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Original Article

Measurement of Serum Survivin to Discriminate Patients with Breast Cancer from Normal Subjects

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ABSTRACT

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Key words
Breast cancer
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Background and Aims: There is now an increasing body of evidence that survivin is a protein, expressed highly in breast cancer. The signaling interaction of protein survivin in breast cancer is still unclear, but physiological regulation of survivin seems to be linked to the breast cancer occurrence and severity of it.

Materials and Methods: Serum samples were obtained from April 2015 to November 2017 out of women enrolled in a group undergoing annual breast cancer testing. Routine blood samples were analyzed at the Biochemical Laboratory of Rouhani Babol University Hospital .

Results: Serum levels of survivin in patients with breast cancer group increased compared to the healthy controls [207.520±110.284 (mean±SD) vs. 126.212±53.130, ng/L, $p<0.001$]. Also, we detected a positive correlation between elevated serum survivin level and clinical characteristics of patients with breast cancer.

Conclusions: Serum survivin measurement was shown to discriminate patients with breast cancer from healthy controls. However, further studies are needed to confirm this role and its benefits.

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Introduction

Despite significant advances in biochemical and clinical techniques, the prognosis for patients with breast cancer remains poor. Identification of noninvasive biomarkers for early detection of breast cancer is important to improve these patients' prognosis. Early detection of breast cancer is very critical, because it gives patients a better chance of treatment and recovery from the disease. The over-expression of survivin in breast cancer cells has been investigated by researchers. Despite these observations, very little is known about the role of survivin [1]. Researchers have recorded a new event where biochemical markers are an important factor in the diagnosis of breast cancer. As reported by the investigators, survivin expression is significantly correlated with the breast cancer status [2]. There is growing evidence suggesting that exhibiting a different expression of survivin can work as a diagnostic biomarker in breast cancer subjects [3]. A study has indicated that survivin is a protein, and expression of survivin in MCF-7 cells has been reported [4]. Researchers have found antibodies that are specific for survivin, but these antibodies are absent in the blood samples of healthy individuals [5]. As indicated previously, surviving is a protein with 142 amino acid residues and plays an important role as the prognostic biomarker for tumor [6]. The expression of survivin is modulated in breast cancer [7]. A previous report has suggested that nuclear survivin expression is significantly correlated with breast cancer status [2]. It is evident that the regulation of expression of survivin in breast cancer provides a promising strategy for the treatment of patients with breast cancer [1]. Morusin regulates the expression of the survivin in breast cancer cells [8]. The mechanism underlying the role of survivin in breast cancer is still a matter of controversy. This study explored the relationship between the levels of survivin content and clinical characteristics in patients with breast cancer.

Materials and Methods

Vortex mixer labnet, centrifuge (Clement 2000, Australia), water bath (Fanazmagostar Co WM22), Dionizer (HastaranTeb Co), Microplate reader with 450±10 nm filter (Raytolife, coated elisa plate, and analytical science Model RT-2100 C, Hamburg, Germany) were used. In our ongoing research projects on the human cancer mechanism, we undertook the present project. In this study, we attempted to determine whether survivin could be used as a biomarker in patients with breast cancer.

All chemicals were of the highest purity available. Human survivin enzyme-linked immunosorbent assay (ELISA) kit, ELISA was purchased from Bioassay Technology laboratory Co.

Between April 2015 and November 2017, patients from the Babol University of Medical Sciences, Rouhani Hospital were asked to take part in the study. Twenty one individuals were enrolled in the research. Some individuals

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(n=4) were excluded because they did not have sufficient quantity for analysis. The serum samplesof the remaining 17 female subjects enrolled are undergoing annual breast cancer testing at first stage, were used. Once the participants signed the informed consent, venous blood specimens were obtained throughout the morning fasting state, with minimal stasis in evacuated tubes. After at least 30 minutes, the tubes were centrifuged at 25˚C for 15 minutes at 1250*g. We determined sera survivin in 17 patients with breast cancer and in 24 healthy control subjects with ELISA method. Healthy controls were defined as women who had been followed for at least 2 years on a study with no breast cancer diagnosis. Exclusion criteria of the patients were: (i) those with other cancer or malignant diseases, (ii) those who had received chemotherapy or radiation therapy. We collected the data for each patient. The subsequent data were noted down: age, body mass index, smoking habit as well as some biochemical characteristics. All the patients yielded written informed consent and accepted to participate in the study. The study protocol and written consent procedures were approved by the Ethics Committee of Babol University of Medical Sciences (MUBABOL.REC.1394.305). Routine blood analyses, including serum biochemical parameters, were analyzed at the Central Laboratory of Rouhani Babol University Hospital. Survivin concentrations were determined by using an ELISA method.

Statistical analysis

Results were expressed as mean±standard deviation (SD) in the study. Descriptive statistics and analysis were performed in SPSS16 for windows.

Results

This study explored the relationships between the levels of survivin content and clinical characteristics in breast cancer patients. Serum levels of survivin in the breast cancer patients [207.520±110.284 (mean±SD)] increased compared to the healthy controls (126.212± 53.130, ng/L, $p<0.001$) as shown in figure 1.

Age, body mass index, smoking habit and as well as some biochemical markers of control and patient groups were demonstrated in table 1.

Table 1. Age, body mass index, smoking habit and some biochemical characteristics of control and patient groups

Variable	Control group	Patients group
Age(years)	29-83	33-78
Body mass Index (kg/m^2)	22.4-29.6	19.9-34.2
Smoking habit	No	No
Fasting blood sugar (mg/dl)	102-247	73-121
Calcium (mg/dl)	9.6-9.7	9.7-10.6
Aspartate aminotransferase (U/L)	10-17	14-28
Alanine aminotransferase (U/L)	14-16	19-47

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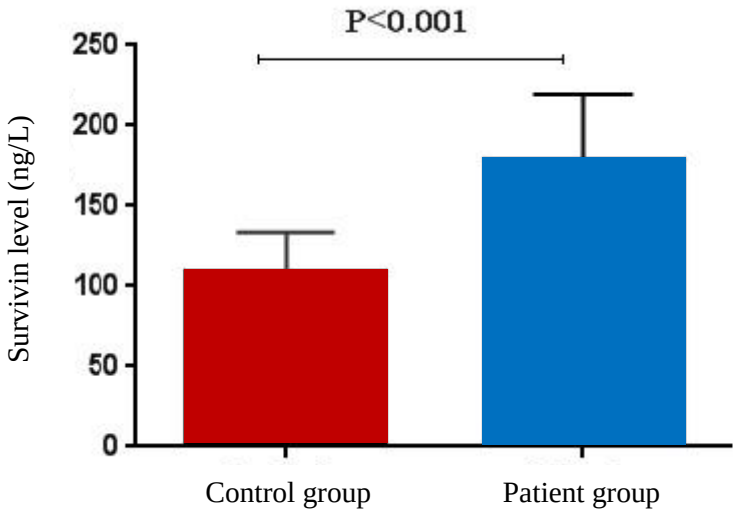

Fig. 1. Serum survivin content in the breast cancer patients group increased compared to that in the healthy controls.

Discussion

The main findings of the current study was that serum survivin levels increases in patients with breast cancer and it correlates with the clinical parameters of breast cancer. There is an association of survivin level with clinical parameters in breast cancer. We suggest additional studies to establish the importance of survivin in breast cancer in terms of pathogenesis and management of that the disease; it improves the characteristics of life in these patients. We suggest that survivin be routinely used as serum markers for detection of breast cancer. Therefore, these findings demonstrate that survivin bears the capacity to be a biomarker for breast cancer diagnosis.

Our results confirms the findings of other investigators [1-3, 7, 12]. Many biomarkers are routinely used as serum markers for detection of cancer [9-11].The expression of survivin is correlated with the proliferation and apoptosis of breast cancer cells [12]. It is difficult, however, to compare our results with other studies because they used different study designs, had different populations, investigated different sample types and utilized a variety of analytical methods to measure survivin.

Despite all these positive findings and recommendations, some limitations and methodological defects of this study should be reminded. Firstly, the number of subjects comprising the experiment was small and it is substantial to include a much larger population and secondly, use additional laboratory methods to confirm the results.

Conclusion

In the current study, we showed that survivin levels in serum samples of patients with breast cancer are significantly higher than those in healthy individuals. Thus, measurement of the serum level of survivin is useful for predicting the prognosis of patients with breast cancer. Based on our present findings, the sera marker can be useful for the early diagnosis of breast

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cancer. Further efforts are required to achieve a greater understanding of the role of survivin in breast cancer.

Conflict of Interest

The authors assert there are no conflicts of interest regarding the publication of this article.

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