible from different geographical location, ages, ethnicity, and genders.

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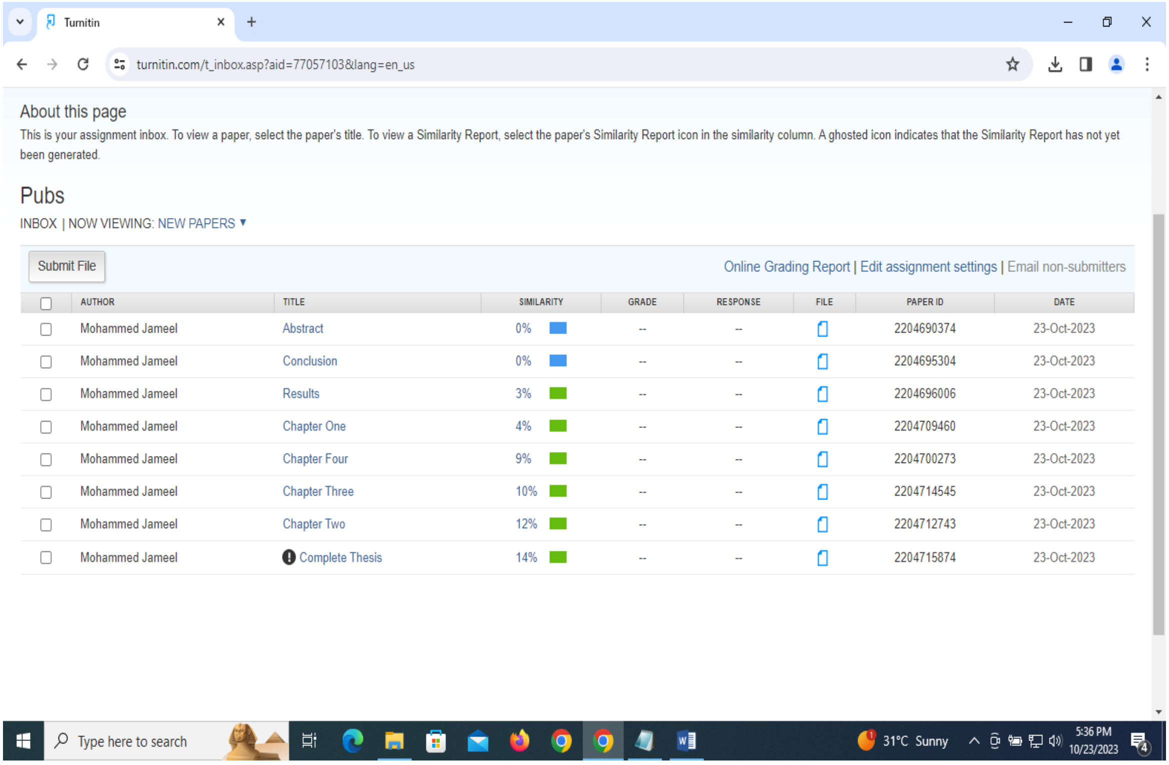
APPENDICES

Appendix A
Summary of the Multi-input Single-output IF THEN Fuzzy Rule of the Proposed System.

Patients	Multi-input Single-output IF THEN Fuzzy Rules
1	IF age (INDICATE) 50, gender (INDICATE) male, biopsy (INDICATE) S, VFSS (INDICATE) YES, and region of patient (INDICATE) AS/A/CA/SA, THEN test result = positive for AC. As shown in figure 5.2
2	IF age (INDICATE) 76, gender (INDICATE) male, biopsy (INDICATE) P, EGD (INDICATE) imaging, and region of patient (INDICATE) NA, E, A/NZ, CI, THEN test result = positive for AC. As shown in figure 5.3
3	IF age (INDICATE) 47, gender (INDICATE) male, biopsy (INDICATE) S, VFSS (INDICATE) no, and region of patient (INDICATE) AS, A, CA, SA, THEN test result = positive for SCC. As shown in figure 5.4
4	IF age (INDICATE) 33, gender (INDICATE) female, biopsy (INDICATE) N, VFSS (INDICATE) no, and region of patient (INDICATE) AS, A, CA, SA, THEN test result = negative for AC. As shown in figure 5.5
5	IF age (INDICATE) 61, gender (INDICATE) male, biopsy (INDICATE) S, VFSS (INDICATE) no, and region of patient (INDICATE) AS, A, CA, SA, THEN test result = suspecious, requires further screening. As shown in figure 5.6
6	IF age (INDICATE) 53, gender (INDICATE) male, biopsy (INDICATE) P, VFSS (INDICATE) yes, and region of patient (INDICATE) AS, A, CA, SA, THEN test result = positive for AC. As shown in figure 5.7

Appendix B

Turnitin Similarity Report



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