A COST EFFECTIVENESS ANALYSIS TO COMPARE MASTECTOMY VERSUS LUMPECTOMY USING A FUZZY APPROACH

AYSUN AKTAŞ

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A COST EFFECTIVENESS ANALYSIS TO COMPARE MASTECTOMY VERSUS LUMPECTOMY USING A FUZZY APPROACH

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Approval of the Graduate School of Natural and Applied Sciences

Prof. Dr. Cüneyt GÜZELİŞ
Director

I certify that this thesis satisfies all the requirements as a thesis for the master degree of Applied Statistics.

Prof. Dr. Ünal UFUKTEPE
Head of Department

We have read the dissertation entitled/A Cost Effectiveness Analysis to Compare Mastectomy Versus Lumpectomy Using a Fuzzy Approach" completed by AYSUN AKTAŞ under supervision of Assoc.Prof. Dr. G. Yazgı Tütüncü and we certify that in our opinion it is fully adequate, in scope and in quality, as a dissertation for the Master degree of Applied Statistics.

Assoc. Prof. Dr. G.Yazgı Tütüncü

Examining Committee Members

Date:

Assoc. Prof. Dr. G. Yazgı TÜTÜNCÜ
Dept. of Mathematics, IUE_

Assoc. Prof. Dr. Güvenç ARSLAN
Dept. of Mathematics, IUE_

Assoc. Prof. Dr. Selma GÜRLER
Dept. of Statistics, DEU_

Ass. Prof. Dr. M. Kaan SÖZMEN
Dept. of Public Health, IKCU_

ABSTRACT

A COST EFFECTIVENESS ANALYSIS TO COMPARE MASTECTOMY VERSUS LUMPECTOMY USING A FUZZY APPROACH

AYSUN AKTAŞ
Master Degree in Applied Statistics
Graduate School of Natural and Applied Sciences
Supervisor: Assoc. Prof. Dr. G. Yazgı Tütüncü
2015

Breast cancer is the most common cancer for women in many countries. Treatment choice for breast cancer depends on many factors. Under certain circumstances, people with early stage breast cancer have the opportunity to choose between total removal of a breast (Mastectomy) and breast-conserving surgery (Lumpectomy) followed by Radiation Therapy (RT). Overall survival chance with lumpectomy plus RT is same as with mastectomy but there are important differences in patient's quality of life (QOL) which affects all emotional, social, and physical aspects of the individual's life. One of the main goals of this study is to evaluate the Cost-Effectiveness Analysis (CEA) of Mastectomy and Lumpectomy operations in breast cancer patients taking into consideration adjuvant therapies in periods, monetary units and patient's satisfaction. A Decision Tree was constructed to project the clinical history of breast carcinoma following surgery. Then, health states used in the model were characterized by transition probabilities and utilities for QOL. In order to capture both costs uncertainty and variation of health benefits over time we recommend a fuzzy cost-effectiveness ratio that will be a powerful tool for decision making, and to handle and manipulate imprecise and noisy data. The necessary data is obtained from hospital records, TUIK databases and the literature.

Keywords: Cost effectiveness Analysis, Fuzzy Approach, Breast Cancer

ÖZ

MASTEKTOMİ VE LUMPEKTOMİ YÖNTEMLERİNİN MALİYET ETKİNLİK ANALİZİ İLE KARŞILAŞTIRILMASINDA BULANIK KÜME YAKLAŞIMININ KULLANILMASI

AYSUN AKTAŞ
Uygulamalı İstatistik Yüksek Lisans
Fen Bilimleri Enstitüsü
Tez Danışmanı: Doç. Dr. G. Yazgı Tütüncü
2015

Meme kanseri çoğu ülkede en yaygın olan kanser türüdür. Meme kanserinin tedavisi birçok faktöre bağlıdır. Erken evre meme kanseri hastaları belirli şartlar altında meme dokusunun çıkarılması (mastektomi) ya da meme koruyucu cerrahi (lumpektomi) yöntemlerinden birini seçebilir. Lumpektomi ve sonrasında uygulanan ışın tedavisi ile mastektominin sağ kalım oranları eşittir fakat hastaların duygusal, sosyal ve fiziksel hallerini etkileyen yaşam kaliteleri arasında önemli bir fark vardır. Bu çalışmanın amacı Mastektomi ve Lumpektomi operasyonlarını hastaların operasyon sonrası tedavilerini, tedavi maliyetlerini ve hastaların memnuniyetini dikkate alarak maliyet etkinlik analizi ile değerlendirmektir. Ameliyat sonrasında hastaların klinik geçmişini özetleyen bir karar ağacı oluşturulmuştur. Modeli tanımlarken geçiş olasılıkları ve yaşam kaliteleri kullanılmıştır. Maliyetlerin ve sağlık durumunun zamana bağlı değişkenliği sebebiyle düzensiz verileri değerlendirmek için güçlü bir karar aracı olan bulanık küme maliyet etkinlik oranı önerilmiştir. Gerekli veriler hastane kayıtlarından, TUIK veri tabanından ve yazılı kaynaklardan elde edilmiştir.

Anahtar kelimeler: Maliyet etkinlik analizi, Bulanık küme yaklaşımı, Meme kanseri

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CHAPTER 1

Introduction

1.1. Breast Cancer

Breast cancer is a malignant tumor that starts in the cells of the breast. A malignant tumor is a group of cancer cells that can grow into surrounding tissues or spread to distant areas of the body. The disease occurs almost entirely in women, but men can get it, too.

Today breast cancer is the most common type of cancer for women worldwide and its occurrence is gradually increasing. Every year more than 250,000 new cases of breast cancer are diagnosed in Europe, with a death rate of over 165,000 patients in Europe. Worldwide, more than 700,000 women die of breast cancer annually, and it is estimated that eight to nine percent of women will suffer from breast cancer in their lifetime. [1]

On the other hand, according to the Turkish Health Ministry resources, the number of breast cancer incidents has increased in the last decades. In 2011, the estimated number of breast cancer patients is over 50,000 which reflects a 22% increase from 2007. The numbers are expected to increase further in the coming years. It is estimated that 1 out of every 8 women develop breast cancer at one point in their lives, but mostly after the age of 50. Young age (<40 years old) and premenopausal breast cancer rates are 20% and 45%, respectively in Turkey. However, the actual number of breast cancer patients is unknown due to a lack of nationwide registry programs. [2]

1.1.1. Risk Factors for Breast Cancer

Breast cancer exact causes are not clearly known however the main factors that influence the risk for breast cancer include, age, sex, heredity (BRCA1 and BRCA2, other genes), prior cancers, hormones, obesity and lack of exercise. Women are much more likely develop breast cancer than men. Men can develop breast cancer, but this disease is about 100 times more common among women than men. Risk of breast cancer increases as women get older [3].

1.1.2. Treatment of Breast Cancer

Choice of treatment for early stage breast cancer depends on many factors, including size and stage of cancer, patient's age, and other health problems of patient, risks and advantages of treatments.

Different types of treatment are available for breast cancer patients. Some treatments are standard which are currently used, and some are being tested in clinical trials which a research study is meant to help improve current treatments. When clinical trials indicate better results than standard treatment, the clinical or new treatment may become the standard treatment. Depending on National Cancer Institute in USA there are six types of standard treatments are used to cure breast cancer patients [3] :

- Surgery
- Sentinel lymph node biopsy followed by surgery
- Radiation therapy
- Chemotherapy
- Hormone therapy
- Targeted therapy

The most common form of treatment for breast cancer is surgery. This involves removing the tumor and nearby margins. The main surgery operations to remove the cancer are mastectomy and lumpectomy. Mastectomy is a surgery method to remove the whole breast that has cancer. Moreover, some of the lymph nodes may be removed for biopsy at the same time as the breast surgery or after the breast surgery. A potential benefit of mastectomy is that radiation therapy may be avoided. Lumpectomy is another surgery to remove a tumour and a small amount of normal tissue around the

tumor. In general, after lumpectomy patients undergo Radiation therapy. The main benefit of lumpectomy plus radiation therapy is that the breast is preserved as much as possible.

After both types of surgery, there still may remain tumor cells. Thus, some patients may be undergo radiation therapy, chemotherapy, or hormone therapy after surgery to kill any cancer cells that are left. Radiation therapy (RT) is another type of cancer treatment that uses high-energy X-Rays or other types of radiation to remove cancer cells or keep them away from growing. The way the radiation therapy is given depends on the type and stage of the cancer being treated. Chemotherapy (CT) is a cancer treatment that uses drugs to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing. In some cases, before the surgery chemotherapy may be given to reduce the amount of tissue and remove the tumor. The way the chemotherapy is given depends on the type and stage of the cancer being treated like radiation therapy. Hormone therapy (HT) is a cancer treatment that removes hormones or blocks their action and stops cancer cells from growing. Hormone therapy with tamoxifen is often given to patients with early stages of breast cancer and those with metastatic breast cancer that has spread to other parts of the body.

Briefly, mastectomy is the surgical removal of an entire breast, which contains cancer; on the other hand, lumpectomy, which is also called breast-conserving surgery, is the surgical removal of the tumor only [4]. One treatment is not better than the other for improving your chances of surviving cancer. The two treatments do differ, however mastectomy results in loss of your breast, and usually no radiation therapy is required. Lumpectomy, on the other hand, involves removal of some part of the breast that contains cancer cells, and in addition, radiation therapy is offered [5].

Since the chance of survival is nearly the same for both surgical treatment options, women's choice among these treatment options often focuses on quality of life issues. Thus, considerable amount of research has focused on the quality of life in breast cancer patients after surgery in order to make a better informed decision on treatment options.

In this study, we considered patients for whom both treatment options can be applicable. To determine the cost-effectiveness of mastectomy versus lumpectomy in Turkish healthcare system, we performed an economic evaluation study using data gathered in a clinical setting at Ege University Hospital Department of General Surgery in Izmir, TURKEY.

1.1.3. Staging of Breast Cancer

Breast cancer staging is very important because choice of treatment for breast cancer depends on the stage that the disease is diagnosed. The American Joint Committee on Cancer (AJCC) staging system provides a strategy for grouping patients with respect to prognosis. Decisions are formulated in part according to staging categories but primarily according to tumor size (T), regional lymph nodes affected (N), distant metastasises (M) and the stages defined by those variables are called TNM stages as shown in Table 1.1 [6].

Tis	Carcinoma in situ
T1	Tumour ≤ 20 mm in greatest dimension
T2	Tumour > 20 mm but ≤ 50 mm in greatest dimension
T3	Tumour > 50 mm in greatest dimension
N0	No regional lymph node metastasis identified histologically
N1	Micro-metastasises; or metastasises in 1–3 axillary lymph nodes
M0	No clinical or radiographic evidence of distant metastasises

Table 1.1: Early stage breast cancer TNM classification parameters

Stage	Tumour size	Node	Metastasis
Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IB	T0	N1	M0
	T1	N1	M0
Stage IIA	T0	N1	M0
	T1	N1	M0
	T2	N0	M0
Stage IIB	T2	N1	M0
	T3	N0	M0
Stage IIIA	T0	N2	M0
	T1	N2	M0
	T2	N2	M0
	T3	N1	M0
	T3	N2	M0
Stage IIIB	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
Stage IIIC	Any T	N3	M0
Stage IV	Any T	Any N	M1

Table 1.2: Anatomic Stage/Prognostic Group

In this study, selected patients are all in early stage of breast cancer (Stage 0, Stage IA, Stage IB, Stage IIA according to anatomic stage) in Table 1.2. The reason is that in the early stages of breast cancer, physicians can give the opportunity to their patients to decide the type of surgery, such as mastectomy and lumpectomy. Moreover it is known that, once the disease is diagnosed in early stages survival rates of the patients and economical resources spent on the treatment and rehabilitation processes will be lower in early stage. Moreover lack of economic activity because of labor force lost and life quality lost due to breast cancer will be lower in earlier diagnosed cases as well [7].

1.2. Aim of the Study

Under certain circumstances, mentioned in section 1.1.3 people with breast cancer have the opportunity to choose between total removal of a breast (Mastectomy) and breast-conserving surgery (Lumpectomy) followed by Radiation Therapy (RT). In early stage breast cancer, overall survival rate with lumpectomy plus RT is the same as with mastectomy. However, there are important differences in patient's quality of life (QOL) after those treatments, which affects all emotional, social, and physical aspects of an individual's life.

The treatment of breast cancer causes economic difficulty for patients and their relatives because of reduced income and costs of treatment types. Lumpectomy preserves the breast and there are only few additional costs when the radiation treatment is completed. However, breast reconstruction after a mastectomy may require several surgeries that add to the cost over time.

One of the main aims of this study is to evaluate the Cost-Effectiveness Analysis (CEA) of Mastectomy and Lumpectomy operations for breast cancer treatment taking into consideration adjuvant therapies in periods, monetary units and patient's satisfaction. A decision model was constructed to project the clinical history of breast carcinoma following a surgery. Then, health states used in this model were characterized by transition probabilities and utilities were used to define QOL.

The second aim of this study is to propose a Fuzzy-Cost Effectiveness Analysis that can be functional when health interventions and costs are measured in different time

units. In order to capture both uncertainties in costs and variation of health benefits over time we recommend a Fuzzy Incremental Cost-Effectiveness Ratio. To do so we focus on defining a reliable fuzzy membership function for the incremental cost-effectiveness ratio to verify problematic and that inference when used in CEA is inconsistent, irrelevant and optional. This measure will be functional when health effects are measured in time units.

In general, the aim of the study can be defined as helping clinicians inform their patients about surgical treatment options for the treatment of breast cancer and to evaluate the impact of the instrument on the clinical encounter. Moreover, as far as we are aware of this study will be the first one that compares mastectomy versus lumpectomy using data from a records in Turkish Hospital and analysis the factors that affect QOL of Turkish woman patients with breast cancer diagnosis.

We hypothesized that lumpectomy is the more cost effective treatment option than mastectomy according to ICER measure for Turkish breast cancer patients who have early stage diagnosis.

CHAPTER 2

Literature Review

In 1990's Cost Effectiveness studies have become popular in health decisions and studies increasingly continued in 2000's. Depending on the improvements in medical technologies, several main treatment options have been developed to extend survival of breast cancer patients. Study in literature is done by Nissen [8] denote that women with early stage breast cancer generally have three surgical options: lumpectomy, mastectomy, and mastectomy plus reconstruction. Since all these treatment methods improve survival, the quality of life and costs the following treatments have become subject of interest while deciding on the type of treatment. Considerable amount of research has investigated quality of life in early stage breast cancer patients and studied cost effectiveness of these options in several countries but not in Turkey.

A study done by Steinberg et. al. [9] examined the psychological outcome of lumpectomy versus mastectomy in the treatment of breast cancer in 1985. They compared the modified radical mastectomy patients versus lumpectomy and radiation for 46 patients in early stage of breast cancer. Lumpectomy patients have less of a loss of femininity and attractivity. Moreover they were more open about their sexual feelings after surgery. In contrast the mastectomy patients, lumpectomy patients saw their husbands' sexuality as increased after surgery. In overall adaptation lumpectomy patients showed better results than mastectomy patients. However, both group indicated similar results for depression and anxious.

In 1986, another study done by Munoz et. al. [10] compared the costs of breast cancer surgery types which are lumpectomy and mastectomy. Total of 79 patients in early stage breast cancer was selected during 1983 and 1984. They use the hospital and physician charges to compare the cost of this surgery options. Mean value of total charges for lumpectomy patients were 14176$ and for mastectomy patients 10345$ and standard deviations were 4262 and 3134 for lumpectomy and mastectomy

groups, respectively. While hospital inpatient cost for mastectomy group was 7328$ and for lumpectomy was 5741$ that was significantly less than mastectomy group. Unlike the mean total physician fees were significantly higher for lumpectomy group. The radiotherapist fees and the substantial radiation therapy hospital outpatient charge for lumpectomy group was 5015$ made the mean total charges for lumpectomy significantly higher than for mastectomy.

A study done in North America by Lasry et. al. [11] examined the depression and body image following mastectomy and lumpectomy in 1987. They used some functional and symptom scales which were depression, body image, fear of recurrence in order to compare this surgery types. Total mastectomy patients showed higher levels of depression and less satisfaction with body image moreover they have a fear of recurrence. The patients which undergoing radiation therapy showed increase in depressive symptoms.

In 1991, a study done by Verhoef et. al. [12] were applied clinical decision analysis to evaluate the impact of local recurrences after lumpectomy on the quality adjusted life expectancy of breast cancer patients. Mastectomy and lumpectomy groups was simulated by a Markov model of medical prognosis. Data obtained from published literature. The results show that lumpectomy provide better quality adjusted life expectancy than mastectomy. Moreover, they examined the subgroups of the lumpectomy groups which preferably undergo lumpectomy. This groups results show that the surgeons recommendations orient the patients preferences.

A study done by Pozo et. al.[13] in 1992, examined 48 women who received mastectomy and 15 who chose lumpectomy patients depending on mood disturbance, perceived quality of life, life satisfaction, marital satisfaction, perceptions of social support, and self-rated adjustment. Results show that lumpectomy patients had a higher-quality sex life at 6 and 12 months post-surgery than mastectomy patients. Choice of surgical procedure predicted higher levels of life satisfaction at 3 months. They concluded that, the lack of difference between surgical groups in areas other than sexual adjustment replicates previous findings, but extends them by (1) using a fully prospective design, (2) providing data on the period surrounding the surgery (as well as later periods), and (3) examining a broader range of indices of well-being than usual.

Another study proposed in Pennsylvania in 1996 by Young et. al.[14] in order to illustrate the usefulness of administrative claims data in describing trends. They used cancer registry data in order to investigate the treatment of local breast cancer between the years 1986 to 1990. They compare the mastectomy versus lumpectomy using clinical dissemination results. The results show that use of lumpectomy increased significantly from 35.2% to 42.4%, in 1990. Lumpectomy was the treatment choice for younger women, patients with private health insurance, absence of axillary node metastasises, and treatment in urban hospitals. On the other hand, only 45.3% of women with Medicaid coverage who had a lumpectomy with radiation therapy, compared with 77.5% of private insurance subscribers and 88.1% of Medicare beneficiaries in Pennsylvania. This finding is troubling even though there was substantially more compliance in the later years of the study, with 60.0% of eligible Medicaid beneficiaries receiving follow-up radiation therapy in 1990. There was an important variation in the use of radiation therapy depending on the insurance type of patients.

A study done by Norum et. al. [15] in 1997 performed cost utility and cost minimization analysis for comparison of lumpectomy and mastectomy in Norway. The cost of treatment for every single lumpectomy patients was 9564$ and for mastectomy patients was 5596$. Using the quality of life gain for lumpectomy was 0.03 and 5% discount rate, the cost gained per QALY calculated in lumpectomy compared with mastectomy. The value was 20508$. In cost-minimizing analysis results indicate that, lumpectomy had a cost of 10748$ and mastectomy followed by reconstructive surgery had a cost of 8538$. In economic terms for both analyses, lumpectomy was expensive than mastectomy.

Hayman et. al. [16] in 1998 analysed cost effectiveness of radiation therapy following conservative surgery for early-stage breast cancer. They used Markov model, a cost-utility analysis was performed to compare a strategy of radiation therapy versus no radiation therapy in following conservative surgery. Local recurrence, distant recurrence, and survival rates used in the model. Utilities for the no metastatic health states were obtained from actual patients. Using the data from a single institution they estimated direct medical costs, transportation and time costs. ICER over a ten years' time horizon were calculated by the model for each strategy. The ICER indicate that

28000$ per QALY gained for patients had a radiation therapy when compared with patients with no radiation therapy. The threshold they used for determining the cost effectiveness of radiation therapy was 50000$ per QALY gained, based on this assumption radiation therapy was cost-effective care compared with other accepted medical interventions.

In general, physicians recommend a treatment according to their past experiences and survival of patient not the quality of life after surgery. Women are more likely to undergo lumpectomy surgery if their physicians graduated from medical school after 1981 compared with the physicians graduated from medical school after 1961. According to a study done by Kotwall et. al. [17] examined the 157 hospital located in North Carolina. Using multiple logistic regression they calculated the yearly prevalence of lumpectomy in order to determine tumor, patient, and surgeon factors associated with lumpectomy. They conclude that woman younger than 50 years old and with small tumors operated by younger surgeons were more likely to undergo lumpectomy. The reason is that the surgeons trained after 1981 were trained to do lumpectomy surgery and are more knowledgeable about the research showing the safety of lumpectomy.

The study done by Whelan et. al. [18] in 1999, developed a Decision Board to improve communication decision making. The Decision Board was administered to 175 patients. The board give information to women early stage breast cancer about risk and benefits of mastectomy and lumpectomy. From different communities, seven surgeons administered the instrument to women with newly diagnosed clinical stage I or II breast cancer over an 18-month period. Patients and surgeons were interviewed regarding acceptability of the instrument. More patients who used the Decision Board were very satisfied with the information exchanged and the decision-making process. Almost all patients felt they were offered a clear choice. Surgeons also reported similar high satisfaction and comfort with administration of the instrument. The results reported that Decision Board is applicable to present information about patients in 91% consultant. The rate of lumpectomy decreased from 88% to %73 when Decision Board was introduced. The observed results were unexpected. However, the reason of decreasing the lumpectomy rate was some women wanted to avoid radiation therapy

and were less concerned about body image.(An example of this decision board is presented in Appendix 4)

Simmons et. al. [19] investigate the local and distant recurrence rates of 99 patients with central or retroareolar breast cancers treated with lumpectomy compared with mastectomy in 2001. The patients were compared with respect to recurrence including: tumor location, tumor size, axillary nodal status, and final surgical margins. The results of the study show that, there was no significant difference in local or distant failure rates of those patients treated with mastectomy versus lumpectomy. However, surgeons suggested that lumpectomy as a reasonable treatment option for selected patients with central or retroareolar breast cancers.

A study done by Barlow et. al. [20] compare the cost of mastectomy versus lumpectomy for early-stage breast cancer. A total of 1675 women early-stage breast cancer were identified in the period 1990 to 1997. The women were treated with mastectomy (N=183), mastectomy with adjuvant hormonal therapy or chemotherapy (N=417), lumpectomy with radiation therapy (n = 405), or lumpectomy with radiation therapy and adjuvant hormonal therapy or chemotherapy (n = 670). The costs of all interventions were computed for each woman, and monthly costs were computed by treatment, adjusting for age and cancer stage. The mean total medical care costs lumpectomy being more expensive than mastectomy 6 months after diagnosis. The adjusted mean costs were 12987$, 14309$, 14963$, and 15779$ for mastectomy alone, mastectomy with adjuvant therapy, lumpectomy plus radiation therapy, and lumpectomy plus radiation therapy with adjuvant therapy, respectively. Following years costs were influenced adjuvant therapy. By 5 years, lumpectomy was less expensive than mastectomy with 5 year adjusted mean costs of 41930$, 45670$, 35787$, and 39926$, respectively. Moreover, women with breast cancer under 65 years having higher treatment costs than older women.

A study done by Hershman et. al. [21] in 2002 conducted a CEA of tamoxifen for primary prevention in women at high risk for breast cancer. Markov modelling was used to show the effects of tamoxifen on quality adjusted survival, and preference ratings were elicited with time trade-off questionnaires. The positive effects may be greater if tamoxifen is started before age 50 years and if the breast cancer risk reduction submitted by tamoxifen lasts more than 5 years. The results indicate that for the woman

who has very high risk of invasive breast cancer, tamoxifen seems to be cost effective in order to prevent the cancer.

In 2002, a study done by Malin et. al. [22] use cost-effectiveness analysis to calculate the additional costs and benefits of various adjuvant therapy strategies, radiation after breast conserving surgery, and reconstruction compared to those of surgery alone in order to define the most cost-effective breast cancer benefits package for uninsured women. They define a minimum breast cancer benefits package that includes only the most cost effective lifesaving breast cancer treatments. They obtain data from 550 breast cancer patients' records. The total cost of treatment was calculated 10200000$. They presented two options. First option was to add an additional cost of 1700000$ to each patient for expanding their benefits that include post-mastectomy radiation and breast reconstruction. Second option was, to provide the Minimum Package to an additional 93 uninsured women. California legislators have two choices to decide whether to offer extensive benefits to a limited number of breast cancer patients or to provide only the most lifesaving treatments to more woman.

A study done by Polsky et. al. [23] in 2003, studied incremental cost effectiveness analysis of lumpectomy and radiation versus mastectomy by using 5 years primary data from early stage breast cancer patients. The outcome measures were quality-adjusted life-years and 5 year medical costs. The results indicate that lumpectomy and radiation therapy has significantly higher costs than mastectomy in the first year after surgery; the adjusted 5 year costs are 14054$ greater than those of mastectomy. The adjusted ICER comparing lumpectomy and radiation to mastectomy was 219594$ per QALY. If the possibility of patient choice from multiple treatments versus restricting choice to mastectomy alone provided 0.031 QALYs, then the CER of this choice option was 80440$ per QALY. The system of providing a choice between mastectomy and lumpectomy is economically attractive when the economic analysis includes the benefit of patient choice of treatment.

In 2005 a study done by Naeim et. al. [24] evaluated adjuvant treatment for early stage breast cancer with hormone therapy, chemotherapy or combination therapy to find out cost effectiveness in older patients. Decision-analysis modelling using life tables integrated the cost of treatment and impact in length and quality of life. The

incremental cost-effectiveness of different treatment strategies were then compared and mapped graphically. The result of study was that adjuvant therapy is cost-effective in 65 year old women with early breast cancer. The study was concluded that decision analytic models could help policy makers who are faced with decisions about adjuvant therapy in older breast cancer patients.

A study done by Hwang et. al. in 2013 [25] indicates lumpectomy patients live longer than mastectomy patients. They obtained data in the state of California from early stage breast cancer patients (N=112154) between 1990 and 2004. They compared mastectomy and lumpectomy groups considering the effect of age and hormone receptor status using Cox proportional hazards modeling to compare overall survival and disease-specific survival. They used age group (younger and older than 50 years old) and tumor hormone receptor status. The results show that for early stage breast cancer patients, lumpectomy and radiation was associated with improved disease-specific survival. Moreover, lumpectomy and radiation was an effective alternative to mastectomy for early stage disease inconsiderate of age or hormone receptor status. Brief summary of the literature review can be found in Table 2.1.

Author-Title	**Comparison parameter**	**Results**
Steinberg et. al. [9] Psychological Outcome of Lumpectomy versus Mastectomy in the Treatment of Breast Cancer. (1985)	Psychological functioning and adjustment.	Lumpectomy were less loss of feelings of attractiveness and femininity, were less self-conscious about their appearance and were more open about their surgery and sexual feelings after surgery.
Munoz et. al. [10] Lumpectomy vs Mastectomy the Costs of Breast Preservation for Cancer. (1986)	Cost parameter.	Total charges for lumpectomy significantly higher than mastectomy.

Lasry et. al. [11] Depression and Body Image following Mastectomy and Lumpectomy. (1987)	Depression and body image	Total mastectomy patients showed higher levels of depression and less satisfaction with body image.
Verhoef et. al. [12] Breast Conserving Treatment or Mastectomy in Early Breast Cancer: A Clinical Decision Analysis with Special Reference to the Risk of Local Recurrence. (1991)	Quality adjusted life expectancy	Lumpectomy provide better quality adjusted life expectancy than mastectomy.
Pozo et. al. [13] Effects of Mastectomy Versus Lumpectomy on Emotional Adjustment to Breast Cancer: A Prospective Study of The First Year Post Surgery.(1992)	Emotional adjustment	Lumpectomy patients reported a higher-quality sexual life than mastectomy patients.
Young et. al. [14] Dissemination of Clinical Results: Mastectomy Versus Lumpectomy and Radiation Therapy. (1996)	Dissemination rate	Lumpectomy operation increased significantly to 42.4% from 35.2%.
Norum et. al. [15] Lumpectomy or Mastectomy? Is Breast Conserving Surgery Too Expensive? (1997)	QALY and cost parameter.	Lumpectomy was expensive than mastectomy.

Hayman et. al. [16] Cost Effectiveness of Routine Radiation Therapy Following Conservative Surgery for Early Stage Breast Cancer. (1998)	ICER	Radiation therapy was cost-effective care compared with other accepted medical interventions.
Kotwall et. al. [17] Conservation Surgery for Breast Cancer at a Regional Medical Centre. (1998)	Tumor, patient, and surgeon factors.	The woman younger than 50 years old and with small tumors operated by younger surgeons were more likely to undergo lumpectomy.
Whelan et. al. [18] Mastectomy or Lumpectomy? Helping Women Make Informed Choices. (1999)	Develop a decision board to help clinicians inform about patients choice of surgery	The rate of lumpectomy decreased when the Decision Board was introduced.
Simmons et. al. [19] Recurrence Rates In Patients With Central or Retroareolar Breast Cancers Treated with Mastectomy or Lumpectomy. (2001)	Recurrence rate	Lumpectomy to be a reasonable treatment option for selected patients with central or retroareolar breast cancers.
Barlow et. al. [20] Cost Comparison of Mastectomy Versus Breast-Conserving Therapy for Early-Stage Breast. Cancer(2001)	Cost parameter.	Lumpectomy may have higher short-term costs but lower long-term costs than mastectomy.

Hershman et. al. [21] Outcomes of Tamoxifen Chemoprevention for Breast Cancer in Very High-Risk Women: A Cost Effectiveness Analysis (2002)	Quality adjusted survival rates	For high risk of invasive breast cancer patients, tamoxifen seems to be cost effective in order to prevent the cancer.
Malin et. al. [22] Using Cost Effectiveness Analysis to Define a Breast Cancer Benefits for the Uninsured.(2002)	ICER	They define the most cost-effective breast cancer package for uninsured women.
Polsky et. al. [23] Economic Evaluation of Breast Cancer Treatment: Considering the Value of Patient Choice.(2003)	ICER	The system of providing a choice between mastectomy and lumpectomy is economically attractive when the economic analysis includes the benefit of patient choice of treatment.
Naeim et. al. [24] Is adjuvant Therapy for Older Patients with Node (-) Early Breast Cancer Cost-Effective. (2005)	ICER	The result of study was adjuvant therapy is cost-effective in 65 year old women with early stage breast cancer.
Hwang et. al. [17] Survival After Lumpectomy and Mastectomy for Early Stage Invasive Breast Cancer: The Effect of Age and Hormone Receptor Status. (2013)	Overall survival and disease-specific survival rates.	The results indicates lumpectomy patients live longer than mastectomy patients.

Table 2.1: Summary table for Literature

CHAPTER 3

Model Description

3.1. Study Population

The sample we used in this study consists of 100 early stage breast cancer patients treated with mastectomy or lumpectomy at Ege University Hospital General Surgery Department in Izmir between January 2011 and December 2013. All socio-demographical features of the patients were not analyzed, only age interval was reported whereas median age of the patients was 54, for lumpectomy patients median age was 54 and for mastectomy patients it was 55. (Range: 31-77). All early stage breast cancer patients underwent surgery in 2011, 44 (44%) lumpectomy and 56 (56%) mastectomy patients followed adjuvant therapy afterwards.

3.2. Model

A decision tree can be used as a model for a sequential decision problem under uncertainty and describes graphically the decisions to be made, the events that may occur, and the outcomes associated with combinations of decisions and events. Probabilities are assigned to the events, and values are determined for each outcome. A major goal of the analysis is to determine the best decisions. Using decision analytic software (TreeAge Pro, 2009) we constructed the Decision Tree given in Figure 3.1 to estimate and compare the direct medical costs and health outcomes associated with the two breast cancer treatment choice. A decision tree consists of 4 types of nodes:

- Decision nodes - represented by squares
- Markov node - purple circle with “M”
- Chance nodes - represented by circles
- End nodes - represented by triangles

The decision node label to describe the basic alternatives of the decision problem is trying to address. Branches off the decision node represent two alternative treatment strategies; mastectomy and lumpectomy. Each strategy node described by its node label.

The Markov node is the start of a Markov Model. In our model Markov node described by surgery label and the model time horizon is given as total 1 cycle. Each direct branch from the Markov node defines two health states of a patient; live and die with health state valuations 1 and 0, respectively. Live health state followed by chance node and die health state followed end nodes. All structures at the right of each health state node is a transition subtree. Each transition subtree describes the events in a cycle, which can occur after a certain health state. Each end point within the transition subtree is a terminal node which sends flow back to a health state for the next cycle. Values (costs, effectiveness, etc.) can be accumulated at any state and at any event.

In the next step, chance nodes, or chance event nodes that identifies an event in a decision tree where a degree of uncertainty exists are defined. In the model chance nodes starts with RT, CT and metastatic cancer which were introduced in section 1.1.2 (treatment of breast cancer). First chance node represents two possible outcomes; continue treatment with radiation therapy (RT+) or without radiation therapy (RT-). Second chance node that follows the first one has also two possible outcomes; undergoing chemotherapy (CT+) or proceed without chemotherapy (CT-). In the third chance node three health state is possible for breast cancer patients; recovered, metastasises and died from other causes. The last chance node after metastasises represents two possible outcomes; live or died from cancer.

In order to terminate the model, end nodes identify following two health states; live and die. End nodes (terminal nodes) is the last location of the model. To sum up, all the nodes presented in Figure 3.1, are defined using TreeAge Pro Suite-2009 software and run for one decision cycle. In this study we will use this model in order to test our

main hypothesis that lumpectomy is the more cost effective treatment option than mastectomy according to ICER measure.

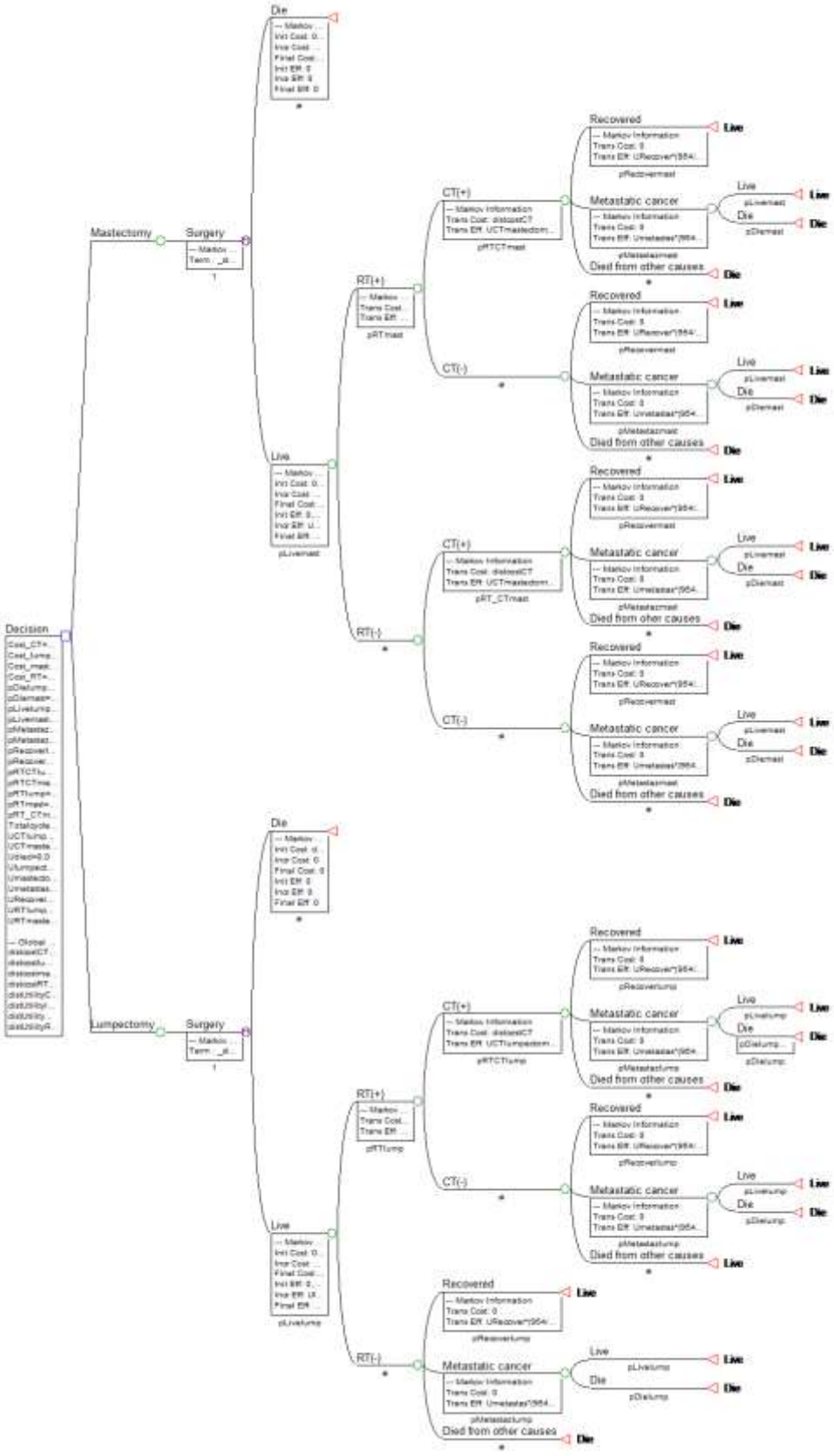

Figure 3.1: Decision Tree Model for Breast Cancer Patients

3.3. Transition Probabilities

There are a number of methods of probability assignment. Empirical clinical studies and statistical data obtained from literature are the most manageable sources for probability assignment. In this study, patient records from Ege University Hospital General Surgery Department have been used. All empirical probabilities related with the health states were calculated from those records and tabulated in Table 3.1.

	Mastectomy	Lumpectomy
Die	0,06	0,03
Live	0,94	0,97
Recover	0,893	0,98
Metastases	0,053	0,01
Radiation therapy	0,197	0,295
Chemotherapy	0,054	0,25
*CT without RT	0,054	0

Table 3.1: Transition Probabilities among the Health States

(*CT: Chemotherapy, RT: Radiation therapy)

These probabilities entered the model by Treeage-Pro software in order to calculate incremental cost effectiveness ratio. We calculated expected value for each course of action using transition probabilities. By calculating the value of each possible chain of events, and weighting uncertain results by the probability of each outcome, we identified the sequence of decisions that will maximize value, minimize costs, or balance multiple attributes.

3.4. Cost Parameters

In 2010 American Cancer Society`s global economic cost of cancer report results show that cancer causes the highest economic loss of all of the leading causes of death worldwide. The top three cancers that caused the most economic impact globally were lung cancer (188billion$), colon/rectum cancer (99billion$), and breast cancer (88billion$) in 2008 reports. The breast cancer is the third biggest economic loss of all of the other cancer types. Breast cancer patients and their relatives face an economic burden due to reduced income and costs related to patients care, as well as adjustments to disability [26]. In this study we examine the breast cancer patients' surgery types using CEA which interest cost of breast cancer and satisfaction of breast cancer patients.

In CEA, different perspectives require including or excluding different costs. In order to standardize CEA it is required that all of these analyses assume the same perspective. For this reason cost were based on the perspective of the health care provider, which included fixed and variable costs. Fixed costs and variable costs make up the two components of total cost. The total cost is calculated by summing up fixed and variable costs.

Fixed costs do not change as total cost varies. These costs were the same value for every patients who were undergone mastectomy or lumpectomy operation. In hospital records, fixed costs are classified into four categories which contain;

- Drugs such as painkiller,
- Other operations such as injection, daily monitoring,
- Medical operations such as medical dressing, establishing vascular access,
- Materials given to every patient such as surgical glove, mask, cautery.

All these costs were obtained from Ege University Hospital billing system for every individual patients in 2011 and prices were converted to 2014 prices level.

On the other hand, variable costs change according to the time period. Variable costs include the cost of pre-surgery and cost of post-surgery. Firstly, we classified pre-surgery costs which include pathology, ultrasound, bone scintigraphy, biochemistry, nuclear medicine, consultation, lymph nodes scintigraphy, intensive care unit,

magnetic resonance, biopsy, microbiology, other costs and hospitalization (There was no difference between average length of hospitalization for mastectomy and lumpectomy patients mean value was 10 days for both). Secondly, we classified post-surgery costs include adjuvant therapy costs and monitoring costs. Adjuvant therapies which is the treatment given after surgery include radiation therapy, chemotherapy, hormonal therapy. Monitoring variable costs include consultation, mammogram, pulmonary function test and ultrasound. Monitoring variable costs period for lumpectomy and mastectomy operation are given in Table 3.2. Summary of cost parameters that have been considered in the decision tree model is given in Table 3.3.

3.4.1. Calculation of Cost Values

All costs were obtained from the Ege University hospital bills. All patients had a surgery in 2011. The time horizon of study was 3 years, and data was gathered for this period. All costs were expressed in Turkish Liras and were converted to 2014 price level. We calculated total cost of lumpectomy group ($\boldsymbol{C_T^L}$) and total cost of mastectomy group ($\boldsymbol{C_T^M}$)using same formulas. All this formulas conducted in the model using Treeage-Pro software for lumpectomy and mastectomy patients. In our study, we summarized the calculation of cost values only lumpectomy patients. In Treeage-Pro software same formulas used for mastectomy patients. However, sample size and adjuvant therapy period numbers was different for lumpectomy and mastectomy groups.

For lumpectomy group, the total cost of the treatment was the summation of fixed costs and variable costs.

$$\boldsymbol{C_T^L = C_F^L + C_V^L},$$

where,

- $\boldsymbol{C_T^L}$:Total cost of lumpectomy treatment
- $\boldsymbol{C_F^L}$:Total fixed cost of the lumpectomy treatment
- $\boldsymbol{C_V^L}$:Total variable cost of the lumpectomy treatment

Firstly, we calculated total fixed costs of lumpectomy group ($\boldsymbol{C_F^L}$), this value was same for every single patient, this costs converted to the 2014 price level. Moreover, the number of compounding periods was the same for every patient (t=3). Fixed costs

include; drugs, other operations costs, medical costs and materials cost. We symbolized these four costs by $\boldsymbol{C_{fi}}$. For example, $\boldsymbol{C_{f1}}$ indicates the total cost of drugs or $\boldsymbol{C_{f2}}$ indicate the the total cost of other operations. The total fixed costs calculated by following formula,

$$\boldsymbol{C_F^L = n.\sum_{i=1}^{4} C_{fi}\,.\,(1+r)^t} \qquad (3.1)$$

where,

n :The number of lumpectomy patients

t :The number of compounding periods

r : Interest rate

$\boldsymbol{C_{fi}}$: i.th intervention cost

Secondly, we calculated variable costs of lumpectomy group ($\boldsymbol{C_V^L}$). This costs include the cost of pre-surgery ($\boldsymbol{C_P^L}$) and cost of post-surgery ($\boldsymbol{C_s^L}$).

$$\boldsymbol{C_V^L = C_P^L + C_s^L}$$

Pre-surgery costs ($\boldsymbol{C_P^L}$) was different number of intervention for every patients. However, the number of compounding periods was the same for every patient and equals 3. These costs include 12 treatment interventions which are pathology, ultrasound, bone scintigraphy, biochemistry, nuclear medicine, consultation, lymph nodes scintigraphy, intensive care unit, magnetic resonance, biopsy, microbiology, other costs and hospitalization. We symbolized these 12 pre surgery costs and number of pre surgery interventions by $\boldsymbol{C_{pi}}$ and $\boldsymbol{n_{pj}}$ respectively. For example, $\boldsymbol{C_{p1}}$ indicates the total cost of pathology or $\boldsymbol{C_{p2}}$ indicate the total cost of ultrasound etc. and $\boldsymbol{n_{p1}}$ show the number of intervention for 1st patient or $\boldsymbol{n_{p2}}$ shows the number of interventions for 2nd patient.The total pre-surgery costs are calculated by,

$$\boldsymbol{C_P^L = \sum_{j=1}^{n}\sum_{i=1}^{12} C_{pi}\,.\,n_{pj}.\,(1+r)^t} \qquad (3.2)$$

where,

n :The number of lumpectomy patients

t :The number of compounding periods

r :Interest rate

$\boldsymbol{C_{pi}}$:i[th] intervention cost

$\boldsymbol{n_{pj}}$:j[th] patient intervention number

Then we calculated post-surgery costs ($\boldsymbol{C_S^L}$). These costs had different number of intervention for every single patient and different number of compounding periods for mastectomy and lumpectomy groups. Post-surgery costs ($\boldsymbol{C_S^L}$) include adjuvant therapy costs ($\boldsymbol{C_A^L}$) and monitoring costs ($\boldsymbol{C_M^L}$). Adjuvant therapy costs include radiation therapy costs, chemotherapy costs and hormonal therapy costs. We symbolized these 3 adjuvant therapy costs and number of adjuvant therapy costs by $\boldsymbol{C_{ai}}$ and $n_{a_{ij}}^t$, respectively. For example, $\boldsymbol{C_{a1}}$ indicates the cost of radiation therapy or $\boldsymbol{C_{a2}}$ shows the cost of chemotherapy etc. The number of consultation operation provided to j[th] patient who had the surgery in 2011 can be denoted by n_{a1j}^2 where 1 denotes the index for the intervention and 2 denotes the period of surgery. This value will be equal to cost of consultation operation ($\boldsymbol{C_{a1}}$) times number of adjuvant therapy for j[th] patient who had surgery in 2011. The total adjuvant therapy costs calculated by,

$$\boldsymbol{C_A^L} = \sum_{t=1}^{4} \sum_{\boldsymbol{j=1}}^{\boldsymbol{n}} \sum_{\boldsymbol{i=1}}^{\boldsymbol{3}} \boldsymbol{C_{ai}} \,.\, n_{a_{ij}}^t .\, (\boldsymbol{1} + \boldsymbol{r})^{\boldsymbol{4-t}} \qquad (3.3)$$

where,

n :The number of lumpectomy patients

t :The number of compounding periods

r :Interest rate

$\boldsymbol{C_{ai}}$:i[th] intervention adjuvant cost

$n_{a_{ij}}^t$:i[th] intervention number for j[th] patient in t[th] period

Monitoring costs ($\boldsymbol{C_M^L}$) include 4 screening tests, which were consultation costs, mammogram costs, pulmonary function test costs and ultrasound costs. We denote these monitoring costs and number of monitoring costs by $\boldsymbol{C_{mi}}$ and $n_{m_{ij}}^t$, respectively. For example, $\boldsymbol{C_{m1}}$ indicate the cost of consultation or $\boldsymbol{C_{m2}}$ show the cost of

mammogram etc. The value of $n_{m_{ij}}^{t}$ can be calculated according to the treatment procedures summarized in Table 3.2. For example, the number of consultation operation provided to j[th] patient who had the surgery in 2011 (2011-2012 is the 1[st] period so, t=1) can be denoted by n_{m1j}^{2} where 1 denotes the index for the intervention and 2 denotes the period of surgery. This value will be equal to cost of consultation operation ($\boldsymbol{C_{m1}}$) times 4 for j[th] patient who had surgery in 2011.The total monitoring costs calculated by,

$$\boldsymbol{C_M^L} = \sum_{t=1}^{4} \sum_{\boldsymbol{j=1}}^{\boldsymbol{n}} \sum_{\boldsymbol{i=1}}^{\boldsymbol{4}} \boldsymbol{C_{mi}} \cdot n_{m_{ij}}^{t} \cdot (\boldsymbol{1} + \boldsymbol{r})^{\boldsymbol{4-t}} \qquad (3.4)$$

where,

n :The number of lumpectomy patients

t :The number of compounding periods

r :Interest rate

$\boldsymbol{C_{mi}}$:i[th] intervention adjuvant cost

$n_{m_{ij}}^{t}$:i[th] intervention number for j[th] patient in t[th] period

	Mastectomy		Lumpectomy	
	First 2 years	Between 2-5 years and more	First 2 years	Between 2-5 years and more
Consultation	4	2	4	1
Mammogram (MMG)	1	1	2	1
Pulmonary Function Test	2	1	2	1
Ultrasound (USG)	2	1	2	1

Table 3.2: Monitoring Variable Costs Period for Lumpectomy and Mastectomy Operation

<table>
<tr><td rowspan="5">TOTAL COSTS(C_T)</td><td rowspan="3">VARIABLE COSTS(C_V)</td><td rowspan="2">Post-Surgery (C_S)</td><td>Adjuvant Therapy (C_A)
Radiation Therapy
Chemotherapy
Hormonal Therapy</td></tr>
<tr><td>Monitoring(C_M)
Consultation
Mammogram (MMG)
Pulmonary Function Test
Ultrasound (USG)</td></tr>
<tr><td colspan="2">Pre-Surgery(C_P)
Pathology
Ultrasound
Bone Scintigraphy
Biochemistry
Nuclear Medicine
Consultation
Lymph Nodes Scintigraphy
Intensive Care Unit
Magnetic Resonance
Biopsy
Microbiology
Other costs
Hospitalization</td></tr>
<tr><td rowspan="3">FIXED COSTS(C_F)</td><td colspan="2">Drugs
Painkiller</td></tr>
<tr><td colspan="2">Other Operations
Injection
Daily Monitoring</td></tr>
<tr><td colspan="2">Medical Operations
Medical Dressing
Establishing Vascular Access</td></tr>
<tr><td colspan="2">Medical Materials
Surgical Glove
Mask
Cautery</td></tr>
</table>

Table 3.3: Summary of Total Costs

Using fixed and variable cost formulas we calculated total costs for lumpectomy and mastectomy patients. We analyzed all data using Statistical Package for the Social Sciences (SPSS 16.0) software. Descriptive statistics for cost values between the years 2011 to 2014 are presented in Table 3.4. The mean cost of treatment per patient in lumpectomy strategy were calculated as 4208,12 TL and 2727,14TL for mastectomy strategy in 2014 price level. This differences in cost was statistically significant based on independent sample t test (p=0,014).

	N	Mean	Std. Deviation	Minimum	Maximum
Cost of Lumpectomy	44	4208,12	2765,45	1179,01	12751,23
Cost of Mastectomy	56	2727,14	1710,75	370,04	6837,15

Table 3.4: Descriptive statistics of cost parameters

	Levene's Test		t-test for Equality of Means						
								95% CI of the Difference	
	F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Equal variances assumed	6,246	,014	3,288	98	,001	1480,976	450,384	587,202	2374,750
Equal variances not assumed			3,115	67,944	,003	1480,976	475,471	532,173	2429,779

Table 3.5: Independent sample t-test of cost values of surgery types

We calculated cost values for every individual patient. Group 1 indicate the lumpectomy group costs (N=44) and group 2 indicate the mastectomy group costs (N=56). Scores show that lumpectomy patients had 4208,12 mean cost and mastectomy patients had 2727,14 mean cost which was less than lumpectomy costs. We hypothesized that;

H_0: Mean cost value was the same for both mastectomy and lumpectomy groups

H_1: Mean cost value differs between mastectomy and lumpectomy groups.

Levene's test indicates that the variances are not equal (p=0,014<0,05) across the two groups, we will rely on the second row of output which is equal variances not assumed. We conclude that, (p=0,003<0,05) we rejectH_0, which means that there is a statistically significant difference between mean cost values of lumpectomy and mastectomy groups.

3.5. Utility Parameters

In this study, Quality-Adjusted Life Years (QALY) was used as an outcome measure. The quality of life adjustment is represented in the form of quality adjusted life years (QALYs). One QALY would represent 1 year spent in perfect health. For example, half a year lived in perfect health is equivalent to 0,5 QALYs the same as 1 year of life lived in a situation with utility 0,5 (0,5years × 1Utility = 1year × 0,5Utility = 0,5 QALYs).

Utility weights for each health state were obtained from Ege University Hospital at General Surgery Department in the period 2011 through to 2014. Patients gave their consent to participate in study and filled in QOL questionnaire. The study was approved by ethics committee of Ege University. No severe and serious comorbidities were reported during the study but there were cases of death in study period although they were early stage breast cancer patients.

All the information was collected between February 2011 and October 2014. Patients were approached for participation during their visit to the Ege University Hospital in Izmir for monitoring and some patient participated questionnaire on phone interview. The interview lasted approximately 30 to 40 minutes, and none of the patients declined participation. No patients were suffering from metastasises of the cancer to other organs, which could further affect their HRQoL negatively.

3.5.1. EuroQol 5D-5L (EQ-5D-5L)

EQ-5D-5L is a standardized measure of health status developed by the EuroQol Group in order to provide a simple, generic measure of health for clinical and economic appraisal. Test reliability and validity of the Turkish versions of EQ-5D-5L questionnaires for Turkish patients presented.[27]

EuroQol 5D-5L provides a simple descriptive profile and a single index value for health status that can be used in the clinical and economic evaluation of health care as well as in population health surveys. EQ-5D-5L is designed for self-completion by respondents and is ideally suited for use in postal surveys, in clinics, and in face-to-face interviews. The EQ-5D-5L consists of 3 pages, page 1 include the logo of EuroQol Group, page 2 include descriptive system and page 3 include EQ Visual Analogue Scale (EQ VAS).

The descriptive system comprises the 5 following dimensions;

- mobility,
- self-care,
- usual activities,
- pain/discomfort,
- anxiety/depression

Each dimension has 5 levels;

- no problems,
- slight problems,
- moderate problems,
- severe problems,
- extreme problems.

EQ VAS records that respondent's self-rated health on a 20 cm vertical, visual analogue scale with endpoints labelled 'the best health you can imagine' and 'the worst health you can imagine'. This information can be used as a quantitative measure of

health as judged by the individual respondents. Scoring procedure and EQ-5D-5L questionnaire is presented in Appendix 1.

3.5.2. EORTC QLQ-C30 Cancer Module

EORTC QLQ-C30 is a questionnaire developed to assess the quality of life of cancer patients by The European Organization for Research and Treatment of Cancer. Structure of the EORTC QLQ-C30 questionnaire have four point response format for individual items;

- not at all,
- a little,
- quite a bit,
- very much.

QLQ-C30 is composed of 30 items assessing global perceived health status and QoL. These items are grouped in five functional scales;

- physical functioning,
- role functioning,
- emotional functioning,
- cognitive functioning,
- social functioning;

three symptom scales;

- fatigue,
- nausea and vomiting,
- pain;

six health status scales;

- dyspnea,
- insomnia,
- appetite loss,
- constipation,
- diarrhea,

- financial difficulties.

All of the scales and single-item measures range in score from 0 to 100. A high scale score represents a higher response level. Therefore;

- a high score for a functional scale represents a high level of healthy functioning,
- a high score for the global health status QoL represents a high QoL,
- however, a high score for a symptom scale represents a lower level of healthy functioning.

The QLQ-C30 survey English and Turkish version presented in Appendix 2.

3.5.3. EORTC BR-23 Breast Cancer Module

The European Organization for Research and Treatment of Cancer (EORTC) developed a cancer-specific core questionnaire (QLQ-C30) which is common to all cancer sites, and also developed site-specific questionnaires for the measurement of QoL of patients with specific cancers. QLQ-BR23 is formed for breast cancer patients.QLQ-BR23 questionnaire has 23 items to assess functional scales;

- body image,
- sexual functioning,
- sexual enjoyment,
- future perspective;

symptom scales;

- systemic therapy,
- side effects,
- breast symptoms,
- arm symptoms
- upset by hair loss.

EORTC questionnaires were proved to have good reliability and validity and were gained widespread use in many countries. However, the original questionnaires are in English, and they should be translated and validated for other languages to be used for

non-English speaking countries. Many of the questionnaires have already been translated to common languages and validated as well [28].

Demirci et. al., [29] present a study to test reliability and validity of the Turkish versions of QLQ-C30 and QLQ-BR23 questionnaires for Turkish breast cancer patients. In this study, internal consistency was demonstrated by Cronbach's alpha which was 0,781 and 0,70 in all QLQ-C30 scales, for lumpectomy and mastectomy patient's scores, respectively. The QLQ-BR23 survey English and Turkish version presented in Appendix 3.

3.5.4. Calculation of Utility Scores

In order to calculate the utility scores of lumpectomy and mastectomy operations the HRQoL (Health-Related Quality of Life) was assessed the breast cancer patients using the standard questionnaire of European Organization for Research and Treatment of Cancer (EORTC QLQ-C30) and (EORTC BR-23) 2 years after the surgery. As the scores in EORTC QLQ-C30 are not utility-based, these scores were mapped to EuroQoL 5D (EQ-5D) using equations in Kontodimopoulos et al.[30]. Published literature was used for utility values of metastasis, recover, RT and CT. [41]. Then, utility scores were calculated in related time period to get QALY gained for each branch.

3.5.4.1. Scoring the EORTC QLQ-C30 and BR-23 version 3.0

The QoL scores were calculated according to the QLQ-C30 scoring manual and missing data were treated according to the published recommendations [31]. All scales are converted to a score ranging from 0 to100. The higher the scores of the overall QoL and functioning scales indicate the better overall QoL; however the higher scores of the symptom scales indicate the lower QoL. This scales summarized for QLQ-C30 questionnaire in Table 3.7and for BR-23 module in Table 3.8.
The formula for scoring these scales is the same in all cases:

1. Calculating raw score which estimate the average of the items that contribute to the scale. For all scales, Raw Score (RS) is the mean of the component items: if items $I_1, I_2, \ldots, I_n$ are included in a scale, RS can be calculated as follows:

$$\text{RawScore} = \text{RS} = \frac{I_1 + I_2 + \cdots + I_n}{n}$$

For example, role functioning have item numbers 6 and 7. Raw score is $\frac{Q_6 + Q_7}{2}$, Q_6 show the response of the patients for question 6 with range 3.

2. In order to standardize the raw score we need to apply a linear transformation, so that scores range from 0 to 100. A higher score represents a higher ("better") level of functioning, or a higher ("worse") level of symptoms.

We need to apply the linear transformation to 0-100 to obtain the score S,

Functional scales: $S = \left(1 - \frac{RS-1}{Range}\right).100$

Symptom scales / items: $S = \left(\frac{RS-1}{Range}\right).100$

Global health status / QoL: $S = \left(\frac{RS-1}{Range}\right).100$

Range is the difference between the maximum possible value of RS and the minimum possible value. The QLQ-C30 has been designed so that all items in any scale take the same range of values. Therefore, the range of RS equals the range of the item values. Most items are scored 1 to 4, giving range is equal 3, but the global health status/QoL, which are 7-point questions with range is equal 6.

	Scale	Number of items	Item range	Item numbers	Function scales
Global Health Status/QoL	QL	2	6	29,30	
Global Health Status/QoL					
Functional Scales					
Physical functioning	PF	5	3	1-5	F
Role functioning	RF	2	3	6,7	F
Emotional functioning	EF	4	3	21-24	F
Cognitive functioning	CF	2	3	20,25	F
Social functioning	SF	2	3	26,27	F
Symptom Scales/items					
Fatigue	FA	3	3	10,12,18	
Nausea and vomiting	NV	2	3	14,15	
Pain	PA	2	3	9,19	
Dyspnea	DY	1	3	8	
Insomnia	SL	1	3	11	
Appetite loss	AP	1	3	13	
Constipation	CO	1	3	16	
Diarrhea	DI	1	3	14	
Financial difficulties	FI	1	3	28	

Table 3.7: Scoring the QLQ-C30 version 3.0

	Scale	Number of items	Item range	Item numbers	Function scales
Functional Scales					
Body image	BRBI	4	3	9-12	F
Sexual functioning	BRSEF	2	3	14,15	
Sexual enjoyment	BRSEE	1	3	16	
Future perspective	BRFU	1	3	13	F
Symptom scales / items					
Systemic therapy side effects	BRST	7	3	1 – 4,6,7,8	
Breast symptoms	BRBS	4	3	20 – 23	
Arm symptoms	BRAS	3	3	17-19	
Upset by hair loss	BRHL	1	3	5	

Table 3.8: Scoring the QLQ-BR-23 version 3.0

In scoring BR-23 questionnaire it was denoted that sexual functioning and sexual enjoyment are scored positively (i.e. “very much” is best) and therefore use the same algebraic equation as for symptom scales; however, the body image scale uses the algebraic equation for functioning scales. QLQ-C30 and BR-23 descriptive statistics presented for both lumpectomy and mastectomy patients in the following 6 tables.

	N	Minimum	Maximum	Mean	Std. Deviation	Skewness	
	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error
QL	44	33,333	100,000	72,538	14,665	-,384	,357
PF	44	13,333	100,000	74,545	18,595	-,978	,357
RF	44	33,333	100,000	88,258	19,216	-1,857	,357
EF	44	,000	100,000	70,644	24,805	-,921	,357
CF	44	,000	100,000	82,955	20,170	-1,934	,357
SF	44	66,667	100,000	94,697	9,354	-1,606	,357
Valid N (list wise)	44						

Table 3.9: Descriptive statistics for lumpectomy patients QLQ-C30 Functional scales

	N	Minimum	Maximum	Mean	Std. Deviation	Skewness	
	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error
FA	44	,000	88,889	32,071	22,379	,252	,357
NV	44	,000	83,333	13,636	23,917	1,621	,357
PA	44	,000	100,000	20,076	22,613	1,366	,357
DY	44	,000	66,667	9,848	18,439	1,756	,357
SL	44	,000	100,000	24,242	28,1778	,808	,357
AP	44	,000	66,667	9,848	19,792	1,912	,357
CO	44	,000	100,000	20,455	28,042	1,097	,357
DI	44	,000	33,333	4,545	11,571	2,195	,357
FI	44	,000	100,000	31,818	31,298	,976	,357
Valid N (list wise)	44						

Table 3.10: Descriptive statistics for lumpectomy patients QLQ-C30 Symptom scales

QLQ-C30 scales for lumpectomy patients, social functioning was the highest mean scoring functional scale (μ=94,697), and emotional functioning the lowest (μ=70,644), indicating best and worst HRQoL, respectively, in these two domains. The best mean symptom scale score (i.e., lowest level of symptoms) was diarrhea (μ=4,545), and the worst (i.e., the most symptoms) was fatigue (μ=32,071) and financial difficulties (μ=31,818).

	N	Minimum	Maximum	Mean	Std. Deviation	Skewness	
	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error
BRBI	44	16,667	100,000	90,341	17,786	-2,669	,357
BRSEF	44	,000	66,667	19,697	20,417	,510	,357
BRSEE	44	,000	66,667	18,182	20,903	,710	,357
BRFU	44	,000	100,000	59,091	34,374	-,318	,357
BRST	44	,000	71,429	29,654	19,044	,113	,357
BRBS	44	,000	66,667	17,614	16,591	,818	,357
BRAS	44	,000	66,667	32,071	25,271	,047	,357
BRHL	44	,000	100,000	28,030	32,899	1,094	,357
Valid N (list wise)	44						

Table 3.11: Descriptive statistics for lumpectomy patients BR-23 module

BR-23 scales for lumpectomy patients, body image was the highest mean scoring functional scale (μ=90,341), and sexual enjoyment the lowest (μ=18,182), indicating best and worst HRQoL, respectively, in these two domains. The best mean symptom scale (i.e., lowest level of symptoms) was breast symptoms (μ=17,614), and the worst (i.e., the most symptoms) was arm symptoms (μ=32,071).

	N	Minimum	Maximum	Mean	Std. Deviation	Skewness	
	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error
QL	56	33,333	91,667	63,244	12,888	,117	,319
PF	56	,000	93,333	63,214	22,055	-1,239	,319
RF	56	,000	100,000	51,190	28,222	-,325	,319
EF	56	8,333	100,000	60,267	28,113	-,376	,319
CF	56	16,667	100,000	70,238	17,324	-,751	,319
SF	56	16,667	100,000	67,857	23,753	,026	,319
Valid N (list wise)	56						

Table 3.12: Descriptive statistics for mastectomy patients QLQ-C30 Functional scales

	N	Minimum	Maximum	Mean	Std. Deviation	Skewness	
	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error
FA	56	22,222	100,000	55,753	18,2870	,580	,319
NV	56	,000	50,000	5,952	10,263	2,027	,319
PA	56	,000	100,000	41,666	22,019	,564	,319
DY	56	,000	100,000	36,309	30,667	,835	,319
SL	56	,000	66,667	25,000	17,115	-,313	,319
AP	56	,000	66,667	9,523	21,755	2,076	,319
CO	56	,000	100,000	30,952	26,097	,363	,319
DI	56	,000	66,667	13,690	22,720	1,407	,319
FI	56	33,333	100,000	65,476	27,680	,068	,319
Valid N (list wise)	56						

Table 3.13: Descriptive statistics for mastectomy patients QLQ-C30 Symptom scales

QLQ-C30 scales for mastectomy patients, cognitive functioning was the highest mean functional scale score (μ=70,238), and role functioning was the lowest (μ=51,190), indicating best and worst HRQoL, respectively, in these two domains. The best mean symptom scale score (i.e., lowest level of symptoms) was nausea and vomiting (μ=5,952), and the worst (i.e., the most symptoms) was financial difficulties (μ=65,476).

	N	Minimum	Maximum	Mean	Std. Deviation	Skewness	
	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error
BRBI	56	,000	83,333	31,845	25,480	,175	,319
BRSEF	56	,000	50,000	19,345	14,486	,021	,319
BRSEE	56	,000	66,667	23,809	18,764	,026	,319
BRFU	56	,000	66,667	26,190	23,539	,331	,319
BRST	56	4,762	57,143	30,782	12,181	-,136	,319
BRBS	56	,000	41,667	16,220	12,249	,274	,319
BRAS	56	,000	88,889	42,857	26,920	,213	,319
BRHL	56	,000	100,000	41,666	37,739	,341	,319
Valid N (list wise)	56						

Table 3.14: Descriptive statistics for mastectomy patients BR-23 module

BR-23 scales for mastectomy patients body image was the highest mean functional scale score (μ=34,845), and sexual functioning is the lowest (μ=19,345), indicating best and worst HRQoL, respectively, in these two domains. The best mean symptom scale score (i.e., lowest level of symptoms) was breast symptoms (μ=16,220), and the worst (i.e., the most symptoms) was arm symptoms (μ=42,857).

	Group	N	Mean Rank	Sum of Ranks
QL	1	44	61,26	2695,50
	2	56	42,04	2354,50
	Total	100		
PF	1	44	58,89	2591,00
	2	56	43,91	2459,00
	Total	100		
RF	1	44	71,58	3149,50
	2	56	33,94	1900,50
	Total	100		
EF	1	44	57,51	2530,50
	2	56	44,99	2519,50
	Total	100		
CF	1	44	62,68	2758,00
	2	56	40,93	2292,00
	Total	100		
SF	1	44	67,86	2986,00
	2	56	36,86	2064,00
	Total	100		

Table 3.15: Rank Scores of functional scales

Group 1 show the lumpectomy patients (N=44) and group 2 show the mastectomy patients (N=56). The mean rank scores was global health status (μ=61,26 and μ=42,04), physical functioning (μ=58,89 and μ=43,91), role functioning (μ=71,58 and μ=33,94), emotional functioning (μ=57,51 and μ=44,99), cognitive functioning (μ=62,68 and μ=40,93), social functioning (μ=67,86 and μ=36,86) for lumpectomy and mastectomy patients, respectively. The value of the mean ranking indicates that the lumpectomy group was significantly had high perceived mean functional scale scores than the mastectomy group.

	QL	PF	RF	EF	CF	SF
Mann-Whitney U	758,500	863,000	304,500	923,500	696,000	468,000
Wilcoxon W	2354,500	2459,000	1900,500	2519,500	2292,000	2064,000
Z	-3,344	-2,593	-6,592	-2,159	-3,919	-5,671
Asymp. Sig. (2-tailed)	,001	,010	,000	,031	,000	,000

Table 3.16: Mann-Whitney U test results for functional scales

A non-parametric test would be needed if the data did not support the assumptions underlying a parametric test (in our case, the two sample t-test). In order to compare the lumpectomy and mastectomy group's functional scales we used Mann-Whitney U test because of ordinal and independent variables. Unlike the t-test which compares the mean values of two groups, the Mann-Whitney U test compares their medians and we hypothesized that;

H_0: Median functional scale scores are the same for both mastectomy and lumpectomy groups

H_1: Median functional scale scores differ between mastectomy and lumpectomy groups

For functional scale score p-values are given for global health status (p=0,001<0,05), physical functioning (p=0,01<0,05), role functioning (p=0,00<0,05), emotional functioning (p=0,031<0,05), cognitive functioning (p=0,00<0,05), social functioning (p=0,00<0,05). Since, all p-values are less than the specified α level so we reject H_0 for all functional scales. We conclude that median functional scale scores differs between mastectomy and lumpectomy groups.

	Group	N	Mean Rank	Sum of Ranks
FA	1	44	34,56	1520,50
	2	56	63,03	3529,50
	Total	100		
NV	1	44	52,33	2302,50
	2	56	49,06	2747,50
	Total	100		
PA	1	44	35,52	1563,00
	2	56	62,27	3487,00
	Total	100		
DY	1	44	35,80	1575,00
	2	56	62,05	3475,00
	Total	100		
SL	1	44	48,11	2117,00
	2	56	52,38	2933,00
	Total	100		
AP	1	44	51,52	2267,00
	2	56	49,70	2783,00
	Total	100		
CO	1	44	43,81	1927,50
	2	56	55,76	3122,50
	Total	100		
DI	1	44	45,41	1998,00
	2	56	54,50	3052,00
	Total	100		
FI	1	44	34,59	1522,00
	2	56	63,00	3528,00
	Total	100		

Table 3.17: Rank Scores of symptom scales

Group 1 show the lumpectomy patients (N=44) and group 2 show the mastectomy patients (N=56). The mean rank scores were nausea and vomiting (μ=52,33 and μ=49,06), appetite loss (μ=51,52 and μ=49,70), for lumpectomy and mastectomy patients, respectively. The value of the mean ranking indicates that lumpectomy group was significantly had more perceived symptom scale scores than the mastectomy

group for nausea and vomiting and appetite loss symptoms. On the other hand, lumpectomy group was significantly had less perceived symptom scale scores than the mastectomy group for remain with the mean rank scores fatigue (μ=34,56 and μ=63,03), pain (μ=35,52 and μ=62,27), dyspnea (μ=35,80 and μ=62,05), insomnia (μ=48,11 and μ=52,38), constipation (μ=43,81 and μ=55,76), diarrhea (μ=45,41 and μ=54,50), financial difficulties (μ=34,59 and μ=63,00).

	FA	NV	PA	DY	SL	AP	CO	DI	FI
Mann-Whitney U	530,50	1151,5	573,0	585,0	1127,0	1187,00	937,50	1008,00	532,00
Wilcoxon W	1520,5	2747,5	1563,0	1575,0	2117,0	2783,00	1927,50	1998,00	1522,00
Asymp. Sig. (2-tailed)	,000	,489	,000	,000	,418	,654	,028	,034	,000

Table 3.18: Mann-Whitney U test results for functional scales

We compare the medians of lumpectomy and mastectomy group's symptom scales using Mann-Whitney U test because of ordinal and independent variables and we hypothesized that;

H_0: Median symptom scale scores are the same for both mastectomy and lumpectomy groups

H_1: Median symptom scale scores differ between mastectomy and lumpectomy groups.

For six symptom scale score were less than the specified α level so we reject H_0. We have sufficient evidence to conclude that fatigue (p=0,00<0,05), pain (p=0,00<0,05), dyspnea (p=0,00<0,05), constipation(p=0,028<0,05), diarrhea (p=0,034<0,05), financial difficulties (p=0,00<0,05) scores was different for mastectomy and lumpectomy groups. The Kruskal Wallis test was used to indicate that there is a statistically significant difference among the lumpectomy and mastectomy groups for fatigue, pain, dyspnea, constipation, diarrhea and financial difficulties scores. On the other hand, there was no difference between the mastectomy and lumpectomy groups using the scales of nausea and vomiting (p=0,489>0,05), appetite loss (p=0,654>0,05), insomnia (p=0,418>0,05).

	Group	N	Mean Rank	Sum of Ranks
BRBI	1	44	76,52	3367,00
	2	56	30,05	1683,00
	Total	100		
BRSEF	1	44	49,88	2194,50
	2	56	50,99	2855,50
	Total	100		
BRSEE	1	44	45,91	2020,00
	2	56	54,11	3030,00
	Total	100		
BRFU	1	44	65,36	2876,00
	2	56	38,82	2174,00
	Total	100		
BRST	1	44	49,60	2182,50
	2	56	51,21	2867,50
	Total	100		
BRBS	1	44	50,60	2226,50
	2	56	50,42	2823,50
	Total	100		
BRAS	1	44	45,44	1999,50
	2	56	54,47	3050,50
	Total	100		
BRHL	1	44	44,89	1975,00
	2	56	54,91	3075,00
	Total	100		

Table 3.19: Rank Scores of breast symptom scales

Group 1 show the lumpectomy patients (N=44) and group 2 show the mastectomy patients (N=56). The mean rank scores were body image (μ=76,52 and μ=30,05) and future perspective (μ=65,36 and μ=38,82) indicates that the lumpectomy group was significantly had high perceived functional breast symptom scale scores than the mastectomy group, respectively. For sexual functioning (μ=49,88 and μ=50,99) and sexual enjoyment (μ=45,91 and μ=54,11) indicates that the lumpectomy group was

significantly had less perceived functional breast symptom scale scores than the mastectomy group, respectively.

The value of the mean ranking indicates that breast symptoms (μ=50,60 and μ=50,42) scale for lumpectomy group was significantly had more perceived breast symptom scale scores than the mastectomy group. On the other hand, lumpectomy group was significantly had less perceived breast symptom scale scores than the mastectomy group for remain with the mean rank scores systemic therapy side effects (μ=49,60 and μ=51,21), arm symptoms (μ=45,44 and μ=54,47), upset by hair loss (μ=44,89 and μ=54,91)

	BRBI	BRSEF	BRSEE	BRFU	BRST	BRBS	BRAS	BRHL
Mann-Whitney U	87,000	1204,50	1030,00	578,00	1192,50	1227,50	1009,500	985,00
Wilcoxon W	1683,00	2194,50	2020,00	2174,00	2182,50	2823,50	1999,500	1975,00
Z	-8,042	-,201	-1,583	-4,747	-,277	-,032	-1,561	-1,804
Asymp. Sig. (2-tailed)	,000	,840	,113	,000	,782	,975	,119	,071

Table 3.20: Mann-Whitney U test results for breast symptom scales

We compare the medians of lumpectomy and mastectomy group's breast symptom scales using Mann-Whitney U test and we hypothesized that;

H_0: Median breast symptom scale scores are the same for both mastectomy and lumpectomy groups

H_1: Median breast symptom scale scores differ between mastectomy and lumpectomy groups

The results indicate that, for two symptom scale score were less than the specified α level so we reject H_0. We have sufficient evidence to conclude that body image (p=0,00<0,05), future perspective (p=0,00<0,05) scores was different for mastectomy and lumpectomy groups. The Kruskal Wallis test was used to indicate there is a statistically significant difference among the lumpectomy and mastectomy groups for BRBI and BRFU. On the other hand, there was no difference between the mastectomy and lumpectomy groups using the scales of sexual functioning (p=0,840>0,05), sexual enjoyment (p=0,113>0,05), systemic therapy side effects

(p=0,418>0,05), breast symptoms (p=0,975>0,05), arm symptoms (p=0,119>0,05), upset by hair loss (p=0,071>0,05).

3.5.4.2. Scoring the EQ-5D Index and Visual Analogue Scale (VAS)

EQ-5D-5L health states, defined by the EQ-5D-5L descriptive system, converted into a single index value. The descriptive system can be represented as a health state, e.g. health state 21543 represents a patient who indicates slight problems on the mobility dimension, no problems on the self-care extreme problems on the usual activities, severe pain or discomfort, and moderate problems on the anxiety/depression dimension. Using EQ-5D-5L calculator, we compute the index scale values. The index scale values, presented in country specific value sets which has not been determined in Turkey. So we calculated index values using United States specific value sets. We multiply index values by 100 to obtain the scores between 0 to100. Than we calculated the EQ-VAS scores which are anchored on 100 is the best health you can imagine and 0 is the worst health you can imagine.

The descriptive statistics for lumpectomy and mastectomy patients presented in Table 3.21 and Table 3.22 respectively. There is a significant correlation between EQ-VAS scores and index score, at the 0.01 level for lumpectomy patients Table 3.23 and for mastectomy patients Table 3.24.

	N	Minimum	Maximum	Mean	Std. Deviation	Skewness	
	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error
VAS	44	40,00	100,00	80,43	14,389	-,547	,357
INDEX_SCALE	44	17,00	100,00	75,82	20,415	-,897	,357
Valid N (list wise)	44						

Table 3.21: Descriptive statistics for lumpectomy patients EQ-5D Index and VAS scores

	N	Minimum	Maximum	Mean	Std. Deviation	Skewness	
	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error
VAS	56	20	90,00	64,79	15,716	-,328	,319
INDEX_SCALE	56	-51,0	100,00	56,007	36,416	-1,786	,319
Valid N (listwise)	56						

Table 3.22: Descriptive statistics for mastectomy patients EQ-5D Index and VAS scores

		VAS	INDEX_SCALE
VAS	Pearson Correlation	1	,667**
	Sig. (2-tailed)		,000
	N	44	44
INDEX_SCALE	Pearson Correlation	,667**	1
	Sig. (2-tailed)	,000	
	N	44	44
**. Correlation is significant at the 0.01 level (2-tailed).			

Table 3.23: Correlation between VAS and Index Scale for lumpectomy patients

		VAS	INDEX_SCALE
VAS	Pearson Correlation	1	,455**
	Sig. (2-tailed)	,000	
	N	56	56
INDEX_SCALE	Pearson Correlation	,455**	1
	Sig. (2-tailed)		,000
	N	56	56
**. Correlation is significant at the 0.01 level (2-tailed).			

Table 3.24: Correlation between VAS and Index Scale for mastectomy patients

	Group	N	Mean Rank	Sum of Ranks
VAS	1	44	65,19	2868,50
	2	56	38,96	2181,50
	Total	100		
INDEX_SCALE	1	44	64,09	2820,00
	2	56	39,82	2230,00
	Total	100		

Table 3.25: Rank scores for VAS and index scale

Group 1 show the lumpectomy patients (N=44) and group 2 show the mastectomy patients (N=56).The Mann-Whitney test compares the distributions of ranks in two groups. The value of the mean ranking indicates that the lumpectomy group (μ=65,19) was significantly had high perceived VAS scores than the mastectomy group (μ=38,96). Similarly for index scales, the value of the mean ranking indicates that the lumpectomy group (μ=64,09) was significantly had high perceived index scale scores than the mastectomy group (μ=39,82).

	VAS	INDEX
Mann-Whitney U	585,500	634,000
Wilcoxon W	2181,500	2230,000
Z	-4,540	-4,165
Asymp. Sig. (2-tailed)	,000	,000

Table 3.26: Mann-Whitney U Test statistic for VAS and index scales

We compare the medians of lumpectomy and mastectomy group's VAS scores using Mann-Whitney U test and we hypothesized that;

H_0: Median VAS scores are the same for both mastectomy and lumpectomy groups
H_1: Median VAS scores differ between mastectomy and lumpectomy groups

As p value was less than the specified α level (p=0,00<0,05), we reject H_0. Thus, we have sufficient evidence to conclude that VAS scores was different for mastectomy and lumpectomy groups (Mann Whitney U=585,500, z = -4,54, p = 0,00). Than we

compare the medians of lumpectomy and mastectomy group's index scale scores using Mann-Whitney U test and we hypothesized that;

H_0: Median index scale scores are the same for both mastectomy and lumpectomy groups

H_1: Median index scale scores differ between mastectomy and lumpectomy groups

For index scales p value was less than the specified α level (p=0,00<0,05), we reject H_0. Thus, we have sufficient evidence to conclude that index scale scores was different for mastectomy and lumpectomy groups (Mann Whitney U=634000, z = -4.165, p = 0,00). The Kruskal Wallis test was used which is the non-parametric version of ANOVA and a generalized form of the Mann-Whitney test method since it permits two groups. The results indicate that (p=0,00<0,05) there is a statistically significant difference among the lumpectomy and mastectomy groups.

		Lumpectomy		Mastectomy	
	Scale	Mean	SD	Mean	SD
Global Health Status(QLQ-C30)					
Global Health Status/QoL	QL	72,538	14,665	63,244	12,888
Functional Scales					
Physical functioning	PF	74,545	18,595	63,214	22,055
Role functioning	RF	88,258	19,216	51,190	28,222
Emotional functioning	EF	70,644	24,805	60,267	28,113
Cognitive functioning	CF	82,955	20,170	70,238	17,324
Social functioning	SF	94,697	9,354	67,857	23,753
Symptom Scales/items					
Fatigue	FA	32,071	22,379	55,753	18,287
Nausea and vomiting	NV	13,636	23,917	5,952	10,263
Pain	PA	20,076	22,613	41,666	22,019
Dyspnea	DY	9,848	18,439	36,309	30,667
Insomnia	SL	24,242	28,177	25,000	17,115
Appetite loss	AP	9,848	19,792	9,523	21,755
Constipation	CO	20,455	28,042	30,952	26,097
Diarrhea	DI	4,545	11,571	13,690	22,720
Financial difficulties	FI	31,818	31,298	65,476	27,680
Functional Scales(BR-23)					
Body image	BRBI	90,341	17,786	31,845	25,480
Sexual functioning	BRSEF	19,697	20,417	19,345	14,486
Sexual enjoyment	BRSEE	18,182	20,903	23,809	18,764
Future perspective	BRFU	59,091	34,374	26,190	23,539
Symptom scales/items					
Systemic therapy side effects	BRST	29,654	19,044	30,782	12,181
Breast symptoms	BRBS	17,614	16,591	16,220	12,249
Arm symptoms	BRAS	32,071	25,271	42,857	26,920
Upset by hair loss	BRHL	28,030	32,899	41,666	37,739
EQ-5D					
	VAS	80,43	14,389	64,79	15,716
	Index	75,82	20,415	56,007	36,416

Table 3.27: Summary table of Utility Scores ‘Mean Values and Standard Deviations (SD)

3.5.4.3. Mapping EORTC QLQ-C30 Questionnaire to EQ-5D Questionnaire

The scores in EORTC QLQ-C30 are not utility-based, these scores were mapped to EuroQoL 5D (EQ-5D) using the regression model proposed in Kontodimopoulos et. al.[30]. Backward elimination was used to model the EQ-5D using the scale scores of QLQ-C30 and BR-23 as predictor variables. Furthermore, forward and stepwise regression models were tried also however we had better predictors using backward regression. At each step, the variable that is the least significant is removed. This process continues until no non-significant variables remain.

In order to examine the difference between predicted and reported utility indicator, root mean square error (RMSE) is calculated. This is also referred as the standard error of the estimate. This was determined the performance measure of the models. For the better performance, RMSE should be small value. RMSE is divided by the range of observed values in order to calculate the normalized root mean squared error (%RMSE) [30].

R	R Square	Adjusted R Square	Std. Error of the Estimate
,781	,610	,546	,138

Table 3.28: Model Summary of lumpectomy group
(Predictors: Constant, QL, PF, RF, CF, BRSEF, BRAS)

R	R Square	Adjusted R Square	Std. Error of the Estimate
,626	,392	,344	,294

Table 3.29: Regression Model Summary of mastectomy group
(Predictors: Constant, RF, EF, PA, BRFU)

In the model, lumpectomy and mastectomy groups' dependent variables were presented by $(INDEX_{SCALE})_{Lumpectomy}$ and $(INDEX_{SCALE})_{Mastectomy}$, respectively. The dependent variable$(INDEX_{SCALE})_{Lumpectomy}$, can be explained by the independent variables; global health status, physical functioning, role functioning, cognitive functioning, sexual functioning and arm symptoms (QL, PF, RF, CF, BRSEF, BRAS) for lumpectomy group. In mastectomy group dependent variable of the model can be

explained by the independent variables; role functioning, emotional functioning, pain and future perspective (RF, EF, PA, BRFU).

For functional scales; role functioning (RF) was significant variables both models whereas global health status (QL), physical functioning (PF), role functioning (RF), cognitive functioning (CF), sexual functioning (BRSEF) were significant only lumpectomy group and emotional functioning (EF), future perspective (BRFU) was significant predictor for mastectomy group. On the other hand, for symptom scales pain (PA) was significant for mastectomy group and arm symptoms (BRAS) was significant scale for lumpectomy group.

R is the square root of R-Squared and is the correlation between the QLQ-C30 and predicted values of dependent variables. In the model R square was 0,61 show that QLQ-C30 indices explain more than half of the variance of EQ-5D indices for lumpectomy group. For mastectomy group this value less than lumpectomy group which was 0,392. This value show that QLQ-C30 indices explain less than half of the variance of EQ-5D indices for mastectomy group. However, lower score of the R-square does not necessarily denote unreliable predictive ability. [30] Thus, the RMSE was the important indicator to examine the predictor ability. For lumpectomy group this score was 0,138 which was less than mastectomy group with 0,294 prediction errors corresponded to the EQ-5D model.

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95% Confidence Interval for B	
	B	Std. Error	Beta			Lower Bound	Upper Bound
(Constant)	,054	,150		,361	,720	-,250	,358
QL	,332	,155	,238	2,139	,039	,018	,646
PF	,378	,151	,344	2,511	,017	,073	,683
RF	,559	,131	,526	4,272	,000	,294	,824
CF	-,240	,122	-,237	-1,967	,050	-,487	,007
BRSEF	-,231	,106	-,231	-2,179	,036	-,445	-,016
BRAS	-,210	,085	-,260	-2,453	,019	-,383	-,037

Table 3.30: Backward Regression Model Coefficients for lumpectomy group

Regression model for lumpectomy patients is;

$$(EQ5D)_i = \beta_0 + \beta_1(\mathrm{QL})_i + \beta_2(\mathrm{PF})_i + \beta_3(\mathrm{RF})_i + \beta_4(\mathrm{CF})_i + \beta_5(\mathrm{BRSEF})_i + \beta_6(\mathrm{BRAS})_i$$

$(\mathrm{QL})_i$ global health status score for i.th lumpectomy patient,

$(\mathrm{PF})_i$ physical functioning score for i.th lumpectomy patient,

$(\mathrm{RF})_i$ role functioning score for i.th lumpectomy patient,

$(\mathrm{CF})_i$ cognitive functioning score for i.th lumpectomy patient,

$(\mathrm{BRSEF})_i$ sexual functioning score for i.th lumpectomy patient,

$(\mathrm{BRAS})_i$ arm symptoms for i.th lumpectomy patient.

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95% Confidence Interval for B	
	B	Std. Error	Beta			Lower Bound	Upper Bound
(Constant)	,521	,222		2,344	,023	,075	,968
RF	-,350	,169	-,271	-2,073	,043	-,689	-,011
EF	,532	,168	,411	3,165	,003	,195	,870
PA	-,501	,244	-,303	-2,055	,045	-,991	-,012
BRFU	,405	,176	,262	2,309	,025	,053	,758

Table 3.31:Backward Regression Model Coefficients for mastectomy group

Regression model for mastectomy patients is;

$$(EQ5D)_i = \beta_0 + \beta_1(\mathrm{RF})_i + \beta_2(\mathrm{EF})_i + \beta_3(\mathrm{PA})_i + \beta_4(\mathrm{BRFU})_i$$

$(\mathrm{RF})_i$ role functioning score for i.th mastectomy patient,

$(\mathrm{EF})_i$ emotional functioning score for i.th mastectomy patient,

$(\mathrm{PA})_i$ cognitive functioning score for i.th mastectomy patient,

$(\mathrm{BRFU})_i$ future perspective for i.th mastectomy patient.

These results are shown in following table. Group 1 shows lumpectomy patients and Group 2 shows mastectomy patients. The mean utility scores were 0,758 and 0,559 for lumpectomy and mastectomy patients, respectively.

GROUP	N	Mean	Std. Deviation	Std. Error Mean
1	44	,758	,159	,024
2	56	,559	,227	,030

Table 3.32: Descriptive statistics for mean utility scores from regression model

	Levene's Test		t-test for Equality of Means						
								95% CI of the Difference	
	F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Equal variances assumed	9,693	,002	4,904	98	,000	,198	,040	,118	,278
Equal variances not assumed			5,112	96,819	,000	,198	,038	,121	,275

Table3.33: Independent sample t-test results from regression model utility scores

We calculated utility scores for every individual patient using the regression model. Group 1 indicates the lumpectomy group (N=44) and group 2 indicates the mastectomy group (N=56). Scores show that lumpectomy patients have 0,758 mean utility scores

and mastectomy patients show less perceived satisfaction than lumpectomy patients with 0,559 mean utility score. We hypothesized that;

H_0: Mean utility score are the same for both mastectomy and lumpectomy groups
H_1: Mean utility scores differ between mastectomy and lumpectomy groups.

Levene's test indicates that the variances are not equal (p=0,002<0,05) across the two groups, we will rely on the second row of output which is equal variances not assumed. We conclude that, (p=0,00<0,05) we reject H_0, which means that there is a statistically significant difference between mean utility scores of lumpectomy and mastectomy groups.

Utility Scores	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	,968	1	,968	24,045	,000
Within Groups	3,947	98	,040		
Total	4,915	99			

Table 3.34: Anova Table for Utility scores from regression model

There is a statistically significant difference (p = 0,00<0,05, F=24,045) in the mean utility scores between the different surgery types of breast cancer patients.

CHAPTER 4

Methods

4.1. Cost Effectiveness Analysis

Cost analysis is a well-known tool that can be used by decision makers to assess and potentially improve the performance of their systems. There are four types of cost analyses for decision making. These include cost-benefit, cost-feasibility, cost-utility and cost-effectiveness analysis. Although each is related to cost-analysis family, each of them is characterized by important differences that make them suitable for specific applications. Cost benefit analysis (CBA) refers to the evolution of alternatives according to their costs and benefits when each is measured in monetary terms. Cost feasibility analysis (CFA) refers to the method of estimating only the costs of an alternative in order to determine whether or not alternatives are within the boundaries of consideration, it cannot be used to determine which ones should actually be selected. Cost utility analysis (CUA) and cost effectiveness analysis (CEA) are very similar methods. Cost effectiveness analysis refers to the evaluation of alternatives according to both their costs and their effects with regard to producing some outcome. However, cost utility analysis uses information on the preferences of individuals in order to express their overall satisfaction with a measure of effectiveness [32].

Cost-effectiveness analysis was developed in the 1950s by the United States Department of Defense as a device for adjudicating among the demands of the various branches of the armed services for increasingly costly weapons systems with different levels of performance and overlapping missions [33]. By the 1960s it had become widely used as a tool for analysing the efficiency of alternative government programs outside of the military, in 1990's Cost Effectiveness studies have become popular in health decisions and studies increasingly continued in 2000's [34].

CEA, has been most frequently employed by health researchers. Cost-effectiveness analysis compares the costs and health effects of an intervention to determine the extent to which it can be regarded as providing value for money. This informs decision-makers who have to determine where to allocate limited healthcare resources. The aim of CEA is to maximize the level of benefits (health effects) relative to the level of resources available. The measure of CEA is incremental cost effectiveness ratio (ICER) which is detailed in section 4.1.1.

The decision criteria for CEA is recommended by the Commission on Macroeconomics and Health, uses gross domestic product (GDP) as a readily available indicator to derive the following three categories of cost-effectiveness [35].

- Highly cost-effective (less than GDP per capita);
- Cost-effective (between one and three times GDP per capita);
- Not cost-effective (more than three times GDP per capita)

4.1.1. Incremental Cost Effectiveness Ratio

Incremental Cost Effectiveness Ratio (ICER), provides information on cost, improvements in health status, and changes in life expectancy, but it also shows that how much should be spend to buy additional health relative to the competing alternative. The incremental cost-effectiveness was calculated as follows:

$$ICER = \frac{COST_{lumpectomy} - COST_{mastectomy}}{QALY_{lumpectomy} - QALY_{mastectomy}}$$

When the measure of benefit is expressed in life-years or quality-adjusted life-years, the ICER will be measured in cost per life-year or QALY gained.

If the incremental cost is negative and the incremental effect is positive, the intervention can be defined as cost effective (it is dominant, higher health effect at lower cost). If the incremental cost is positive and the incremental effect is negative, the intervention can be defined as unequivocally not cost effective (it is dominated, lower health effects at higher cost). If both the incremental cost and

the incremental effect are negative, or both the incremental cost and the incremental effect are positive no such unequivocal statements can be made [40].

In this study, the mean cost of treatment per patient in lumpectomy strategy were 4208,12TL and 2727,14TL for mastectomy strategy. The lumpectomy strategy provided 0,758 mean QALYs as compared with 0,559 for the mastectomy strategy. This resulted in an ICER of 4962,067TL per QALY gained for lumpectomy when compared with mastectomy.

Strategy	Cost (TL)	Incr Cost (TL)	Eff (LY)	Incr Eff(LY)	C/E (TL/LY)	ICER (TL/LY)
Mastectomy	2803,6		1,093		2565,926	
Lumpectomy	4213,0	1409,4	1,377	0,284	3060,289	4962,067

Table 4.1: Incremental Cost Effectiveness Ratio TreeAge Pro Outputs

The threshold we used for determining the cost effectiveness of Lumpectomy was 4962,067 TL per QALY gained, we based this assumption on the report from the Commission on Macroeconomics and Health [35], which defines interventions with a cost effectiveness ratio that is less than the per capita gross domestic product (10576TL for Turkey in 2014) as highly cost effective. (Turk Stat, GDP nominal per capita, 2014) [36].

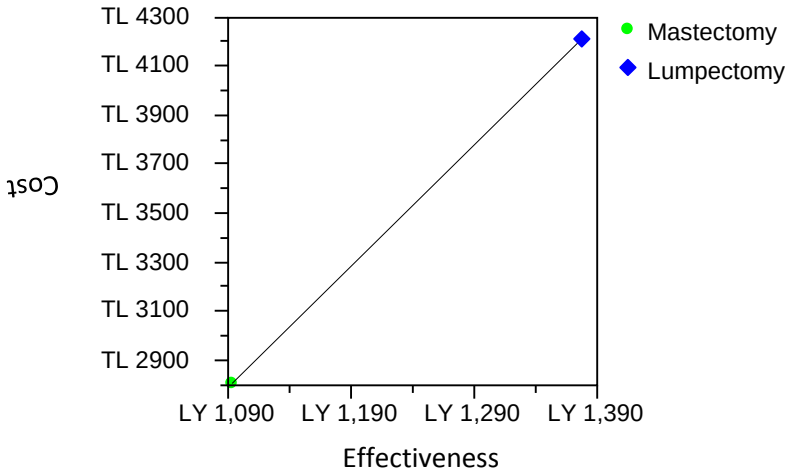

Figure 4.1: Cost-Effectiveness Analysis At Decision

4.1.2. Fuzzy Approach

Fuzzy logic was introduced with the 1965 proposal of fuzzy set theory by Zadeh in 1965. Today, an increasing number of applications of fuzzy logic is encountered in all fields of science and in health care as well. Fuzzy logic is an extension of classical logic and uses fuzzy sets rather than classical sets. A fuzzy set is defined by a membership function which assigns to each element in the set under consideration a membership grade. Membership grade is a value in the interval [0, 1]. By defining a set using a membership function, it is possible for an element to belong partially to a set. But in classical sets we have only two choices; objects belong to a set or not.[39]

Definition (Fuzzy set): Fuzzy set A is defined by;

A= {(x, $\mu_A(x)$): $x \in A$, $\mu_A(x) \in [0.1]$}.

In the pair (x,$\mu_A(x)$), the first element x belongs to the classical set A, the second element $\mu_A(x)$, is a value in the interval [0, 1], called membership function.

Definition (Support of Fuzzy Set): The support of fuzzy set A* is the set of all points x in X such that $\mu_A(x) > 0$.Hence,

A* = Support (A) = {x |$\mu_A(x) > 0$}.

Definition (α-cut): The α-cut of α-level set of fuzzy set A is a set consisting of those elements of the universe X which membership values exceed the threshold level α and can be define as follows,

$A_\alpha = \{x/\ \mu_A(x) \geq \alpha\}$.

Definition (Fuzzy Number): A fuzzy set A on R must possess at least the following three properties to qualify as a fuzzy number,

- A must be a normal fuzzy set
- The support of A, A* must be bounded.
- A* must be closed interval for every α∈[0,1]

Definition (Triangular Fuzzy Number): Among the various shapes of fuzzy number, triangular fuzzy number (TFN) is the most popular one. It is a fuzzy number represented with three points as follows: $A = (a_1, a_2, a_3)$. This representation is interpreted as membership functions and holds the following conditions.

- $a_1 \ \ to \ \ a_2$ is increasing function
- $a_2 \ \ to \ \ a_3$ is decreasing function
- $a_1 \leq \ a_2 \leq a_3$.

The membership function of triangular fuzzy number A, is given $\forall\, x \in \Re$ as follows;

$$\mu_A(x) = \begin{cases} 0 & x < a_1 \\ \dfrac{x - a_1}{a_2 - a_1} & a_1 \leq x \leq a_2 \\ \dfrac{a_3 - x}{a_3 - a_2} & a_2 \leq x \leq a_3 \\ 0 & x > a_3 \end{cases}$$

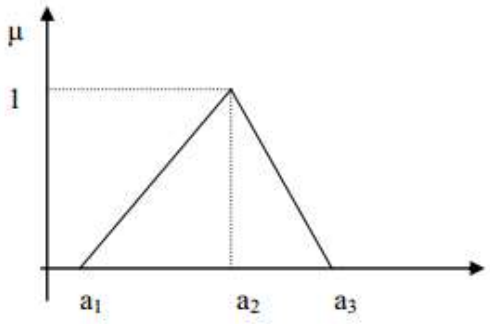

Figure 4.2: Triangular Fuzzy Number

$$A = (a_1, a_2, a_3)$$

4.1.3. Fuzzy Cost Effectiveness Ratios

In this study we noted that statistical analysis for the cost-effectiveness ratio can be useful to make inference when the data used in CEA has been gathered in similar time horizon, otherwise all the statistics used in CEA are incompatible, irrelevant and optional. As we observed from our sample patients costs and health effects don't necessarily coincide in time. Thus, comparing them is not realistic if we don't convert them so that they are all situated in the same point of time. The traditional way to do so is to use some other statistical methods such as time series analysis but even those methods assumes that the change in cost and effects can be predicted in time. However, for real cases it is known that these types of models are not dominated to the ones

based on an expert's opinion. In order to account for time when valuing health costs and effects, we propose a different approach than the one based on the changes in time. Our approach is based on the satisfaction of the patient which can be seen by an individual expert of his/her health condition today, tomorrow and yesterday. In this regard, if a patient gets a different satisfaction over time, then we can account for the different time locations of health effects and this will be corresponding to a cost that enables us to capture the difference in terms of satisfaction. In this study we make two considerations:

i) the patient feels more satisfied today than in the future

ii) the patient will get more satisfaction in the future than in the present time.

In order to consider both possibilities we propose an approach based on triangular fuzzy numbers which can represent positive and negative corrections to current cost and effect of a treatment depending on the patients' satisfaction levels. This approach will enable decision making when the health conditions are defined by the patients with considering change in their own conditions in time. Therefore, to obtain cost effectiveness ratio in fuzzy sense we need to consider both costs and effects as fuzzy numbers.

- We define a triangular fuzzy number for the cost of health intervention *j* for a given time period:

$$C_j = (c_1, c_2, c_3) \quad c_1, c_2, c_3 \in \Re \quad c_1 \leq c_2 \leq c_3$$

$$\forall\, x \in \Re \qquad \mu_C(x) = \begin{cases} 0 & x < c_1 \\ \dfrac{x - c_1}{c_2 - c_1} & c_1 \leq x \leq c_2 \\ \dfrac{c_3 - x}{c_3 - c_2} & c_2 \leq x \leq c_3 \\ 0 & x > c_3 \end{cases} \qquad (4.1)$$

In the given membership function c_1 is the subjective minimum cost which covers only operation cost. This cost include fixed costs and pre surgery costs. c_2 is the cost of the treatment which include also post-surgery costs. c_3 is subjective maximum costs over time that is possible to account adjuvant therapy costs.

- For lumpectomy groups we define a $\mu_{C_L}(x)$ which is the triangular fuzzy number for the cost of health intervention *j* for a given time period:

$$C_{j_L} = (1468,28;\ 4139,64;\ 8014,24)$$

$$\forall\, x \in \Re \qquad \mu_{C_L}(x) = \begin{cases} 0 & x < 1468,28 \\ \dfrac{x - 1468,28}{2671,31} & 1468,28 \le x \le 4139,64 \\ \dfrac{8014,24 - x}{3874,60} & 4139,64 \le x \le 8014,24 \\ 0 & 8014,24 > c_3 \end{cases} \qquad (4.2)$$

c_1 is the subjective minimum cost which covers only the lumpectomy operation cost. This cost include fixed costs and pre surgery costs. c_2 is the cost of the treatment which include also post-surgery costs. c_3 is subjective maximum costs over time that is possible to account adjuvant therapy costs.

- For mastectomy groups we define a $\mu_{C_M}(x)$ which is the triangular fuzzy number for the cost of health intervention *j* for a given time period:

$$C_{j_M} = (1468,28;\ 2727,14;\ 4110,01)$$

$$\forall\, x \in \Re \qquad \mu_{C_M}(x) = \begin{cases} 0 & x < 1468,28 \\ \dfrac{x - 1468,28}{1258,86} & 1468,28 \le x \le 2727,14 \\ \dfrac{4110,01 - x}{1382,87} & 2727,14 \le x \le 4110,01 \\ 0 & 4110,01 > c_3 \end{cases} \qquad (4.3)$$

In the given membership function$c_1$is the subjective minimum cost which covers only the lumpectomy operation cost. This cost include fixed costs and pre surgery costs. c_2 is the cost of the treatment which include also post-surgery costs. c_3 is subjective maximum costs over time that is possible to account adjuvant therapy costs.

We define a triangular fuzzy number for the present health effects intervention *j* for a given time period:

$$E_j = (e_1, e_2, e_3) \quad e_1, e_2, e_3 \in \Re \quad e_1 \le\ e_2 \le e_3$$

$$\forall\, x \in \Re \quad \mu_E(x) = \begin{cases} 0 & x < e_1 \\ \dfrac{x - e_1}{e_2 - e_1} & e_1 \le x \le e_2 \\ \dfrac{e_3 - x}{e_3 - e_2} & e_2 \le x \le e_3 \\ 0 & x > e_3 \end{cases} \qquad (4.4)$$

The minimum effect of the treatment perceived by the patients at the time of the operation is given bye_1. e_2 is the perceived effect of the treatment at any time during the treatment which was determined by the patients using visual analogue scale (VAS). e_3 is the maximum value that is possible for the perceived maximum satisfaction over time.

We define a triangular fuzzy number for lumpectomy patients the present health effects intervention *j* for a given time period:

$$E_{j_L} = (0{,}4;\ 0{,}804;\ 1)$$

$$\forall\, x \in \Re \quad \mu_{E_L}(x) = \begin{cases} 0 & x < 0{,}4 \\ \dfrac{x - 0{,}4}{0{,}804 - 0{,}4} & 0{,}4 \le x \le 0{,}804 \\ \dfrac{1 - x}{1 - 0{,}804} & 0{,}804 \le x \le 1 \\ 0 & x > 1 \end{cases} \qquad (4.5)$$

The minimum effect of the lumpectomy treatment perceived by the patients at the time of the operation is given bye_1. e_2 is the perceived effect of the treatment at any time during the treatment which was determined by the patients using visual analogue scale (VAS). e_3 is the maximum value that is possible for the perceived maximum satisfaction over time.

We define a triangular fuzzy number for mastectomy patients the present health effects intervention *j* for a given time period:

$$E_{j_M} = (0{,}2;\ 0{,}648;\ 0{,}9)$$

$$\forall\, x \in \Re \quad \mu_{E_M}(x) = \begin{cases} 0 & x < 0{,}2 \\ \dfrac{x - 0{,}2}{0{,}648 - 0{,}2} & 0{,}2 \le x \le 0{,}648 \\ \dfrac{0{,}9 - x}{0{,}9 - 0{,}648} & 0{,}648 \le x \le 0{,}9 \\ 0 & x > 0{,}9 \end{cases} \qquad (4.6)$$

The minimum effect of the mastectomy treatment perceived by the patients at the time of the operation is given bye_1. e_2 is the perceived effect of the treatment at any time during the treatment which was determined by the patients using visual analogue scale (VAS). e_3 is the maximum value that is possible for the perceived maximum satisfaction over time.

After $\mu_C(x)$ and $\mu_E(x)$ are defined for each strategy we define a triangular fuzzy number for the ICER. The incremental cost effectiveness ratio at the time of the treatment in the given membership function is given by i_2 where i_1 and i_3 are subjective values that are possible to account for the difference of satisfaction and inflation rate for costs over time. Then we define an ICER,

$$ICER = (i_1, i_2, i_3) \quad i_1, i_2, i_3 \in \Re \quad i_1 \le i_2 \le i_3$$

The membership function of triangular fuzzy number $\mu_{ICER}(x)$, is given by $\forall\, x \in \Re$ as following Formula (4.7);

$$\mu_{ICER}(x) = \begin{cases} 0 & x < (\Delta c_1/\Delta e_1) \\ \dfrac{x - (\Delta c_1/\Delta e_1)}{(\Delta c_2/\Delta e_2) - (\Delta c_1/\Delta e_1)} & (\Delta c_1/\Delta e_1) \le x \le (\Delta c_2/\Delta e_2) \\ \dfrac{(\Delta c_3/\Delta e_3) - x}{(\Delta c_3/\Delta e_3) - (\Delta c_2/\Delta e_2)} & (\Delta c_2/\Delta e_2) \le x \le (\Delta c_3/\Delta e_3) \\ 0 & x > (\Delta c_3/\Delta e_3) \end{cases}$$

$$\forall\, x \in \Re \quad \mu_{ICER}(x) = \begin{cases} 0 & x < i_1 \\ \dfrac{x - i_1}{i_2 - i_1} & i_1 \le x \le i_2 \\ \dfrac{i_3 - x}{i_3 - i_2} & i_2 \le x \le i_3 \\ 0 & x > i_3 \end{cases} \quad (4.8)$$

where,

$$(\Delta c_1/\Delta e_1)=(c_{1L} - c_{1M})/(e_{1L} - e_{1M})= i_1$$
$$(\Delta c_2/\Delta e_2)=(c_{2L} - c_{2M})/(e_{2L} - e_{2M})=i_2$$
$$(\Delta c_3/\Delta e_3)=(c_{3L} - c_{3M})/(e_{3L} - e_{3M})=i_3$$

$$\mu_{ICER}(x) = \begin{cases} 0 & x < 0 \\ \dfrac{x - 0}{9027.78 - 0} & 0 \le x \le 9027.78 \\ \dfrac{59140.8 - x}{59140.8 - 9027.78} & 9027.78 \le x \le 59140.8 \\ 0 & x > 59140.8 \end{cases} \quad (4.9)$$

Using our sample results we calculated the ICER which was 4962,067 TL per QALY gained for lumpectomy when compared with mastectomy. This value was between $i_1\ and\ i_2$ and the membership function $\mu_{ICER}(x)$ is calculated as following,

$$\mu_{ICER}(4962.067\ TL/QALY) = 0{,}55$$

We can conclude that lumpectomy is highly cost effective than mastectomy with a possibility of 0,55. As we mentioned in section 4.1. the cost effectiveness criteria is about the ICER and in order to conclude for an intervention to be cost effective ICER of that intervention should be more than one to three times of the GDP per capita. Since we have the information about the GDP per capita in 2014 and it is 10576TL for Turkey and it is between $i_2\ and\ i_3$ and the membership function $\mu_{ICER}(x)$can be calculated as fallowing,

$$\mu_{ICER}(10576\ TL/QALY) = 0{,}97$$

And we can conclude that lumpectomy is cost effective operation when using the GDP per capita in 2014 for Turkey as a criteria with the possibility of 0,97. This fuzzy number will help us to analyse the interventions in terms of cost effectiveness ratio in a fuzzy phenomenon.

CHAPTER 5

Results

5.1. Conclusion and Discussion

When different health care treatment methods are not expected to produce the same outcomes the costs and the effects of the alternatives need to be assessed. This can be done by cost-effectiveness analysis, where the costs are compared with outcomes such as, per life saved and per life year gained. Many cost-effective analyses rely on existing published studies for effectiveness data as it is often too costly or time consuming to collect data on cost and effectiveness during a clinical trial. In this study we represent the first cost effectiveness analysis in Turkey for comparing mastectomy versus lumpectomy for patients with early stage breast cancer using data collected at Ege University Hospital General Surgery Department in İzmir. The HRQoL (Health-Related Quality of Life) was assessed with 100 breast cancer patients using the standard questionnaire of European Organization for Research and Treatment of Cancer (EORTC QLQ-C30 and BR-23) and EuroQol Group measure of health status to calculate the utility scores.

EQ-5D-5L is a standardized measure of health status. EQ-5D includes index scale scores and Visual Analogue Scale. There is a significant correlation between EQ-VAS scores and index scores, at the 0,01 level for lumpectomy patients and for mastectomy patients. The value of the mean ranking indicates that the lumpectomy group was significantly high perceived VAS scores than the mastectomy group. Similarly for index scales, the value of the mean ranking indicates that the lumpectomy group was significantly high perceived index scale scores than the mastectomy group.

EORTC QLQ-C30 is a questionnaire developed to assess the quality of life of cancer patients. QLQ-C30 scales for lumpectomy patients, social functioning was the highest

mean scoring functional scale, and emotional functioning the lowest, indicating best and worst HRQoL, respectively, in these two domains. The best mean symptom scale score was diarrhea, and the worst was fatigue and financial difficulties.QLQ-C30 scales for mastectomy patients, cognitive functioning was the highest mean functional scale score, and role functioning was the lowest, indicating best and worst HRQoL, respectively, in these two domains. The best mean symptom scale score was nausea and vomiting, and the worst was financial difficulties. The value of the mean ranking indicates that the lumpectomy group was significantly had high perceived mean functional scale scores than the mastectomy group for all functional scales. Furthermore, median functional scale scores differs between mastectomy and lumpectomy groups. The value of the mean ranking indicates that lumpectomy group was significantly had more perceived symptom scale scores than the mastectomy group for NV and AP symptoms. On the other hand, lumpectomy group was significantly had less perceived symptom scale scores than the mastectomy group for fatigue, pain, dyspnea, insomnia, constipation, diarrhea and financial difficulties. For six symptom scale score fatigue, pain, dyspnea, constipation, diarrhea, financial difficulties scores was different for mastectomy and lumpectomy groups. There is a statistically significant difference among the lumpectomy and mastectomy groups for fatigue, pain, dyspnea, constipation, diarrhea and financial difficulties scores. On the other hand, there was no difference between the mastectomy and lumpectomy groups using the scales of nausea and vomiting, appetite loss, and insomnia.

The European Organization for Research and Treatment of Cancer developed site-specific questionnaires for the measurement of QoL of patients with specific cancers. QLQ-BR23 is formed for breast cancer patients. BR-23 scales for mastectomy patients body image was the highest mean functional scale score, and sexual functioning is the lowest, indicating best and worst HRQoL, respectively. The best mean symptom scale score was breast symptoms, and the worst was arm symptoms.BR-23 scales for lumpectomy patients, body image was the highest mean scoring functional scale, and sexual enjoyment the lowest, indicating best and worst HRQoL, respectively. The best mean symptom scale was breast symptoms, and the worst was arm symptoms. The mean rank scores were bosy image and future perspective indicates that the lumpectomy group was significantly had high perceived functional breast module scale scores than the mastectomy group. For sexual functioning and sexual enjoyment

indicates that the lumpectomy group was significantly had less perceived functional breast symptom scale scores than the mastectomy group. The value of the mean ranking indicates that BRBS scale for lumpectomy group was significantly had more perceived breast module symptom scale scores than the mastectomy group. On the other hand, lumpectomy group was significantly had less perceived breast symptom scale scores than the mastectomy group for remain with the mean rank scores systemic therapy side effects, arm symptoms, upset by hair loss. For breast module symptom scale body image, future perspective scores was different for mastectomy and lumpectomy groups. There is a statistically significant difference among the lumpectomy and mastectomy groups for body image and future perspective. On the other hand, there was no difference between the mastectomy and lumpectomy groups using the scales of sexual functioning, sexual enjoyment, systemic therapy side effects, breast symptoms, arm symptoms, upset by hair loss.

As the scores in EORTC QLQ-C30 are not utility-based, these scores were mapped to EuroQoL 5D (EQ-5D) using the regression model proposed in Kontodimopoulos et. al.[30]. In the regression model; for lumpectomy and mastectomy groups' dependent variables were index scale of lumpectomy and index scale of mastectomy, respectively. The dependent variable for lumpectomy group, can be explained by the independent variables; global health status, physical functioning, role functioning, cognitive functioning, sexual functioning and arm symptoms (QL, PF, RF, CF, BRSEF, BRAS). In mastectomy group dependent variable of the model can be explained by the independent variables; role functioning, emotional functioning, pain and future perspective (RF, EF, PA, BRFU). For functional scales; role functioning was a significant variable for both models whereas global health status, physical functioning, role functioning, cognitive functioning, sexual functioning were significant only lumpectomy group and emotional functioning, future perspective were significant predictor for mastectomy group. On the other hand, for symptom scales pain was significant for mastectomy and arm symptoms variable was significant scale for lumpectomy group.

We calculated utility scores for every individual patient using this regression model. Scores show that lumpectomy patients have 0,758 mean utility scores and mastectomy patients show less perceived satisfaction than lumpectomy patients with 0,559 mean

utility score. There is a statistically significant difference between mean utility scores of lumpectomy and mastectomy groups. RMSE was the important indicator to examine the predictor ability. For lumpectomy group this score was 0,138 which was less than mastectomy group with 0,294 prediction errors corresponded to the EQ-5D model.

In order to compare lumpectomy and mastectomy operations we calculate incremental cost effectiveness ratio (ICER) which provides information on cost, improvements in health status. If one intervention is more effective and less expensive than alternative intervention we conclude that the more cost effective intervention is preferable. In this case an intervention is said to be dominant. If one intervention is more expensive but will improve the health condition of the patient then the patient have to decide about willing to pay price. If intervention is more expensive and less effective than the alternative intervention it is said to be dominated [40]. In our study, the mean cost of treatment per patient in lumpectomy strategy were 4208,12 TL and 2727,14 TL for mastectomy strategy. This differences in cost was statistically significant. The lumpectomy strategy provided 0,758 mean QALYs as compared with 0,559 for the mastectomy strategy. Published literature was used for utility values of metastasis, recover, RT and CT. [41]. This resulted in an ICER of 4962,067 TL per QALY gained for lumpectomy when compared with mastectomy. Since the incremental cost effectiveness ratio is less than the per capita gross domestic product for lumpectomy it can be categorized as highly cost effective intervention.

In order to account for time when valuing health costs and effects, we propose a different approach than the one based on the changes in time. Our approach is based on the satisfaction of the patient on different time periods. The results of the fuzzy approach presented that lumpectomy is more cost effective than mastectomy with a possibility of 0,55 when using the GDP per capita in 2014 for Turkey as a criteria with the possibility of 0,97. This fuzzy membership value will help us to analyse the interventions in terms of cost effectiveness ratio in a fuzzy phenomenon.

Moreover, the proposed approach also provides a new decision tool for the surgeons' decisions about the type of the treatment where there is uncertainty about the costs and effectiveness of the treatments. We propose an approach based on fuzzy numbers which can represent positive and negative corrections to current cost and effect of a

treatment depending on the patients' satisfaction levels and time interval that this satisfaction was measured. This approach will enable decision making when the health conditions are defined by the patients with considering change in their own conditions in time.

5.2. Future Work

In this study we used Ege University Hospital General Surgery Department for 100 breast cancer patient records. The study can be expand other regions of Turkey. We calculated QALY only one time period. But the utility scores can be calculated different time periods (0, 4, and 8 months) to see the difference on time. The results of the questionnaire can be evaluated considering socio demographic factors of patients. Additionally, Structural Equation Modeling (SEM) method can be used to assess the questionnaires of the patients in order to estimate the utilities of interventions. Moreover using the Fuzzy Approach a new decision criteria can be defined for assessing Incremental Cost Effectiveness Ratio other than the gross domestic product.

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Appendix

Appendix 1: EQ-5D-5L Questionnaire

Appendix 2: QLQ-C30 Questionnaire

Appendix 3: QLQ-BR23 Questionnaire

Appendix 4: Decision Board

Appendix 1

Sağlık Anketi

Türkiye için Türkçe sürümü

(Turkish version for Turkey)

Her başlık altında BUGÜNKÜ sağlık durumunuzu en iyi ifade eden BİR kutuyu işaretleyiniz.

HAREKET EDEBİLME

Yürüyerek dolaşırken bir güçlük yaşamıyorum ❑
Yürüyerek dolaşırken çok az güçlük yaşıyorum ❑
Yürüyerek dolaşırken orta derecede güçlük yaşıyorum ❑
Yürüyerek dolaşırken şiddetli güçlük yaşıyorum ❑
Yürüyerek dolaşamıyorum ❑

KENDİ KENDİNE BAKABİLME

Kendi kendime yıkanırken veya giyinirken bir güçlük yaşamıyorum ❑
Kendi kendime yıkanırken veya giyinirken çok az güçlüğüm oluyor ❑
Kendi kendime yıkanırken veya giyinirken orta derecede güçlüklerim oluyor ❑
Kendi kendime yıkanırken veya giyinirken şiddetli güçlüklerim oluyor ❑
Kendi kendime yıkanacak veya giyinebilecek durumda değilim ❑

OLAĞAN İŞLER *(örneğin iş, ders çalışma, ev işleri, aile içi veya boş zaman faaliyetleri)*

Olağan işlerimi yaparken bir güçlük yaşamıyorum ❑
Olağan işlerimi yaparken çok az güçlüğüm oluyor ❑
Olağan işlerimi yaparken orta derecede güçlüklerim oluyor ❑
Olağan işlerimi yaparken şiddetli güçlüklerim oluyor ❑
Olağan işlerimi yapabilecek durumda değilim ❑

AĞRI / RAHATSIZLIK

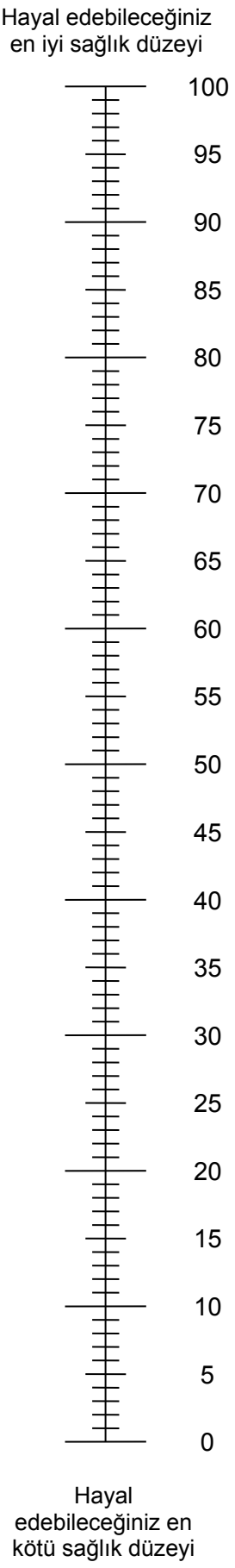
Ağrı veya rahatsızlığım yok ❑
Hafif ağrı veya rahatsızlığım var ❑
Orta derecede ağrı veya rahatsızlığım var ❑
Şiddetli ağrı veya rahatsızlığım var ❑
Aşırı derecede ağrı veya rahatsızlığım var ❑

ENDİŞE/MORAL BOZUKLUĞU

Endişeli veya moral bozukluğu içinde değilim ❑
Hafif derecede endişeliyim veya moralim bozuk ❑
Orta derecede endişeliyim veya moralim bozuk ❑
Şiddetli derecede endişeliyim veya moralim bozuk ❑
Aşırı derecede endişeliyim veya moralim çok bozuk ❑

- Sağlığınızın BUGÜN ne kadar iyi veya kötü olduğunu bilmek istiyoruz.
- Bu ölçek 0'dan 100'e kadar numaralandırılmıştır.
- 100 hayal edebileceğiniz <u>en iyi</u> sağlık düzeyini göstermektedir
  0 ise hayal edebileceğiniz <u>en kötü</u> sağlık düzeyini göstermektedir
- BUGÜNKÜ sağlığınızın nasıl olduğunu göstermek için ölçeğe bir X işareti koyun.
- Şimdi de lütfen ölçekte işaretlediğiniz sayıyı aşağıdaki kutuya yazın.

BUGÜNKÜ SAĞLIK DURUMUNUZ = ☐



Appendix 2 TURKISH

EORTC QLQ-C30 (version 3.0)

Siz ve sağlığınız hakkında bazı şeylerle ilgileniyoruz. Lütfen soruların tamamını size uygun gelen rakamı daire içine alarak yanıtlayınız. Soruların "doğru" veya "yanlış" yanıtları yoktur. Verdiğiniz yanıtlar kesinlikle gizli kalacaktır.

Lütfen ad ve soyadınızın başharflerini yazınız: ⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋

Doğum gününüz (Gün, Ay, Yıl): ⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋

Bugünkü tarih (Gün, Ay, Yıl): 31 ⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋

		Hiç	Biraz	Oldukça	Çok
1.	Ağır bir alışveriş torbası veya valiz taşımak gibi zorlu hareketler yaparken güçlük çeker misiniz?	1	2	3	4
2.	Uzun bir yürüyüş yaparken herhangi bir zorluk çeker misiniz?	1	2	3	4
3.	Evin dışında kısa bir yürüyüş yaparken zorlanır mısınız?	1	2	3	4
4.	Günün büyük bir kısmını oturarak veya yatarak geçirmeye ihtiyacınız oluyor mu?	1	2	3	4
5.	Yemek yerken, giyinirken, yıkanırken ve tuvaleti kullanırken yardıma ihtiyacınız oluyor mu?	1	2	3	4

Geçtiğimiz hafta zarfında:

		Hiç	Biraz	Oldukça	Çok
6.	İşinizi veya günlük aktivitelerinizi yapmaktan sizi alıkoyan herhangi bir engel var mıydı?	1	2	3	4
7.	Boş zaman aktivitelerinizi sürdürmekten veya hobilerinizle uğraşmaktan sizi alıkoyan bir engel var mıydı?	1	2	3	4
8.	Nefes darlığı çektiniz mi?	1	2	3	4
9.	Ağrınız oldu mu?	1	2	3	4
10.	Dinlenme ihtiyacınız oldu mu?	1	2	3	4
11.	Uyumakta zorluk çektiniz mi?	1	2	3	4
12.	Kendinizi güçsüz hissettiniz mi?	1	2	3	4
13.	İştahınız azaldı mı?	1	2	3	4
14.	Bulantınız oldu mu?	1	2	3	4
15.	Kustunuz mu?	1	2	3	4

Lütfen arka sayfaya geçiniz

Geçtiğimiz hafta zarfında:		**Hiç**	**Biraz**	**Oldukça**	**Çok**
16.	Kabız oldunuz mu?	1	2	3	4
17.	İshal oldunuz mu?	1	2	3	4
18.	Yoruldunuz mu?	1	2	3	4
19.	Ağrılarınız günlük aktivitelerinizi etkiledi mi?	1	2	3	4
20.	Televizyon seyretmek veya gazete okumak gibi aktiviteleri yaparken dikkatinizi toplamakta zorluk çektiniz mi?	1	2	3	4
21.	Gerginlik hissettiniz mi?	1	2	3	4
22.	Endişelendiniz mi?	1	2	3	4
23.	Kendinizi kızgın hissettiniz mi?	1	2	3	4
24.	Bunalıma girdiniz mi?	1	2	3	4
25.	Bazı şeyleri hatırlamakta zorluk çektiniz mi?	1	2	3	4
26.	Fiziksel durumunuz veya tıbbi tedaviniz aile yaşantınıza engel oluşturdu mu?	1	2	3	4
27.	Fiziksel durumunuz veya tıbbi tedaviniz sosyal aktivitelerinize engel oluşturdu mu?	1	2	3	4
28.	Fiziksel durumunuz veya tedaviniz maddi zorluğa düşmenize yol açtı mı?	1	2	3	4

Aşağıdaki sorular için 1 ila 7 arasındaki size en uygun rakamı daire içine alınız

29. Geçen haftaki sağlığınızı genel olarak nasıl değerlendirirsiniz?

1	2	3	4	5	6	7
Çok kötü						Mükemmel

30. Geçen haftaki hayat kalitenizi genel olarak nasıl değerlendirirsiniz?

1	2	3	4	5	6	7
Çok kötü						Mükemmel

Appendix 3

TURKISH

EORTC QLQ - BR23

Hastalar bazen aşağıda sözü geçen belirti ve sorunlardan bahsederler. Lütfen geçen hafta süresince bu belirti ve sorunlardan hangilerini ne derecede yaşadığınızı belirtiniz.

	Geçtiğimiz hafta boyunca:	**Hiç**	**Biraz**	**Oldukça**	**Çok**
31.	Ağzınızda kuruma oldu mu?	1	2	3	4
32.	Yediklerinizde ve içtiklerinizde her zamankinden farklı bir tat var mıydı?	1	2	3	4
33.	Gözlerinizde batma, yanma veya sulanma oldu mu?	1	2	3	4
34.	Saçınız döküldü mü?	1	2	3	4
35.	Bu soruyu yalnızca saçınız döküldü ise yanıtlayınız: Saçınızın dökülmesinden dolayı üzüldünüz mü?	1	2	3	4
36.	Kendinizi hasta veya rahatsız hissettiniz mi?	1	2	3	4
37.	Bu hastalıktan dolayı sıcak (ateş) basmaları oldu mu?	1	2	3	4
38.	Başınızda ağrı oldu mu?	1	2	3	4
39.	Hastalığınız veya tedaviniz nedeni ile kendinizi daha az çekici (cezbedici) hissettiniz mi?	1	2	3	4
40.	Hastalığınız veya tedaviniz sonucunda kendinizi daha az kadınsı hissediyor musunuz?	1	2	3	4
41.	Kendinizi çıplak olarak görmekte zorlandığınız oldu mu?	1	2	3	4
42.	Vücudunuzdan memnuniyetsizlik duyduğunuz oldu mu?	1	2	3	4
43.	Gelecekteki sağlığınız için endişe duydunuz mu?	1	2	3	4

	Geçen <u>dört</u> hafta boyunca:	**Hiç**	**Biraz**	**Oldukça**	**Çok**
44.	Cinsellikle ne derece ilgiliydiniz?	1	2	3	4
45.	Cinsel birleşme olsun yada olmasın cinsel olarak ne kadar aktiftiniz?	1	2	3	4
46.	Bu soruyu, geçen dört hafta boyunca cinsel faaliyetiniz olduysa yanıtlayınız: Cinsel hayatınız yada ilişkinizden ne derece zevk aldınız?	1	2	3	4

Lütfen arka sayfaya geçiniz

	Geçtiğimiz hafta boyunca:	**Hiç**	**Biraz**	**Oldukça**	**Çok**
47.	Kolunuzda veya omzunuzda ağrı oldu mu?	1	2	3	4
48.	Kolunuzda veya elinizde şişme oldu mu?	1	2	3	4
49.	Kolunuzu kaldırmakta veya hareket ettirmekte zorlandınız mı?	1	2	3	4
50.	Hasta olan memenizin bulunduğu bölgede ağrı hissettiniz mi?	1	2	3	4
51.	Hasta memenizin bulunduğu bölgede şişme oldu mu?	1	2	3	4
52.	Hasta olan memenizin bulunduğu bölgede aşırı hassasiyet oldu mu?	1	2	3	4
53.	Hastalanan meme bölgenizde cilt sorunlarınız oldu mu? (örn: kaşıntı, kuruma, döküntü, kızarıklık, yanma)	1	2	3	4

Appendix 4

DECISION BOARD

TREATMENT CHOICE

MASTECTOMY
(Surgical Removal of the Breast)

- Entire breast will be removed
- Some lymph nodes under your arm will be removed
- You are left with a healing scar that runs across your chest
- A drain is inserted near the scar under the arm, for 5-10 days, to remove excess fluid
- After surgery, you may be referred to the Cancer Centre for consideration of other treatments (hormonal therapy or chemotherapy)
- Radiation is not normally required

LUMPECTOMY
(Surgical Removal of the Cancerous Lump)

- Only the cancerous lump and some surrounding tissue will be removed
- Some of the lymph nodes under your arm will be removed
- You are left with two healing scars, one on the breast and one under the arm
- Often, a drain is inserted near the scar under the arm, for 5-10 days, to remove excess fluid
- In some instances (in about 1 out of 10 women), all the cancer in the breast may not be removed and you may require further surgery
- Once the breast has healed, 3-4 weeks after surgery, you will be referred to the Cancer Centre for consideration of radiation

PLUS

RADIATION
(X-ray Treatment)

- You will need to come to the Cancer Centre for planning of the radiation and for treatments
- Your treatments will be daily for 5 weeks, excluding weekends
- Each visit lasts approximately 30 to 45 minutes
- The time between your surgery and the beginning of your radiation treatments may be 6-12 weeks
- Other treatments (hormonal therapy and chemotherapy) may be considered
- If you are treated with chemotherapy, your radiation will begin after chemotherapy

SIDE EFFECTS

MASTECTOMY

OFTEN

- Numbness and discomfort on the inside of the arm where nerves were cut
- Pain, discomfort or numbness of the chest

SOMETIMES

- Stiffness of the shoulder
- Collection of fluid in the scar that may need to be drained

RARELY

- Infection
- Arm swelling

LUMPECTOMY

OFTEN

- Numbness and discomfort on the inside of the arm where nerves were cut
- Pain or discomfort of the breast

SOMETIMES

- Stiffness of the shoulder
- Collection of fluid in the scar that may need to be drained

RARELY

- Infection
- Arm swelling

PLUS

RADIATION

OFTEN

- Redness of the skin like a sunburn

SOMETIMES

- Increased tiredness
- Tanning of the skin
- Slight increase in the size of the breast
- Slight increase in firmness of the breast

RARELY

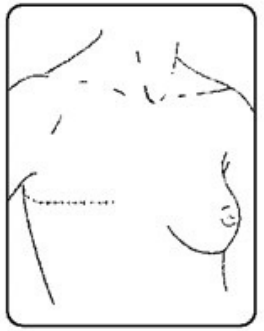
- Blood vessels may become visible on small areas of the skin
- Pneumonia

RESULTS OF TREATMENT CHOICE

For Breast | **For Survival**

MASTECTOMY

- Healed scar across your chest
- Some women may be upset by the loss of their breast
- A breast prosthesis or breast form can be fitted
- A breast can be reconstructed using plastic surgery
- Cancer may come back on the chest. About 5 to 10 out of 100 women will experience this in the next 10 years
- Cancer that comes back on the chest is usually treated by surgery, radiation, or both



MASTECTOMY

*Your chance of surviving cancer is the **SAME** as with Lumpectomy plus Radiation*

LUMPECTOMY PLUS RADIATION

- Two healed scars, one on the breast and one under the arm
- Some indentation where the lump was removed or thickening of the breast tissue
- Some women may be upset by the way the breast looks, but most (8 out of 10) are satisfied
- Cancer may come back in the breast. About 5 to 10 out of 100 women will experience this in the next 10 years.
- Cancer that comes back in the breast is usually removed by further surgery (lumpectomy or mastectomy). Radiation cannot be given again.

LUMPECTOMY PLUS RADIATION

*Your chance of surviving cancer is the **SAME** as with Mastectomy*