

Iranian Quarterly Journal
of Breast Disease. 2022;
14(4):21-30.

Original Article

Evaluation of Salivary Level of Heat Shock Protein 70 in Patients with Breast Cancer

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Receive: 23/8/2021
Accepted: 5/12/2021

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Ethics Approval:
IR.TBZMED.REC.1399.349

Abstract

Introduction: Breast cancer is the most common cancer diagnosed among women worldwide. Increased molecular and genetic information about cancer has improved diagnostic, screening, and treatment methods for cancer. Heat shock protein 70 (HSP70) is overexpressed in breast cancer patients and involved in malignant properties of breast cancer. Due to the noninvasive nature of saliva collection and the fact that no study has been performed on salivary HSP70 levels in patients with breast cancer, the aim of this study was to evaluate the diagnostic value of salivary HSP70 in these patients.

Methods: Saliva samples from 45 patients with breast cancer and 45 age-matched healthy subjects were collected. Salivary HSP70 was measured with the enzyme-linked immunosorbent assay method. The results were analyzed using a Mann-Whitney test. The sensitivity, specificity, and diagnostic value of this protein were evaluated through the ROC curve and cutoff point determination. The software used in this study was SPSS 25, and a P value of less than 0.05 was considered significant.

Results: The mean salivary HSP70 level was 15.41 ± 8.82 ng/ml in patients compared with 15.03 ± 6.28 ng/ml in the control group ($P > 0.05$). Also, the area under the ROC curve was 0.497.

Conclusion: The results showed that salivary HSP70 levels were not significantly different between patients with breast cancer and healthy individuals, and according to the ROC curve, the salivary level of this protein has no diagnostic value in these patients.

Keywords: Axillary lymph Node, Breast Cancer, HSP70, Saliva

Introduction

Breast cancer is the most common cancer diagnosed among women worldwide (1). Heat shock proteins (HSPs) are produced by cells in stressful conditions. Recent studies have reported increased expression of HSP70 in breast cancer and shown that this protein plays an important role in tumor cell proliferation, differentiation, invasion, and metastasis (2-4). The high prevalence of breast cancer and its high mortality necessitates the identification of tumor-associated molecular markers for early diagnosis and better treatment of this cancer. Because of the easy and noninvasive nature of saliva collection, our aim in this study was to evaluate salivary HSP70 levels and the diagnostic value of this marker in patients with breast cancer. It is also noted that there is no study on the evaluation of salivary HSP70 levels in breast cancer patients.

Materials and Methods

In this study, salivary samples from 45 patients with breast cancer and 45 age-matched healthy subjects were used. Also, the group with breast cancer was divided into two subgroups with and without axillary lymph node involvement. Salivary HSP70

was measured by the enzyme-linked immunosorbent assay method. The results were analyzed using a Mann-Whitney test. The sensitivity, specificity, and diagnostic value of this protein were evaluated through the ROC curve and cutoff point determination. Data were analyzed with SPSS 25, and a P value of less than 0.05 was considered significant.

Results

In this study, the mean salivary HSP70 level was 15.41 ± 8.82 ng/ml in patients and 15.03 ± 6.28 ng/ml in the control group ($P > 0.05$). There was also no significant difference in the mean HSP70 level between patients with axillary lymph node involvement and patients without axillary lymph node involvement ($P = 0.673$). Figure 1 shows the ROC curve. The optimal cutoff point is shown on the curve with an arrow. Also, the area under the ROC diagram was 0.497, which indicates that salivary HSP70 does not perform well in the correct diagnosis of healthy individuals and patients with breast cancer.

The standard error (P-value) and 95% confidence interval for the cutoff point are reported in Table 1.

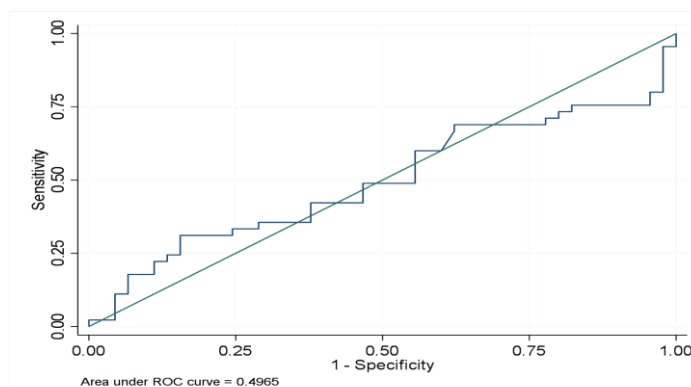


Figure 1: ROC curve to show the salivary diagnostic value of HSP70

Table 1 :Measurement of Diagnostic Value of HSP70 Saliva in the ROC cCurve

Specificity	Sensitivity	The Area Under the Curve	95% Confidence Interval	Standard Error (P-value)
40%	71%	0.497	0.37-0.62	0.063

Discussion

Early detection of breast cancer plays an important role in preventing the progression of this disease. The results showed that the salivary level of HSP70 has no diagnostic value in patients with breast cancer. Jagadish et al. (3) showed that there is an increase in HSP70 expression in 83% of breast cancer patients. They also showed that removing HSP70 from cancer cells significantly reduced cell growth and stopped the cell cycle in the animal model and suggested that decreasing HSP70 reduced oncogenes and increased tumor suppressor genes. Several studies have also shown that increased expression of HSP70 is associated with poor differentiation of breast cancer cells, lymph node metastasis, increased tumor size, p53 mutation, and higher tumor grade (2-6). Gunaldi et al. (4) showed that serum HSP70 levels in breast cancer patients were significantly higher than in the control group, but no significant difference was found between different types of breast cancer. They suggested that HSP70 may be involved in proliferation, cell cycle, migration, and invasion of cancer cells. It has also been suggested that HSP70 induces the expression of oncogenes such as cyclins

and mutations in tumor suppressor genes, inhibiting apoptosis and leading to the proliferation of cancer cells. Studies have also shown that 10 to 25 percent of breast cancer patients have anti-p53 antibodies in their blood, and all tumors have the p53-HSP70 complex, indicating that HSP70 is involved in the presenting of the p53 antigen (2-6).

Because salivary HSP70 levels had not been measured in breast cancer, it was not possible to compare this study with previous studies. Regarding the different nature of the serum and saliva, and considering that no association between serum and salivary HSP70 has been shown so far, it is not possible to compare the results of the current study with those measuring HSP70 in patients' serum.

Conclusion

The results of the present study showed that salivary HSP70 levels were not significantly different between breast cancer patients and healthy individuals. The ROC curve showed that the salivary level of this protein has no diagnostic value in these patients.

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