Prioritization of Factors of Breast Cancer Treatment Using Fuzzy AHP

Hatice Camgöz-Akdağ, Aziz Kemal Konyalıoğlu, Tuğçe Beldek

Abstract Breast cancer is a widespread disease that can both be seen at males or females. According to so many different factors such as age, sex, genetics, the shape and size of the tumor, environmental situations and so on that effects cancer type directly. With so many alternative cancer types and thus treatment preference changes it is vital to make the diagnosis as soon as possible to decide and start the treatment process. Diagnosis time is dependent on both technological equipment and also medical personnel. This study aims to support medical personnel, radiologists, doctors, surgeons, via proposing a multi criteria decision model to find out which factor is more effective on the breast cancer type. Fuzzy Analytic Hierarchy process is used to prioritize factors of breast cancer treatment alternatives and results are compared to another study which already used Analytic Hierarchy Process but in certain conditions.

Keywords breast cancer • multi-criteria decision making • fuzzy • analytical hierarchy process • healthcare support systems

H. Camgöz-Akdağ (✉) • A. K. Konyalıoğlu • T. Beldek
Management Engineering Department, Management Faculty, Istanbul Technical University, Istanbul, Turkey
e-mail: camgozakdag@itu.edu.tr

A. K. Konyalıoğlu
Management Engineering Department, Management Faculty, Istanbul Technical University, Istanbul, Turkey
e-mail: konyalioglua@itu.edu.tr

T. Beldek
Management Engineering Department, Management Faculty, Istanbul Technical University, Istanbul, Turkey
e-mail: beldek@itu.edu.tr

Introduction

Today, cancer is a worldwide disease that is usually uncontrollable. With some type of treatments, people try to survive against the speed of the abnormal cell reproduction. At this point, age is a very important criterion as a young body produces abnormal/normal cells faster than an old body. With the technological improvement and development in medicine area, people can cope up with different cancer types such as pancreatic, breast, prostate, lung and so on. One of the most common cancer type is breast cancer, which may both seen on males or females. There are also types of breast cancer, which also differentiate the treatment options. It may start with drugs or chemotherapy, or an operation than using medicine. It is important to diagnose breast cancer at its early stage and decide the way of the surviving process. For this study two different drug types are considered for HER2+ type of breast cancer. One of them is Kadcyla and the other one is Lapatinib plus Capecitabine. Medical personnel are giving a decision for the patient to use which of these drugs in terms of their own disease's properties.

According to so many different factors such as age, sex, genetics, the shape and size of the tumor, environmental situations and so on that effects cancer treatment directly. With so many alternatives cancer type and thus treatment preference changes. It is vital to make the diagnosis as soon as possible to decide and start the treatment process. Diagnosis time is dependent on both technological equipment and also medical personnel. This study aims to support medical personnel, radiologists, doctors, surgeons, via proposing a multi criteria decision model (MCDM) to find out which factor is more effective on the breast cancer type. Fuzzy Analytic Hierarchy process is used to prioritize factors of breast cancer treatment alternatives which are mentioned above and results are compared to another study which already used the Analytic Hierarchy Process but in certain conditions. After the introduction part, a literature review will cover up MCDM and F-AHP. Then F-AHP will be detailed in the methodology part and analysis will show the results which belongs to the selected study. At the end, conclusion and future studies will be mentioned.

Literature Review

Breast Cancer Treatment

First treatment called Trastuzumab approved in 1998, which is a monoclonal antibody targeting the extracellular domain of the HER2 protein, used as a combination of another type of treatment for HER2 positive (HER2+) breast cancer (Slamon et al., 2001). There are also different types of drugs for HER2+ breast cancer type that

are being preferred according to the patients' specific properties. Kadcyla is a combination of Trastuzumab and Emtansine. The main reason to use Kadcyla is the breast cancermetastatic characteristic. It may spread to the other parts of the body of the patient. Duty of Trastuzumab is finding cancer cells and Emtansine tries to destroy the cell because of its toxic structure. This process of the drug minimizes the damage of healthy cells so this treatment is more preferred than the others to increase the survival rate of the patients (URL-1).

Another drug combination of Lapatinib and Capecitabine helps to heal HER2+ breast cancer. Lapatinib has a duty to stop the reproduction of the cancer cells. The material of the drug blocks the receptors of HER2+ cancer cells and it slows down its growth (URL-2). It may be used as a combination with Capecitabine which is a regular chemotherapy drug, that is more effective when used together for metastatic breast cancer (Geyer et al., 2006).

There are very different scenerios, which are already studied at literature based on breast cancer. Rostami et al., made a literature review of brain metastasis in brain cancer in 2016. They mentioned about different types of treatments according to patients' genetics and the microenvironment of the brain (Rostami et al., 2016). Wanchai et al. conducted another study, about breast cancer related lymphedema. This type of disease may treated by combinations of compression therapy, pharmacotherapy, modality approaches and therapeutic excercises (Wanchai et al., 2016). Borin et al., presented a statistical study that shows melatonin decreases the rate of breast cancer metastasis (Borin et al., 2016).

Fuzzy Analytic Hierarchy Process

Saaty studied the traditional Analytic Hierarchy Process (AHP) for multi criteria decision making (Saaty, 1980). AHP makes a question as the subjective numbers of decision makers' and the environment of uncertainity, however it is easier than the other decision making methods in terms of mathematical calculations. Fuzzy AHP is more suitable for fuzziness and uncertainity for conducting a hierarchical rating (Zyoud, 2016).

Under fuzziness, there are different methods that may be used, while the most common one is fuzzy AHP (F-AHP). An extend analysis is preferred by using F-AHP because of its easy steps despite its disadvantages. F-AHP can cope up with the uncertain environment and it is steadier than the others. Different criteria are being compared pairly with the help of triangular fuzzy numbers (Kumar et al., 2017). Methodology part is clearly giving the details of the F-AHP method steps one by one.

There are different examples from literature that already used F-AHP. At one of the studies, human capital indicators are ranked by using F-AHP (Bozbura et al., 2007). Huang et al., preferred using F-AHP to select a governmental R&D project (Huang et al., 2008). Lee et al. studied F-AHP in Taiwan to evaluate IT departments of production sector (Lee et al., 2008). An evaluation of hazardous waste transportation by using F-AHP was another study found in literature (Gumus, 2009). Another waste management study is done by Lung Hung, which evaluated municipal solid waste management with F-AHP (Hung et al., 2007).

Methodology

More complex and realistic problems may have uncertainities. Solving these kind of situations under uncertainity is sometimes difficult with deterministic models. Fuzzy sets help to make models that include uncertainities within and thus it is easier to solve those problems (Kahraman et al., 2003). Uncertainity and fuzziness are the important factors of Fuzzy Analytic Hierarchy Process. This multi criteria decision making model is also preferred by decision makers for it natural language to understand the complex model easily (Kahraman et al., 2003).

There are different management and engineering studies that use F-AHP in literature that are already mentioned. To understand methodology of this process Chang introduced triangular fuzzy numbers (Chang, 1996). Membership function is assigned between 0-1 for fuzzy sets, which can be seen at Figure 1 (Kahraman et al., 2003).

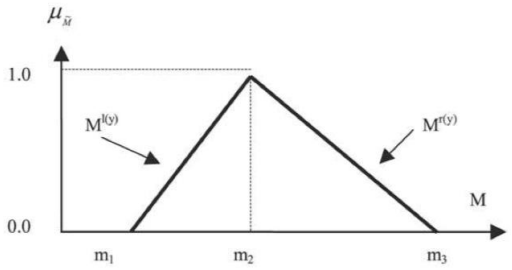

Fig. 1. Triangular fuzzy numbers (Kahraman et al., 2003).

Which is also expressed as the linear presentations interpreting as piecewise function on left and right sides, $\widetilde{M}$, in (1).

$$\mu(x|\widetilde{M}) = \begin{cases} 0, & x < m_1 \\ (x - m_1)/(m_2 - m_1), & m_1 \le x < m_2 \\ (m_3 - x)/(m_3 - m_2), & m_2 \le x < m_3 \\ 0, & x \ge m_3 \end{cases} \quad (1)$$

Equation (2) shows right and left side expression, which are $l(y)$ and $r(y)$, of fuzzy numbers of membership degrees (Chan et al., 2008).

$$\widetilde{M} = \left(M^{l(y)}, M^{r(y)}\right) = (m_1 + (m_2 - m_1)y, m_3 + (m_2 - m_3)y)$$
$$where\ y \in [0,1] \quad (2)$$

Fuzzy AHP procedure is given below (Huang et al., 2008):

- A scale is defined for each criteria related to their relative strength. Each criteria must assigned according to the relative strength by triangular fuzzy numbers [9].

- Decision makers have to make a pairwise comparison with matrix $\widetilde{A_k}$ to construct a fuzzy jugdement matrix which is $\tilde{E}$ (3).

$$\widetilde{A_k} = \begin{pmatrix} 1 & \tilde{a}_{12} & \cdots & \widetilde{a_{1(n-1)}} & \widetilde{a_{1n}} \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ \tilde{a}_{n1} & \widetilde{a_{n2}} & \cdots & \widetilde{a_{n(n-1)}} & 1 \end{pmatrix} \quad (3)$$

Where $i = j, a_{ij} = 1$ and $e_{ij} = 1$,

$$\tilde{E} = \begin{pmatrix} 1 & \tilde{e}_{12} & \cdots & \widetilde{e_{1(n-1)}} & \widetilde{e_{1n}} \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ \tilde{e}_{n1} & \widetilde{e_{n2}} & \cdots & \widetilde{e_{n(n-1)}} & 1 \end{pmatrix} \quad (4)$$

$\tilde{A}_{kl} = \left[\tilde{a}_{ij}^{kl}\right]$ and $\tilde{E}_l = \left[\tilde{e}_{ij}^{l}\right]$, it follows that $\tilde{a}_{ij}^{l} = (\tilde{a}_{ij}^{kl} \Theta \ldots . \Theta \tilde{a}_{ij}^{kn})^{1/n}$ and

$\widetilde{e_{ij}} = (\tilde{e}_{ij}^{1} \Theta \ldots . \Theta \tilde{e}_{ij}^{n})^{1/n}$

i^{th} object's fuzzy value is:

$S_i = \sum_{j=1}^{m} M_{gi}^{j} \otimes \left[\sum_{i=1}^{n} \sum_{j=1}^{m} M_{gi}^{j}\right]^{-1}$

where

$\sum_{j=i}^{m} M_{gi}^{j} = \left(\sum_{j=1}^{m} l_j, \sum_{j=1}^{m} m_j, \sum_{j=1}^{m} u_j\right)$

- Possibilities are calculated such as

$M_2 = (l_2, m_2, u_2) \geq M_1 = (l_1, m_1, u_1)$ can be defined as

$V(M_2 \geq M_1) = sup_{y \geq x}\left[\min(\mu_{M_1}(x), \mu_{M_2}(x))\right]$

Furthermore, we need to compare M_2 *and* M_1 values by
$V(M_2 \geq M_1)$ *and* $V(M_1 \geq M_2)$

Then, $d'(A_i) = minV(S_i \geq S_k)$

- Normalized weights are figured out for $k = 1,2, \dots n; k \neq i$, the weight vector can be found as $W' = (d'(A_1), d'(A_2), \dots d'(A_n)^T$, and the normalized weights,

$W = (d(A_1), d(A_2), \dots d(A_n))^T$, where W is crisp value.

Model Analysis and Results

In this study, it is aimed to prioritize breast cancer treatment factors by using fuzzy AHP method. Camgöz-Akdağ et al., studied breast cancer treatment factors' prioritization using AHP (Camgöz-Akdağ et al., 2019). Factors are gathered from this study to compare AHP and F-AHP results in equality. Firstly, the criteria are evaluated and explained. Table 1 shows the criteria of the model.

Table 1. Main and subcriteria of the model

Main criteria	Sub-criteria
C1: Patient Related Factors	C11: Age
	C12: General Health Condition
	C13: Manopause
	C14: Preference
	C15: Ethnicity
C2: Tumor Related Factors	C21: Size
	C22: Location
	C23: Stage
C3: Drug Related Factors	C31: Therapeutic Index
	C32: Structure
	C33: Delivery
	C34: Adverse Effect Grade

C35: Median Survival Time
C36: Recurrence Probability
C37: Frequent Usage
C38: Maximum Dosage

Figure 2 shows the hierarchical tree for the selection of the breast cancer treatment.

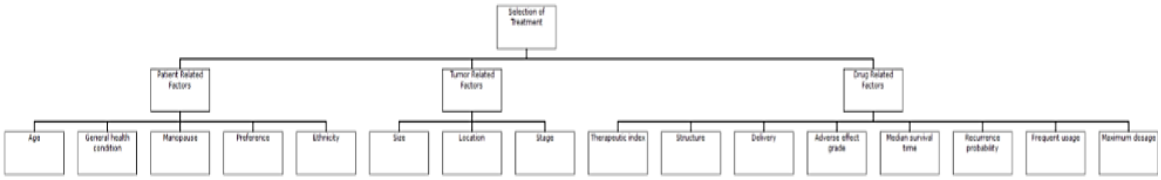

Fig. 2. A hierarchy for selection of the breast cancer treatment

These criteria are asked to the experts to make pairwise comparisons in terms of five-point scale. After their relative weighting, F-AHP results are taken. Table 2 shows priorities with respect to treatmen selection.

Table 2. Priorities with respect to treatment selection

Rank	Name	Weight
3	Patient Related Factors	0.113
1	Tumor Related Factors	0.549
2	Drug Related Factors	0.338

As shown in the table above, according to the Selection of Treatment, Tumor Related Factors is the first priority. Next priorities are assigned to Drug Related Factors and Patient Related Factors according to the obtained weights.

Following tables are the results of the analysis of subcriteria prioritization. Table 3 shows the patient related factors' subcriteria ranking.

Table 3. Priorities with respect to patient related factors' sub-criteria

Rank	Name	Weight
2	Age	0.283
1	General health condition	0.446
4	Manopause	0.044
3	Preference	0.227
5	Ethnicity	0

As shown in the table above, according to the Patient Related Factors, General health condition is the first priority. Next priorities are assigned to Age, Preference,

Manopause and Ethnicity according to the obtained weights. Table 4 shows the tumor related factors' subcriteria ranking.

Table 4. Priorities with respect to treatment selection

Rank	Name	Weight
2	Size	0.049
3	Location	0
1	Stage	0.951

Table 5 shows the drug related factors' subcriteria ranking.

Table 5. Priorities with respect to drug related factors' sub-criteria

Rank	Name	Weight
4	Therapeutic index	0.102
5	Structure	0.08
6	Delivery	0.06
3	Adverse effect grade	0.196
1	Median survival time	0.267
2	Recurrence probability	0.258
7	Frequent usage	0.034
8	Maximum dosage	0.002

As shown in the table above, according to the Drug Related Factors, Median survival time is the first priority. Next priorities are assigned to Recurrence probability, adverse effect grade, Therapeutic index, Structure, Delivery, Frequent usage and Maximum dosage according to the obtained weights.

Discussion and Conclusion

The results of the F-AHP model of this study is similar to the reference paper. Cmagöz-Akdağ et al., used AHP to prioritize breast cancer treatment selection criteria and found that the first rank belongs to tumor related factors with a nearly 50 percent of total. This study inserted fuzziness and uncertaintiy to the model and solved F-AHP. The results were same but a few point differences. All main and subcriteria rankings are the same but when numbers are considered, there are slight gaps.

Other multi criteria decision-making models, with more detailed criteria can be modelled to reach decisions that are more accurate. Because of a healthcare problem, errors must be eliminated if possible. These kind of technological supports for medical personnel will decrease diagnosis time, which is very important when considering a cancer treatment process.

References

Borin, T. F., Arbab, A. S., Gelaleti, G. B., Ferreira, L. C., Moschetta, M. G., Jardim-Perassi, B. V., ... & Fabri, V. A. (2016). Melatonin decreases breast cancer metastasis by modulating Rho-associated kinase protein-1 expression. Journal of pineal research, 60(1), 3-15.

Bozbura, F. T., Beskese, A., & Kahraman, C. (2007). Prioritization of human capital meas-urement indicators using fuzzy AHP. Expert Systems with Applications, 32(4), 1100-1112.

Camgöz-Akdağ, H., Alemdar, Ç., & Aydın, E. (2019). A MCDM Model Design for HER2+ Breast Cancer Treatment Technique Using AHP Method. PONTE Journal, Vol. 75. No. 1/1.

Chan, F. T., Kumar, N., Tiwari, M. K., Lau, H. C., & Choy, K. L. (2008). Global supplier selection: a fuzzy-AHP approach. International Journal of production research, 46(14), 3825-3857.

Chang, D. Y. (1996). Applications of the extent analysis method on fuzzy AHP. European journal of operational research, 95(3), 649-655.

Geyer, C. E., Forster, J., Lindquist, D., Chan, S., Romieu, C. G., Pienkowski, T., . . . Cameron, D. (2006). Lapatinib plus Capecitabine for HER2-Positive Advanced Breast Cancer. New England Journal of Medicine,355(26), 2733-2743. doi:10.1056/nejmoa064320

Gumus, A. T. (2009). Evaluation of hazardous waste transportation firms by using a two step fuzzy-AHP and TOPSIS methodology. Expert systems with applications, 36(2), 4067-4074.

Huang, C. C., Chu, P. Y., & Chiang, Y. H. (2008). A fuzzy AHP application in govern-ment-sponsored R&D project selection. Omega, 36(6), 1038-1052.

Hung, M. L., Ma, H. W., & Yang, W. F. (2007). A novel sustainable decision making mod-el for municipal solid waste management. Waste management, 27(2), 209-219.

Kahraman, C., Cebeci, U., & Ulukan, Z. (2003). Multi-criteria supplier selection using fuzzy AHP. Logistics information management, 16(6), 382-394.

Kumar, D., Rahman, Z., & Chan, F. T. (2017). A fuzzy AHP and fuzzy multi-objective line-ar programming model for order allocation in a sustainable supply chain: A case study. In-ternational Journal of Computer Integrated Manufacturing, 30(6), 535-551.

Lee, A. H., Chen, W. C., & Chang, C. J. (2008). A fuzzy AHP and BSC approach for eval-uating performance of IT department in the manufacturing industry in Taiwan. Expert sys-tems with applications, 34(1), 96-107.

Rostami, R., Mittal, S., Rostami, P., Tavassoli, F., & Jabbari, B. (2016). Brain metastasis in breast cancer: a comprehensive literature review. Journal of neuro-oncology, 127(3), 407-414.

Saaty, T. L. (1980). The Analytic Hierarchy Process: Planning, Priority Setting, Resources Allo-cation.,(McGraw: New York.).

Slamon, D. J., Leyland-Jones, B., Shak, S., Fuchs, H., Paton, V., Bajamonde, A., ... & Baselga, J. (2001). Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2. New England Journal of Medicine, 344(11), 783-792.

URL-1 Kadcyla may help you live longer. (n.d.). Retrieved April 15, 2018, from https://www.kadcyla.com/patient/about-kadcyla/benefits- risks.html

URL-2 Lapatinib (Tyverb ®). (n.d.). Retrieved April 14, 2018, from https://www.macmil-lan.org.uk/cancerinformation/cancertreatment/treatmenttypes/biologicaltherapies/can cer-growthinhibitors/lapatinib.aspx

Wanchai, A., Armer, J. M., Stewart, B. R., & Lasinski, B. B. (2016). Breast cancer-related lymphedema: A literature review for clinical practice. International Journal of Nursing Sci-ences, 3(2), 202-207.

Zyoud, S. H., Kaufmann, L. G., Shaheen, H., Samhan, S., & Fuchs-Hanusch, D. (2016). A frame-work for water loss management in developing countries under fuzzy environment: In-tegration of Fuzzy AHP with Fuzzy TOPSIS. Expert Systems with Applications, 61, 86-105.