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Original scientific paper

The Level of Serum Pro-Matrix Metalloproteinase-2 as a Prognostic Factor in Patients with Invasive Ductal Breast Cancer

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A B S T R A C T

This paper analyses data of 150 female patients undergoing surgical treatment for invasive ductal breast cancer at the University Hospital for Tumors from January 2006 to January 2007. The control group consisted of 50 healthy women. The patients were classified into three groups, depending on their tumor differentiation, i.e. grade I, II and III tumor groups. Each group consisted of 50 patients. Traditional prognostic factors including: age, tumor size and differentiation grade, axillary lymph node status, presence of distant metastases, steroid receptor findings, vascular invasion of the primary tumor, presence of an extensive intraductal component (EIC) in the primary tumor, HER-2 protein expression were evaluated. Both the patients' and controls' serum levels of proMMP-2 (pro-matrix metalloproteinase-2) were assessed using the ELISA method. The aim of the study was to assess pathohistological prognostic factors and the level of serum proMMP-2 in the three patient groups and the controls, compare the relationship between the prognostic factors and the level of serum proMMP-2 in the patient groups, and upon the results, determine possible features of proMMP-2 as a prognostic factor in breast cancer patients. The study results showed no difference in proMMP-2 concentrations between the three patient groups and the controls. No statistically significant difference in the serum proMMP-2 concentration was found between the patient groups, although the grade III group values were the highest showing a trend toward statistical significance. Comparison of proMMP-2 and prognostic factors revealed a statistically significant correlation between proMMP-2 and age in patients with histologic grade I tumors. There was no statistically significant correlation between circulating proMMP-2 and other pathohistological prognostic factors.

Key words: *circulating proMMP-2, ELISA, serum, invasive ductal breast cancer, breast cancer, prognostic factors*

Introduction

Breast cancer is the most common female malignant tumor representing 27% of all female cancers, while the disease is rare among men.

Breast cancer must be regarded as a disease that is dependent on numerous interactions of both external and internal (genetic, hormonal and metabolic) factors.

Invasive ductal carcinoma is the most common type of breast cancer, accounting for 65–80% of all mammary carcinomas. Its histological picture is characteristically diverse as regards the growth pattern, cell appearance and their mitotic activity.

This is an explicitly heterogeneous group of tumors that covers a full spectrum of favorable to greatly unfa-

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vorable prognostic factors of which the most important are lymph node status, histologic tumor grade and tumor size, presence of steroid receptors and HER2/neu status[1].

The HER2/neu is a biological prognostic factor, a proto-oncogene occurring in locus 17q21 and encoding the 185-KDA transmembrane domain of the epidermal growth factor receptor. Gene amplification and protein overexpression of HER2/neu are characteristics of breast cancer. Several studies have confirmed that HER2/neu onco-gene overexpression is associated with a poorer prognosis. The good side of HER2/neu expression is the possibility of using Herceptin (trastuzumab) therapy, i.e. monoclonal antibody therapy which specifically targets HER2/neu protein[2,3].

Besides cellular proteins, there are also extracellular proteins that play a role in the tumor growth and development. These include matrix metalloproteinases that constitute a large family of proteolytic enzymes and are involved in physiological (the menstrual cycle, bone remodeling process, and normal immune response to infection) and pathological processes of the body. To date, twentyfive MMPs are described, all of them showing a zinc-dependent catalytic domain (Zn++) and classified on the basis of their substrate specificity[4].

MMP-2 is a matrix metalloproteinase that plays a key role in the processes of tumor invasion and metastasis for their capacity to degrade extracellular matrix protein[5,6]. This is especially important in the degradation process of collagen type IV and gelatin type that forms basis of the cell basement membrane. MMP-2 includes a special activation mechanism that requires the presence of both tissue inhibitor matrix metalloproteinase-2 (TIMP-2) and membrane type-1 matrix metalloproteinase (MT1-MMP). TIMP-2 binds to the MT1-MMP catalytic domain of the cell surface. Full activation is achieved through either intramolecular autocatalytic mechanisms or plasminogen-plasmin system activation. At low concentrations, TIMP-2 functions as a positive regulator of MT1-MMP, whereas at high concentrations, TIMP-2 as well as TIMP-3 and TIMP-4 may completely inhibit the activity of proMMP-2[4,7,8].

Experimental murine breast carcinoma with brain metastases shows an increased expression of gelatinases and MMP-2 activity as compared to normal brain tissue[7–11].

There are not enough data available for circulating matrix metalloproteinases in relation to malignant tumor progression. For this reason, the aim of this study was to assess the preoperative circulating serum levels of both proMMP-2 and proMMP-2/TIMP-2 complex in 150 patients with invasive ductal carcinoma of the breast. The preoperative evaluation included pathohistologic prognostic factors (tumor size and differentiation grade, axillary lymph node status, distant metastases, steroid receptors, vascular invasion, presence of an extensive intraductal component (EIC) in the primary tumor, HER-2/neu protein expression) and their relationship with serum concentrations of proMMP-2 and proMMP-2/TIM-2. The aim of the study was to compare serum concentrations proMMP-2 and proMMP-2/TIM-2 in cancer patients with healthy controls.

Materials and Methods

The study included 150 patients with primary breast cancer treated at the Surgical Oncology Department, University Hospital for Tumors in Zagreb.

According to their tumor differentiation (grade I, II, III), the patients were classified into three groups of 50 patients each.

All patients underwent either conservative breast surgery (segmentectomy) with the adjacent lymph node dissection or breast ablation with axillary dissection. After surgery, the material obtained was pathohistologically processed. This includes fixation of the resection material using 10% buffered formalin, paraffin embedding of tissue specimens, tissue sectioning in 5ìm slices and staining with hemalaun-eosin. The slides were examined by light microscopy to determine tumor grade, and assess axillary lymph node status, vascular invasion of tumor tissue and the presence of an extensive intraductal component (EIC). Immunohistochemical staining using murine monoclonal antibodies to identify steroid receptors was performed following Microwave Streptavidin ImmunoPeroxidase (MSIP) protocol on the DAKO Autostainer Universal Staining System. The results of immunohistochemical staining were assessed by a semi-quantitative method, as follows:

- negative reaction (0) – less than 5% of tumor cells were positive
- weak positive reaction (+) – 5–10% of tumor cells were positive
- moderate positive reaction (++) – 10–50% of tumor cells were positive
- strong positive reaction (+++) – more than 50% of tumor cells were positive.

HER-2 protein expression was assessed using Hercep-Test (DAKO kit, NoK 5204). The test uses standard reagents to be placed on a third section of each tumor, and the scores are defined according to the manufacturer's recommendations as follows:

- negative reaction (–): 0–30% of tumor cells with negative reaction or weak membrane staining
- weak positive reaction (+): >30% positive tumor cells with partial membrane standing
- moderate positive reaction (++):>30% positive tumor cells with moderate strong membrane staining
- strong positive reaction (+++): >30% positive tumor cells with complete strong membrane staining.

Patients in whom immunohistochemical analysis of HER-2 receptor showed moderate strong positivity (2+) underwent retesting by use of a hybridization method. These are molecular methods based on mutual hybridization of single-stranded complementary nucleic acid sequences. The hybridization phase includes two different

components: a labeled nucleic acid sequence (probe) and homologous nucleic acid sequence (DNA, RNA) from fixed cytogenetic material to be used for diagnostic purposes. The probes are labeled with fluorochrome or macromolecules that are strong immune genes (digoxigenin, biotin). Depending on probe labeling, two hybridization techniques are distinguished, i.e. FISH – fluorescence in situ hybridization and CISH – chromogenic in situ hybridization.

Blood samples for MMP-2 test were collected from patients at primary diagnosis. Serum for MMP-2 test was separated from venous blood that was collected in a test-tube, left to clot at room temperature for 30 min and further centrifuged at 3000 rpm for 10 min. The separated serum was kept frozen at –20 °C until needed for use. The control group consisted of 50 healthy women.

Enzyme-linked immunosorbent test (ELISA) was used to detect free circulating pro-MMP-2 and proMMP-2--TIMP-2 complex levels. A commercial assay kit – Human Biotrak ELISA system by Amersham Biosciences, Buckinghamshire, UK – was used to detect MMP-2. The assay for total proMMP-2 (RPN2617) identifies the free form of circulating proMMP-2 and proMMP-2-TIMP-2 complex. The ProMMP-2-TIMP-2 complex level was assessed in microtiter plates coated with the monoclonal anti-TIMP--2 antibody (clone T2-101, SBA Sciences, Oulu, Finland). Diluted serum sample and the polyclonal anti-MMP-2 antibody (clone DB-202, SBA Sciences, Oulu, Finland) were also added. The present MMP-2 was all bound to the microtiter plate walls, while other serum components were removed by washing and aspiration. MMP-2 was detected with the anti-MMP-2 antibody coated with peroxidase enzyme that serves as enzyme conjugate (Chemocon International, Temecula, Calif), and the reaction was demonstrated by adding o-phenylendiamine dihydrochloride enzyme substrate (Sigma, Steinheim, Germany). Readings were taken on the 450 nm wave--length spectrophotometer (Photometer Spectra 2, Tecan--Ortho). The sensitivity of the assay for proMMP-2 is 0.37 ng/mL.

All the results were processed using descriptive statistical methods. The ANOVA (one-way analysis of variance) was used to test the differences between quantitative variables. To assess the correlation between proMMP-2 and other prognostic factors for breast cancer linear correlation analysis was employed.

Results

The study included 150 patients. The mean age of all patients was 59.5 years. According to their tumor differentiation grade, the patients were assigned to one of three groups of 50 patients each.

The age range in the grade I, grade II and grade III group was 37–81 years (mean age 59), 45–82 years (mean age 55.5 years) and 36–83 years (mean 59.5 years) respectively.

Analysis of axillary involvement by lymph node metastases showed 89 lymph node-negative patients (59.3%), and 61 patients (40.6%) had lymph node metastases.

Analysis of estrogen (ER) and progesterone (PR) receptors revealed the following: 92 patients (61.3%) with ER+PR+, 37 patients (24.66%) with ER-PR-, 19 patients (12.6%) with ER+PR- and 2 patients with ER-PR+. A comparison of hormone receptors by tumor grade showed a statistically significant difference between grade I and grade III, and between grade I and grade III tumors.

Among the 150 study patients with invasive ductal breast cancer, 48 (32%) patients tested positive for the HER-2 protein, while in 102 (68%) patients the result was negative.

The presence of vascular invasion was observed in 24 (16%) patients, and its absence was shown in 126 (84%) patients.

An extensive intraductal component was found in 46 (30.6%) patients, and not documented in 104 (69%) patients.

A comparison of tumor diameter by tumor grades showed a statistical significance between grades I and II, grades I and III, and grades II and III. The largest mean tumor diameter was in the grade III group, and the smallest mean tumor diameter was observed in the grade I group.

Vascular invasion as a negative prognostic factor was shown to be most pronounced in the grade III. The HER-2 protein as an important predictor and prognosticator was shown to be comparable in the grade II and III groups, and the least expressed in the grade I group.

ProMMP-2

A comparison of the serum proMMP-2 level in healthy controls and patients classified into three histologic tumor grade groups is shown in Table 1. No statistically significant difference in the proMMP-2 level was found between of the controls and patient groups ($p=0.337$). The highest levels and the highest overall mean of proMMP-2 were reported for the grade III group (Table 1). To substantiate the statistical significance in a larger patient sample a further investigation is required

The correlation between the healthy control proMMP-2 level and age was not statistically significant ($p=0.175$).

TABLE 1
COMPARISON OF PROMMP-2 LEVELS BETWEEN CONTROLS AND THREE PATIENT GROUPS

ProMMP-2 ng/L	Controls	Grade I	Grade II	Grade III
N	50	50	50	50
$\overline{X}$	1292.54	1224.67	1268.10	1321.82
SD	239.55	293.81	333.44	274.42
sem	33.88	41.55	47.16	38.81
Maximum	1728	1875	1815	2125
Minimum	783	380	255	497

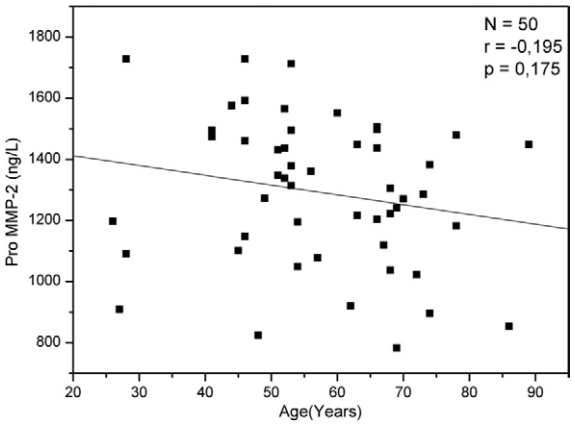

Fig. 1. Correlation proMMP-2 and age of the healthy control.

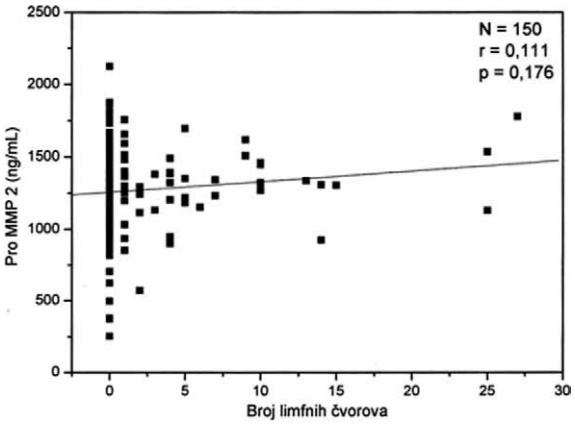

Fig. 3. Correlation proMMP-2 level with the number of positive lymph nodes.

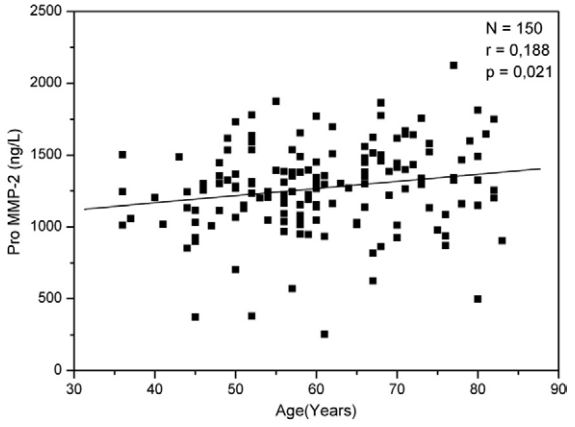

Fig. 2. Correlation proMMP-2 and age of all study patients.

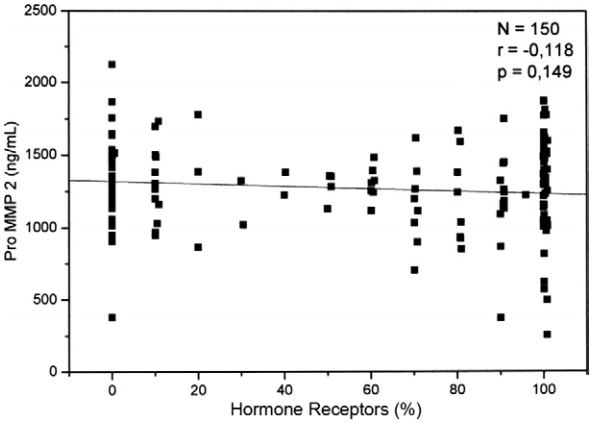

Fig. 4. Correlation proMMP-2 level and steroid receptor levels.

The serum proMMP-2 level in old age had a tendency towards lower values. The correlation between the proMMP-2 level and age of all breast cancer patients showed a tendency towards an increase of proMMP-2 concentrations in old age; the finding was statistically significant (p=0.0021) and actually contrary in relation to this in healthy controls (Figures 1 and 2).

A comparison of the proMMP-2 level with the number of positive lymph nodes did not reveal any statistically significant correlation (p=0.176) between the two variables. Patients with a larger number of tumor-involved lymph nodes presented higher levels of serum proMMP-2 (Figure 3).

The correlation of proMMP-2 and steroid receptor levels was shown to be weak negative and statistically insignificant (p=0.149). Patients with positive steroid receptors showed a tendency towards lower levels of serum proMMP-2 (Figure 4).

The serum proMMP-2 level in correlation with vascular invasion showed a weak, statistically insignificant correlation (p=0.156).

PromMP-2 in relation to EIC also showed a weak, negative and statistically insignificant correlation (p= 0.72). In patients with histologically confirmed EIC component the level of serum proMMP-2 had a tendency towards lower values.

A comparison of proMMP-2 and HER-2 protein did not show any statistical significance (p=0.776). HER-2-positive patients had lower serum proMMP-2 levels compared to HER-2-negative patients in whom the levels of serum proMMP-2 were higher.

Discussion

Breast tumor is a pathohistologically and clinically heterogeneous disease, and of different prognostic patterns. The most common is a malignant female tumor that accounts for 27% of all malignant diseases in women.

It has been generally accepted that the different clinical course and different outcomes of the disease in patients with the same histologic tumor type are the result of molecular differences between carcinomas.

Recently, the importance of proteases related to the tumor, tumor invasion and metastasis has been shown in various tumors, including the tumor of the breast. Matrix metalloproteinases are being intensely investigated as a potential prognostic factor in breast cancer patients[7,8].

MMP-2 is one of MMP family members involved in the process of tumor invasion and metastasis, first of all for its unique ability to disintegrate the type IV collagen, which is the main component of cell basement membrane, and this is considered to play a crucial role in invasion of malignant tumors. Recent studies show MMP-2 to be intensely and invariably related to breast cancer, and this can be found in serum, urine, plasma and tissue of breast cancer patients. In biological systems and fluids, MMPs occur as inactive proenzymes, active enzymes and inactive enzymes bound by various inhibitors[5,10,12].

Some authors show the high level of serum MMP-2 to be related to a poorer prognosis in patients with positive axillary lymph nodes. Moses et al. report that that urine MMP-2 concentrations are increased in patients with breast cancer. For diagnostic purposes, Duffy recommends the assessment of MMP-2 as a prognostic factor in breast cancer[13,14].

Several recent studies have shown that the increased expression of tissue MMP-2 in breast carcinoma is related to poorer prognosis[15,16]. While the results of a series of studies of matrix metalloproteinase-2 expression in tumor tissue are largely in accord that the increased expression is an adverse predictor and prognosticator in breast cancer patients, this cannot be confirmed for the circulating MMP-2.

Which form of the circulating MMP-2 yields the best information about tumor progression and survival remains to be elucidated.

La Rocca et al. report on the results of their study showing a negative correlation between MMP-2 and estrogen receptors[17]. Sheen-Chen et al. publish their study demonstrating a statistically significant difference between MMP-2 concentrations assessed for two groups of breast cancer patients and report on the higher concentration of MMP-2 in patients with lymph node positive cancer and higher stage of the disease[18].

In their publication, Kuvaja et al. report for the first time on the inverse correlation of the concentration of total proMMP-2 and traditional prognostic factors (positive lymph nodes, high histologic tumor grade, higher stage of the disease) in breast cancer patients. There is a reference that the level of the circulating MMP-2 does not correlate with the tissue levels. It is assumed that the total proMMP-2 and proMMP-2-TIMP-2 complex levels in patients' sera prior to surgery suggest the presence of the disease, whereas the active form of MMP-2 could be related to the progression and spread of cancer and might suggest overall patient survival[4].

At the tissue level, the increased concentration of active MMP-2 may be explained by proteolysis and cell migration during the metastatic spread of the disease. This could also explain the concurrent lower value of serum active MMP-2 for its efficacy at the tissue level during the spread of carcinoma.

This study is aimed at assessing the significance of the obtained levels of proMMP-2 and proMMP-2-TIMP-2 complex as the pro-enzyme form of MMP-2 in preoperative serum of breast cancer patients. It has been assumed that the proMMP-2 concentration should differ in patients with different histologic grade of the disease. An attempt has been made to assess the significance of proMMP-2 in relation to tumor size, hormone receptor status, axillary lymph nodes, patient age, EIC, vascular invasion and HER-2 protein. Patients were classified into three groups according to the histologic grade of their tumor to be compared with the control group of 50 healthy women.

A comparison of the serum proMMP-2 level between the healthy controls and patients classified into histologic grade groups does not show any statistical significance of the difference between proMMP-2 concentrations, although the grade III group had the highest values of proMMP-2.

The study of Kuvaja et al. showed that the patients had higher serum levels of proMMP-2 in relation to healthy controls, and also lower serum levels of proMMP--2-TIMP-2 complex than the healthy controls[4].

The correlation between the healthy control proMMP-2 level and age showed a tendency towards lower values in old age, although without any statistical significance ($p=0.175$). In older age, levels of the majority of enzymes are physiologically reduced, and this correlation can thus be explained as a physiological event. On the other hand, comparing proMMP-2 levels with patient age a positive, statistically significant correlation was found, i.e. proMMP-2 had a tendency of increase towards higher levels in the grade I patients of old age ($p=0.0147$) as compared to all study patients ($p=0.0021$).

A comparison of proMMP-2 by tumor diameter, i.e. tumor size revealed a weak positive and statistically insignificant correlation ($p=0.157$). In their study Shu-Chih Liu et al. report also about the positive linear correlation between tissue and serum proMMP-2 levels and tumor size[19]. ProMMP-2 in relation to the number of positive lymph nodes in the axilla showed a weak positive and statistically insignificant correlation. Sirpa Leppa et al. did not find any statistically significant correlation between the serum MMP-2 levels and lymph node status, age and hormone receptors, and in larger tumors, the MMP-2 level showed a tendency towards an increase[20].

A comparison of proMMP-2 and HER-2 protein did not show any statistical significance. Patients who were HER-2-positive had lower proMMP-2 levels, and HER--2-negative patients showed higher levels of serum proMMP-2. These correlation results for HER-2 protein comply with the results obtained by the Finnish authors[4].

This study was aimed at comparing the proMMP-2 enzyme levels obtained in three patient groups with their HER-2 protein status as a prognostic factor and patients' age. The assessed correlation values showed to be statistically significant in relation to age of grade I patients and overall age in all patient groups. The total MMP-2 level was also assessed in this study. The study to distinguish the proMMP-2 from proMMP-2-TIMP-2 complex levels by Kuvaja et al. show the proMMP-2 levels to be

higher in patients in relation to healthy controls, in contrast to the proMMP-2-TIMP-2 complex levels which show to be higher in healthy controls[21].

In this study, a comparison of proMMP-2 levels in three patient groups did not show any statistically significant difference. The highest proMMP-2 levels, including the highest overall mean, were reported for the grade III group.

The obtained results apply to the total proMMP-2 without its dividing into proMMP-2 and proMMP-2--TIMP-2 complexes. The prognostic value of the circulating MMP-2 remains to be documented on a larger patient sample and a longer follow-up. Simplicity in obtaining samples as well as sample availability are also of utmost importance for both the assessment and longer follow-up of the circulating MMP-2.

Conclusion

The serum proMMP-2 levels did not show any statistically significant difference between the study patients classified into three groups according to their tumor differentiation grade (grades I, II and III). The proMMP-2 levels obtained from patients' sera in relation to their pathohistological prognostic factors revealed a statistically significant correlation between proMMP-2 and age in patients with histologic grade I tumors, including overall age in patient groups.

REFERENCES

1. ELSTON CW, ELLIS IO, GOULDING H, PINDER SE, Role of pathology in the prognosis and management of breast cancer. In: ELSTON CW, ELLIS (Eds) The Breast (3rd edition, Churchill Livingstone, London, 1998). — 2. ANDRULIS IL, BULL SB, BLACKSTEIN ME, SUTHERLAND D, MAK C, SIDLOFSKY S, PRITZKER KP, HARTWICK RW, HANNA W, LICKLEY L, WILKINSON R, QIZILBASH A, AMBUS U, LIPA M, WEIZEL H, KATZ A, BAIDA M, MARIZ S, STOIK G, DACAMARA P, STRONGITHARM D, GEDDIE W, MCCREADY D, J Clin Oncol, 16 (1998) 1340. — 3. ROSEN PP, Invasive ductal carcinoma. In: ROSEN PP (Eds) Rosen's breast pathology (2nd edition, Lippincott Williams and Wilkins, Philadelphia, 2001). — 4. KUVAJA P, TALVENSARI-MATTILA A, PAAKKO P, TURPEENNIEMI-HUJANEN T, Hum pathol, 37 (2006) 1316. DOI: 10.1016/2006.04.021. — 5. JINGA DC, BLIDARU A, CONDREA I, ARDELEANU C, DRAGOMIR C, SZEGLI G, STEFANESCU M, MATACHE C, J Cell Mol Med, 10 (2006) 499. DOI: 10.1111/1582-4934. 2006.00415. — 6. KALLAKURY BVS, KARIKEHALLI S, HAHOLU A, SHEEHAN CE, AZUMI N, ROSS JS, Clin Cancer Res, 7 (2001) 3113. — 7. ANDREW CN, Cardiovascular Research, 69 (2006) 614. — 8. BACHMEIER BE, NERLICH AG, LICHTINGHAGEN R, SOMMERHOFF CP, Anticancer Res, 21 (2001) 3821. — 9. BJORKLUND M, KOIVUNEN E, Biochim Biophys Acta, 1755 (2005) 37. — 10. CHAKARBOTI S, MANDAL M, DAS S, MANDAL A, CHAKARBOTI T, Mol Cell Biochem, 253 (2003) 269. DOI: 10.1023/1026093016148. — 11. DAVIS GE, SAUDERS WB, J Investig Dermatol Symp Proc, 11 (2006) 44. DOI: 10.1038/565 0008. — 12. BURRAGE PS, MIX KS, BRICKERHOFF CE, Front Biosci, 11 (2006) 529. DOI: 10.2741/1817. — 13. DUFFY MJ, Clinical Chemistry, 51 (2005) 494. DOI: 10.1373/2004.046227. — 14. LEPPA S, SAARTO T, VEHMANEN L, BLOMQVIST C, ELOMA I, Clin Cancer Res, 10 (2004) 1057. DOI: 10.1158/1078-0432. — 15. MARGARITONI M, Rak dojke – prevencija, detekcija, terapija (Školska knjiga, Zagreb, 1993). — 16. MOOK ORF, FREDERIKS WM, VAN NOORDEN CJF, Biochim Biophys Acta, 1705 (2004) 69. DOI: 10.1016/2004.09.006. — 17. LAROCCA G, PUCCI-MINAFARA I, MARRAZZO A, TAORMINA P, MINAFARA S, Br J Cancer, 90 (2004) 1414. — 18. SHEEN-CHEN SM, CHEN HS, ENG HL, SHEEN CC, CHEN WJ, Cancer Lett, 173 (2001) 79. — 19. SHU-CHIH L, SHUN-FA Y, KUN-TU Y, CHUNG-MIN Y, HUI-LING C, CHING-YI L, MING-CHIH C, YIH-SHOU H, Clin Chim Acta, 371 (2006) 92. — 20. SIRPA L, TIINA S, LEENA V, CARL B, INKERI E, Clin Cancer Res, 10 (2004) 1057. — 21. LI G, FRIDMAN R, KIM HR, Clin Cancer Res, 59 (1999) 6267.

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RAZINA SERUMSKE PRO-MATRIKS METALOPROTEINAZE -2 KAO PROGNOSTIČKOG POKAZATELJA U BOLESNICA S DUKTALNIM INVAZIVNIM KARCINOMOM DOJKE

SAŽETAK

U ovoj studiji analizirano je 150 bolesnica s duktalnim invazivnim karcinomom dojke koje su operirane u Klinici za tumore od siječnja 2006. do siječnja 2007. godine. Kontrolnu skupinu činilo je 50 zdravih žena. Bolesnice su svrstane u tri skupine, ovisno o stupnju diferenciranosti tumora, gradus I, II, III. Svaka supina sadržavala je po 50 bolesnica. Kod bolesnica su analizirani dob, veličina i stupanj diferenciranosti tumora, stanje pazušnih limfnih čvorova, postojanje udaljenih metastaza, nalaz steroidnih receptora, vaskularna invazija u primarnom tumoru, prisutnost intraduktalne komponente (EIK-a) u primarnom tumoru, izraženost proteina HER-2. ProMMP-2 određivana je i u kontrolnoj skupini. Određivana je ELISA metodom. Rezultati istraživanja pokazali su da nije bilo razlike u koncentraciji proMMP-2 između tri skupine bolesnica i kontrolne skupine. Nije nađena statistički značajna razlika u serumskoj koncentraciji proMMP-2 između tri skupine bolesnica premda je skupina gradusa III imala najviše vrijednosti i težnju ka statističkoj značajnosti. Usporedbom proMMP-2 s prognostičkim čimbenicima u skupini histološkog gradusa I nađena je statistički značajna korelacija proMMP-2 i dobi bolesnica. Nije nađena statistički značajna povezanost cirkulirajuće proMMP-2 s ostalim patohistološkim prognostičkim čimbenicima.