

## The prognostic value of tumor markers and cytokines in patients with squamous cell cervical cancer

Optimal management of cervical cancer consists of appropriate treatment methods after the precise staging, following detection as early as possible, and the best salvage therapy. Early detection of recurrence, especially at the early stages in cervical cancer patients, is of main importance. The survival improvement from early detection of disease relapse has been found. So far, several methods are available for recurrence detection, but the disease is usually advanced with the accompanying clinical symptoms. The main problem is detection of the disease in the preclinical phase, with no visible lesions in imaging studies, while the chance for a cure is the highest. Investigation of the most sensitive useful marker to detect disease recurrence at the earliest stage is needed. Of the gynaecologic cancers, squamous cell cervical cancer (SCC) does not have a poor prognosis, but having the possibility of long-term follow-up of these patients (about 10 years) we observed progression and deaths due to cancer in a high proportion of patients in the early stages of advancement (I-II), which was very interesting from our point of view.

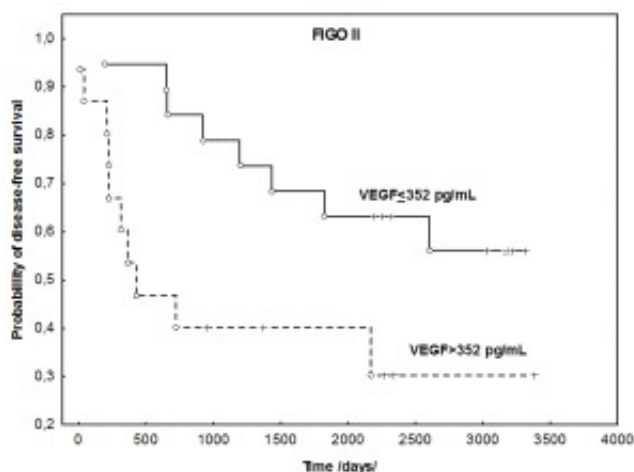


Fig. 1. Disease free survival (DFS) and VEGF concentrations in FIGO stage II.

The aim of the study was to determine the prognostic value of pretreatment serum levels of the cytokines interleukin 6 (IL-6), vascular endothelial growth factor (VEGF), soluble tumor necrosis factor receptor (sTNF RI) and sTNF RII in patients with squamous cell cervical cancer and the tumor markers SCCAg and cytokeratin -19 fragment (CYFRA 21.1).

The subjects of analysis were 138 patients: 78 with stage I+II and 60 with III+IV according to the FIGO classification. During the 10 years of follow-up 56 relapses and 53 deaths were observed. The probability of disease-free survival (DFS) and overall survival (OS) was evaluated using the log-rank test and the Cox regression model.

Within the group of patients who, during a 10- year period of observation, have had recurrence of the disease, concentrations of all markers were significantly higher compared to concentrations noted in patients who were in remission. Furthermore, in cases of patients with progression, the highest diagnostic sensitivity was noted for concentrations of SCCAg and IL-6. In the group of patients who died, the highest diagnostic sensitivity was noted for VEGF, as well as SCCAg and IL-6.

As is known, the classic and widely recognized prognostic factor in patients with malignancy is the degree of development. However, in our studied group, recurrence had already been observed in 45% of patients in FIGO II stage. Because of this, we searched for additional prognostic factors in this specific group of patients. Our studies have demonstrated the prognostic value of VEGF for DFS in patients with FIGO stage II SCC. Therefore, it appears that the relationship we have established between VEGF concentrations and DFS in patients in FIGO stage II may prove to be useful in clinical practice (Fig. 1). A similar analysis of OS in the first stage was conducted in patients in stage FIGO I + II. The analysis demonstrated the important role of proinflammatory cytokines IL-6 and CYFRA 21.1 as independent prognostic factors (Fig. 2).

### FIGO I+II

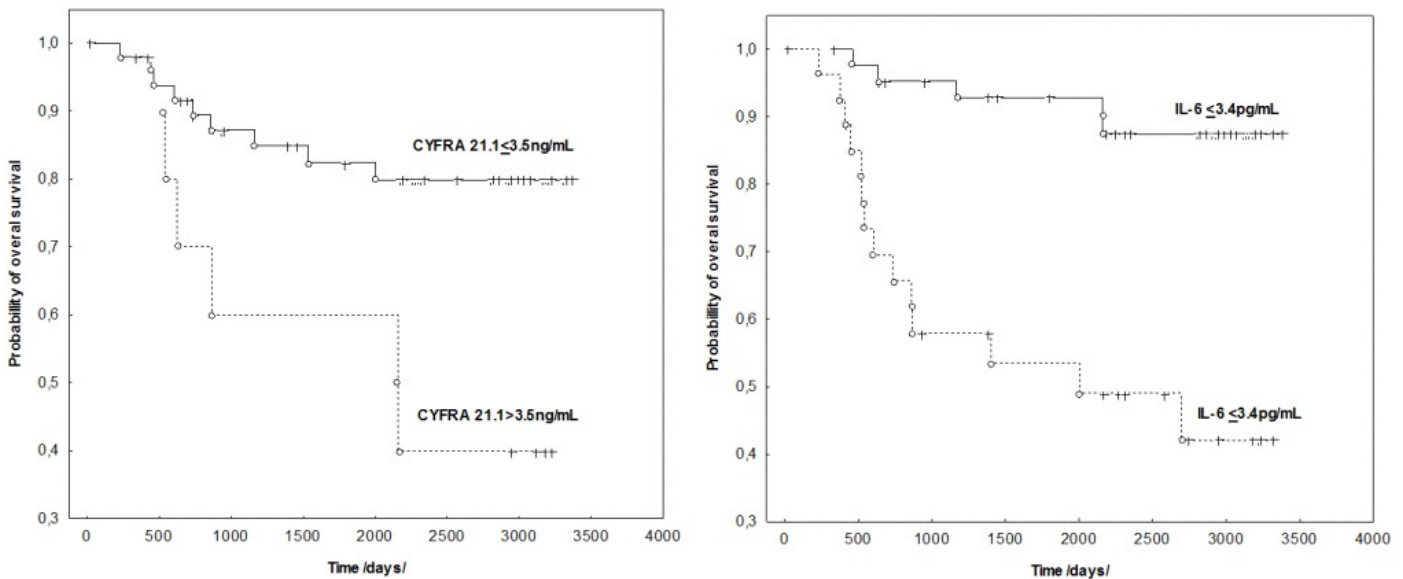


Fig. 2. The relationship between overall survival (OS), CYFRA 21.1 and IL-6 in FIGO stages I-II.

In conclusion, our study illustrated that elevated VEGF and CYFRA 21.1 concentrations before beginning treatment in patients with SCC of the cervix at the earlier stages of clinical development can be poor prognostic factors. Moreover, we demonstrated that in patients with SCCAg concentration levels that are not increased before beginning treatment, measuring interleukin 6

may be helpful in the prognosis of the disease.

We would like to emphasize that the studies represent a summary of many years of our work and follow-up of patients with SCC of the cervix. The collected research material comes from one oncology center.

## **Publication**

[The assessment of the prognostic value of tumor markers and cytokines as SCCAg, CYFRA 21.1, IL-6, VEGF and sTNF receptors in patients with squamous cell cervical cancer, particularly with early stage of the disease.](#)

Kotowicz B, Fuksiewicz M, Jonska-Gmyrek J, Bidzinski M, Kowalska M  
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