Structured abstract

Study objectives:

Ovarian carcinoma

1/ comparison of sensitivities among monitored markers CA 125, HE4, CA 19-9, CEA, TK, TPS, MonoTotal

2/ comparison of false positivity of markers CA 125 and HE4

3/ use of CA 125, HE4 and ROMA index in the diagnostics of ovarian carcinoma

4/ use of CA 125 and HE4 in the follow-up of ovarian cancer

Endometrial carcinoma

1/ feasibility of use of biomarkers CA125 and HE4 in patients with endometrial cancer in pre-operative management

Study design: Retrospective data analysis

Settings: Department of Obstetrics and Gynecology, Medical Faculty and Teaching Hospital in Pilsen

Patients and Methods:

Ovarian cancer

1/ Sensitivity of markers CA 125, HE4, CA 19-9, CEA, TK, TPS, and MonoTotal was assessed in 266 patients - 19 with ovarian cancer and 247 with benign disorders.

2/ False positivity of markers CA125 and HE4 was evaluated in a total of 390 patients with benign diagnoses – 60 women with endometriosis, 70 pregnant patients, 67 patients with ascites, 60 with pleural effusion, 25 with cardiac failure , 80 with renal insufficiency and 28 with hepatic failure.

3/ As a part of this objective we evaluated 552 patients with abnormal pelvic abnormality - 30 women had a histologically confirmed malignant ovarian tumor. Other 522 women had a benign condition. The women were divided to premenopausal and postmenopausal in both groups based on the level of FSH (Follicle-stimulating hormone).

4/ A four-year follow-up evaluation of 70 patients with ovarian cancer.

Endometrial carcinoma

1/ A total of 34 patients diagnosed with endometrial carcinoma and 32 healthy controls were enrolled in this part of the study.

Blood was taken for examination of monitored tumor markers in all women. The marker values were assessed using immunoanalytical methods and correlated with studied variables.

Results:

Ovarian carcinoma

1/ Marker CA 125 reached the highest sensitivity (89.5%) at 95% specificity, marker HE4 showed sensitivity of 73.3%, while marker MonoTotal was merely at the level of utility (63.2%).

2/ Marker CA 125 showed a high false positivity in virtually all selected non-oncologic diagnoses. Conversely, the false positivity of marker HE4 was around 10% in all abovementioned conditions. Both markers showed virtually a 100% increase in case of renal insufficiency.

3/ Postmenopausal women and a combination of both CA125 and HE4 are associated with the highest diagnostic yield of one-step procedure, i.e. immediate examination of the panel of tumor markers associated with clinical and ultrasound examination. ROMA2 reached 92.3% sensitivity, 88.5 % specificity and PV- 99.3% for a cut-off 25.3%, or the closest calculated value 26.4%, in postmenopausal women defined by FSH level above 40 IU/l. If we reduced the cut-off for FSH for laboratory assessment of menopausal status to 22 IU/l, the ROMA2 reached 95.2% sensitivity, 87.8% specificity and PV- 99.5% at the cut-off 25.3%, or the closest calculated value 26.3%.

4/ Marker HE4 was proven to be more suitable in follow-up. Marker CA125 was often false positive in a long-term and did not correlate with the clinical picture.

Endometrial carcinoma

1/ A statistically significant difference in median serum levels of HE4 was found in women with endometrial cancer compared to healthy women (75.5 pmol/l vs. 40.0 pmol/l, $p<0.0001$). In case of CA125, the difference was not statistically significant (19.0 IU/l vs. 15 IU/l, $p=0.4442$).

Conclusions:

Ovarian carcinoma

1/ Assessment of CA 125 and HE4 improves the primary detection of ovarian cancer and narrows differential diagnosis.

2/ HE4 has a minimum incidence of false positive results and may thus be used inter alia in a cohort of multimorbid patients with unclear findings in clinical and ultrasound examination.

3/ Combination of markers HE4 and CA125 with a simultaneous calculation of ROMA index is a suitable method for improvement of ovarian cancer detection especially in postmenopausal women.

4/ Marker HE4 assessment was proven more suitable in follow-up monitoring. It preceded the progression of the disease by up to 6 months, correlated well with the course of the disease and did not show false negativity or positivity.

Endometrial carcinoma

1/ In our pilot group we found that simultaneous assessment of biomarkers HE4 and CA125 may contribute to preoperative verification of ultrasound findings as a correlate of a benign or malignant process that contributes to the ultrasound abnormal findings and clinical symptomatology.