Non comunicable disease

# Machine learning techniques to identify risk factors of breast cancer among women in Mashhad, Iran

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## Keywords

Random forest • Logistic regression • Decision tree • Principal component analysis • Breast cancer

## Summary

**Background**. *Low survival rates of breast cancer in developing countries are mainly due to the lack of early detection plans and adequate diagnosis and treatment facilities.*
**Objectives**. *This study aimed to apply machine learning techniques to recognize the most important breast cancer risk factors.*
**Methods**. *This case-control study included women aged 17-75 years who were referred to medical centers affiliated with Mashhad University of Medical Science between March 21, 2015, and March 19, 2016. The study had two datasets: one with 516 samples (258 cases and 258 controls) and another with 606 samples (303 cases and 303 controls). Written informed consent has been observed. Decision Tree (DT), Random Forest (RF), Logistic Regression (LR), and Principal Component Analysis (PCA) were applied using R studio software.*
**Results**. *Regarding the DT and RF, the most important features that impact breast cancer were family cancer, individual history of breast cancer, biopsy sampling, rarely consumption of a dairy, fruit, and vegetable meal, while in PCA and LR these features including family cancer, pregnancy number, pregnancy tendency, abortion, first menstruation, the age of first childbirth and childbirth number.*
**Conclusions**. *Machine learning algorithms can be used to extract the most important factors in the diagnosis of breast cancer in developing countries such as Iran.*

## Introduction

The most prevalent malignancy of women in the world is breast cancer [1]. Globally, there were 2.3 million new instances of breast cancer in 2020, and this disease claimed 685,000 lives [2]. By 2040, it is expected that there will be more than 3 million new cases and 1 million deaths due to breast cancer worldwide [3]. Breast cancer has been identified as the fifth-leading cause of mortality among Iranian women [4]. In Iran, 15,492 new cases of breast cancer were diagnosed in 2022, making up 11.3% of all new cancer cases [5]. The exact causes of breast cancer are still unknown, but there are both modifiable and non-modifiable risk factors associated with this malignancy [6]. Some of the main non-modifiable risk factors include aging [7], being a woman [8], having a family history of breast cancer [9], possessing certain genetic mutations [10], late menopause, and early menarche [11]. On the other hand, modifiable risk factors for breast cancer include obesity [8], alcohol, smoking [12], postmenopausal hormone therapy [13], and being single [14].
Early detection of breast cancer can lead to lower treatment costs and more effective treatment. Thus, knowledge about the main risk factors that affect this mysterious cancer is a crucial task [15].

Machine learning algorithms have a significant impact on the healthcare system by analyzing large data sets, and assisting to make decisions about a patient's health status, disease progression, and optimal treatment plans [16]. Several machine learning algorithms are used in the medical field for prediction and classification including Decision Trees (DTs), Logistic Regression (LR), random forests (RFs), Principal Component Analysis (PCA), and Support Vector Machines (SVMs) [16]. Decision trees use a tree-like structure to represent decisions and their potential outcomes [17], while logistic regression predicts the probability of an observation belonging to a specific class [18]. Random forest is a method that improves the accuracy and robustness of predictions by combining multiple decision trees [19]. Principal component analysis is an algorithm that reduces the number of dimensions in large datasets with many features, making the data simpler to analyze and interpret [20]. By accounting for time-varying information and managing multiple predictors, interactions, and missing values, these models can improve the accuracy of clinical risk predictions [21].
Unfortunately, the majority of women in developing countries know little about the principal factors that escalate the risk of breast cancer. Moreover, breast

cancer is diagnosed at a younger age in many developing countries such as Iran, Tunisia, and Pakistan [22, 23]. Determining the inhibitory policies and decisions from responsible people to diminish the occurrence of breast cancer requires having knowledge of the risk factors of this cancer. Reviews on risk factors of breast cancer from various published articles in developed countries may not provide a practical solution, since the findings of these studies cannot be applied to women in developing countries. To the best of our knowledge, despite the importance of risk factors associated with this disease, few studies have been conducted in Iran using machine learning methods. Thus, the aim of this study was to determine the most important risk factors of breast cancer using machine learning algorithms in Mashhad, northeastern Iran.

## Materials and methods

### Study population

In this case-control study, data was collected from two different data sets. All women aged 17-75 years who were referred to medical centers affiliated with Mashhad University of Medical Science (MUMS) between March 21, 2015, and March 19, 2016, were enrolled. From these women, the case group was composed of individuals who had positive mammography and were confirmed to have breast cancer through histology. Women without breast cancer were selected as the control group. The smaller data set contained 516 samples, divided into 258 cases and 258 controls. The larger data set contained 606 samples, divided into 303 cases and 303 controls. To account for the effect of age, frequency matching was performed for group matching. However, other factors were not matched in order to measure their effects [24].

### Data preprocessing

Data preprocessing involves several steps. In the parsing step, individual data elements were identified in the source files and isolated in the target files. These parsed data elements were then corrected using sophisticated data algorithms in R, and the data was standardized and transformed into its preferred format.

To handle missing data, imputation methods such as mice in R were used to fill in missing values. The missing data was also removed to compare the results of these two approaches, and the results were found to be the same. As a result, removing the missing data was chosen as the preferred method for proceeding with the analysis.

### Breast cancer prediction models

This paper proposes a method that combines feature selection techniques with machine learning methods to predict prospective cases. Four different methods were used to extract features. The first method is the information.gain decision tree algorithm, which selects the best combination of features based on their correlation with class attributes using a function based on entropy. The second method is the Elastic net algorithm, which balances between LASSO and ridge penalties to address over-regularization. This is achieved by setting a hyper-parameter called Alpha, where Alpha = 1 results in a LASSO model and Alpha = 0 results in a ridge model. This technique, known as Elastic net, is a regularization regression that uses the cv.glmnet function with the family set to 'binomial'.

The third method used in this paper is Random Forest, which uses the built-in random Forest function to extract important variables using the importance function. This feature selection method falls under the category of embedded methods. Each random forest contains 4 to 12 hundred decision trees, each built using a random sample of observations and features from the dataset. Each individual tree consists of a sequence of yes-no questions based on single or combined features.

The fourth method used is principal component analysis, which is a widely recommended method for reducing a dataset with many variables. This is achieved by projecting the data onto fewer variables using linear combinations of the original variables, using the prcomp function in the latest version of R Studio software.

## Results

When using the Information.gain algorithm on a small sample size of the data set, the 10 most important factors that had an effect on breast cancer were identified and ranked according to their coefficients. These factors, in order of importance, were: family cancer, scancerb (Individual history of breast cancer), sampling B (Biopsy sampling), rarely consumption of a dairy meal, fruit meal, and vegetable meal daily, table salt, fast food consumption, oil consumption and type of job. As shown in Figure 1, the results for this method using a large sample size of the data set are the same as those for a small sample size, with the exception of the type of job. For the larger sample size, age with a coefficient of 0.05 was identified as an important factor instead of type of job.

As shown in Figure 2, the Elastic net results identified the 10 most effective factors on breast cancer as family cancer, pregnancy number, pregnancy tendency, first menstruation, abortion, childbirth (the age when they gave birth to the first child), childbirth number, stillbirth, scancerb (Individual history of breast cancer), sampling B (Biopsy sampling).

The results for the Elastic net algorithm were the same for both large and small sample sizes of the dataset.

According to the Random Forest algorithm, for the small sample size, the 10 most important factors that affected breast cancer were identified as family cancer, sampling B, scancerb, rarely consumption of dairy, fruit, and vegetable meals daily, job type, table salt, fast food consumption, and first menstruation (Fig. 3).

**Fig. 1.** The 10 most important risk factors of breast cancer in the larger sample selected by Information.gain function from the Decision Tree algorithm.

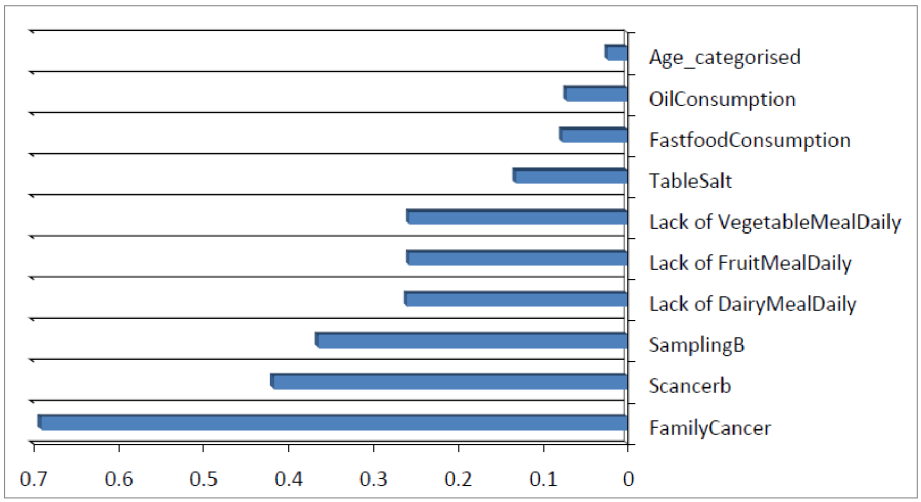
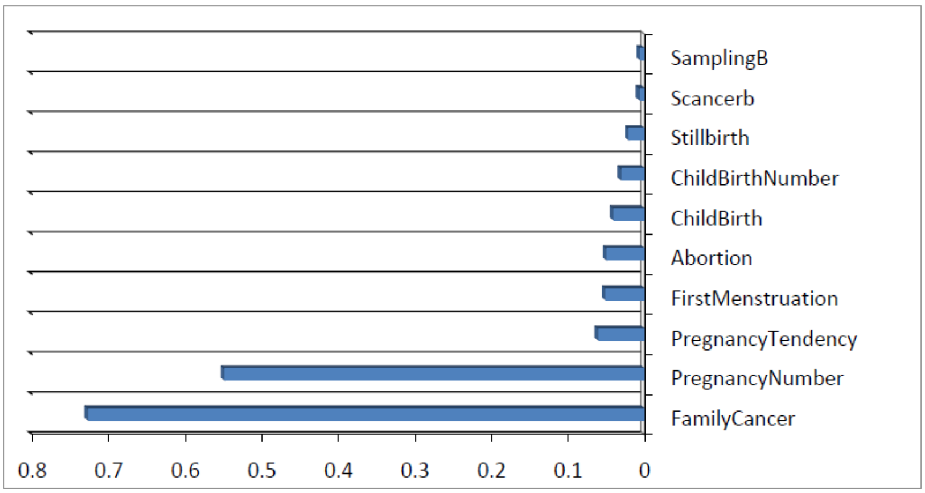



**Fig. 2.** The 10 most important risk factors of breast cancer selected by the Elastic Net algorithm.




For the large sample size of the dataset using the Random Forest algorithm, two different factors were identified as important: age and number of pregnancies, instead of type of job and age at first menstruation.

When using Principal component analysis, as shown in Figure 4, the 10 most important risk factors for breast cancer were identified as the same in both sample sizes including pregnancy tendency, first menstruation, pregnancy number, childbirth number, childbirth (the age of first giving birth), abortion, stillbirth, scancerb, sampling B and family cancer (Fig. 4).

## Discussion

This case-control study investigated the most important risk factors associated with breast cancer among Iranian women. Four machine learning methods were performed in this study including Decision Tree (DT), Random Forest (RF), Logistic Regression (LR), and Principal Component Analysis (PCA). Based on all 4 machine learning algorithms, family history of cancer, biopsy sampling, and individual history of breast cancer were the most important risk factors for breast cancer.

A case-control study indicated that family and personal history of breast cancer were the most important risk factors for breast cancer [25]. Women with two or more persons of breast cancer in their family among women younger than 50 years, or three or more persons at any age, but who do not have BRCA mutations, are about 4 times more likely to have breast cancer [26]. These studies are consistent with the findings of all four machine learning methods in our research. Thakur P et.al found that early menstruation increases the risk of breast cancer by more than two times [27]. Numerous other studies have also corroborated this finding [28, 29]. Based on the RF, LR, and PCA in our study, early menarche was among the top 10 associated risk factors of breast cancer. However, a cohort study found no association between early menstruation age and the risk of breast cancer [30].

**Fig. 3.** The 10 most important risk factors of breast cancer selected by the Random Forest algorithm.

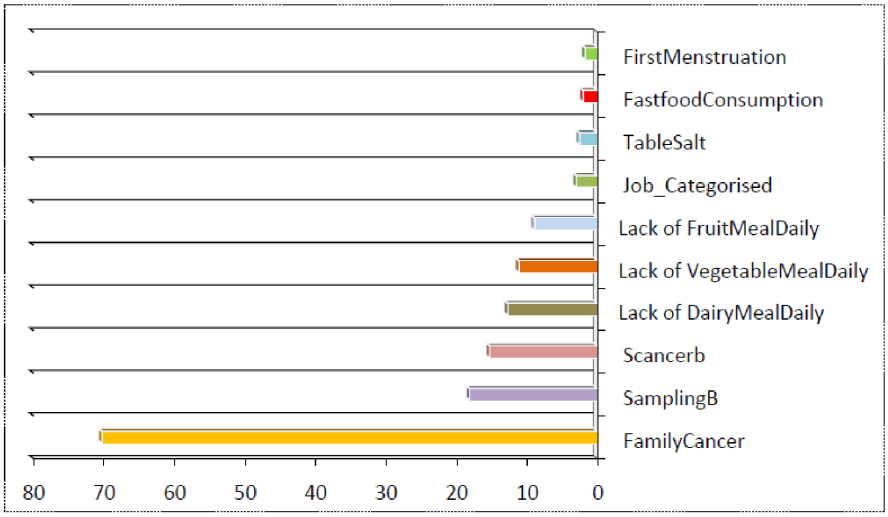
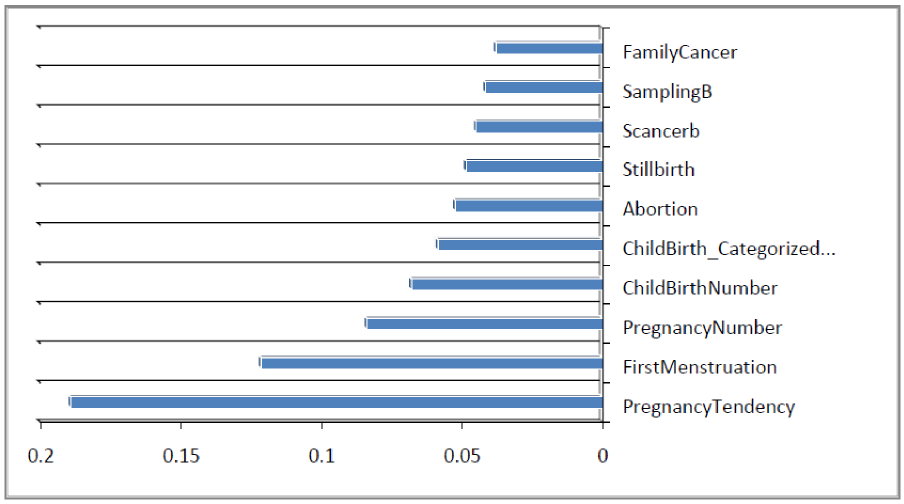



**Fig. 4.** The 10 most important risk factors of breast cancer selected by the Principal Component Analysis algorithm.




According to a case-control study, the risk of breast cancer is inversely related to the number of children born. Women who have had five or more children have a 50% lower risk of developing breast cancer compared to women who have never given birth [31]. Also, a systematic review and meta-analysis in the Eastern Mediterranean region found that having no history of live birth was among the factors that had the largest odd ratios for breast cancer [32]. Our observations showed that the number of pregnancies was only in LR and PCA models among the 10 risk factors associated with breast cancer.

Diet can play an important role in the prevention and management of many diseases, including breast cancer. A systematic review and meta-analysis showed that there was only an association between milk consumption and breast cancer among dairy products. Consumption of more than 450 grams of milk per day was associated with an increased risk of breast cancer. Also, a diet rich in vegetables, fruits, and soy products, and low in red meats, has been associated with a lower risk of breast cancer [33]. Our DT and RF models showed that low consumption of dairy products, fruits, and vegetables was associated with breast cancer risk. However, Patricia M et al. found that there was no significant relationship between dairy consumption and the risk of breast cancer [34].

It is important to note that this study has some limitations that should be considered. First, we only used four machine learning models in our study. Second, the data for this study was collected from hospitals affiliated with Mashhad University of Medical Sciences. As a result, there is uncertainty about whether the prediction model developed in this study can be applied to other datasets from different populations or regions.

## Conclusions

Our study showed that the use of machine learning methods can play an effective role in predicting breast

cancer risk factors in Iranian population with large sample size and different characteristics. Future research could involve using classification techniques to train machine learning models on the data. These models could then be used to make predictions or classifications based on the patterns and relationships identified in the data.

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## Conflict of interest statement

The authors declare that they have no conflicting interests.

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This study had no specific funding and was done with the authors' interest.

## Ethical statement

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, *etc.*) have been completely observed by the authors.
The study has ethical approval from Mashhad University of Medical Sciences (ID: IR.MUMS.REC.1397.125).

## Author's contributions

MT-S, E-MF, Z-SH, AK, S-MT, MY: study conception and design; MY, Z-SH: data collection; AK, S-MT: analysis and interpretation of results; AT, S-MT: draft manuscript preparation; MT-S, Z-SH, E-MF, AK, S-M, T, MY: reviewed the results and approved the final version of the manuscript.

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