# Serum CA-125 tumor marker in endometrial adenocarcinoma

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**Summary**

One hundred and seventy-four patients, mean age 61.23 ± 9.41 years old, with irregular perimenopausal haemorrhage were included in the study. Fractional curettage was performed in all patients. When the pathohistologic findings were adenocarcinoma the concentration of CA-125 tumor marker was determined. Hysterectomy with bilateral salpingo-oophorectomy was determined. In 142 cases carcinoma was restricted to the uterus and in 32 patients extrauterine metastatic disease was found. In the former group CA-125 was positive in 130 patients with a mean value of 64.12 ± 22.41 U/ml serum. In the latter group the cancer antigen was positive in 29 patients with a mean value of 244.82 ± 68.11 U/ml. High production is associated with increased metastatic potential.

*Key words:* CA-125; Endometrial cancer.

## Introduction

Tumor markers are generated by the tumor itself or by the normal tissue after it has been invaded by carcinomatous cells. They are not found in healthy subjects nor in benign disease. In general, tumor markers are radioimmunologically determined in patient sera, their values directly reflecting the mass of the malignancy. Tumor markers are divided into antigens, hormones, proteins and enzymes. CA-125 in peripheral blood takes a particular place among tumor markers. The presence of an elevation more than 35 U/ml appears to be significant [1]. The use in patients with endometrial cancer has been widely discussed in the literature regarding its value in the metastatic potential of disease.

## Materials and Methods

One hundred and seventy-four patients mean age 61.23 ± 9.41 years were included in the study. Irregular premenopausal and postmenopausal haemorrhage was reported by 32 and 142 patients, respectively. Only 11 of them were taking hormonal replacement. Fractional curettage was performed in all patients and the material was sent for pathohistologic testing. On day 5 after curettage, when the findings were obtained, the concentration of CA-125 tumor marker was determined for all patients who were then prepared for surgery. Hysterectomy with bilateral salpingo-oophorectomy including peritoneal cytology and palpation of pelvic paraaortic lymph nodes was performed. The preparation was sent to the pathohistology department for diagnosis. Thus, stage of endometrial carcinoma, histology and grade of maturation, as well as depth of penetration into the myometrium were evaluated. Serum concentrations of CA-125 tumor marker were determined using a radioimmunoassay method and monoclonal antibodies (Abbott CA-125 EIA Monoclonal test with 5 U/ml serum sensitivity). For the statistical data analysis we employed the Student's t-test.

## Results

All of the 174 patients had adenocarcinoma of the endometrium, 122 (70.12%) well or moderately differentiated and 52 (29.88%) poorly or not differentiated. In 142 cases carcinoma was restricted to the uterus, 132 (75.86%) Stage I and ten (5.75%) Stage II, using the FIGO nomenclature. Following surgical staging and including peritoneal cytology 32 patients were found to have extrauterine metastasis disease, 26 (14.94%) Stage III and six (3.45%) Stage IV (Table 1).

In this study, none of 20 healthy women from our biochemical laboratory, examined as control subjects, had positive CA-125 test results, i.e., concentrations of CA-125 were below 5 U/ml serum. Therefore, any positive value recorded in our patients was considered significant, and this was confirmed by postoperative pathohistologic analysis. In the group of patients where the carcinoma was restricted to the uterus CA-125 was negative in 12 and positive in 130 cases with a mean value of 64 ± 22.41 U/ml serum. In the group where extrauterine metastatic disease was found the cancer antigen was negative in

Table 1. — *Stage of endometrial carcinoma (FIGO).*

| Stage of disease | Number of cases | % |
|---|---|---|
| I | 132 | 75.86 |
| II | 10 | 5.75 |
| III | 26 | 14.94 |
| IV | 6 | 3.45 |
| TOTAL | 174 | 100.00 |

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Table 2. — *Relationship between extention of carcinoma and serum CA-125 concentration (U/ml).*

| Stage of disease | Number of cases | % |
|---|---|---|
| I and II | 130 | 64.12 ± 22.41 |
| III and IV | 29 | 244.82 ± 68.11 |
| TOTAL | 174 | 100.00 |

t = 13.92 p < 0.001

three and positive in 29 patients with a mean value of 244.82 ± 68.11 U/ml. The difference is statistically significant (t = 13.92; p < 0.001) Table 2).

## Discussion

Elevations of CA-125 were first described in patients with recurrent and advanced endometrial cancer by Niloff et al in 1984 [2]. Elevated CA-125 greater than 35 U/ml correlated with higher stage, higher grade, increased depth of myometrial invasion, positive cytology and lymph-node metastases [3]. Recent studies have suggested that a CA-125 cut-off level of 20 U/ml may be more appropriate in endometrial carcinoma than the traditional level of 35 U/ml used in ovarian cancer. This level could detect myometrial invasion to more than one-half of the myometrium with a sensitivity of 69.9%, specificity of 74.1%, positive predictive value of 58.8%, and negative predictive value of 81.6% [4]. Either a CA-125 level of > 20 U/ml or grade 3 tumor or both of these correctly predicted 87% of patients requiring surgical staging [5]. The combination of serum CA-125 with a cut-off of 15 U/ml and histological grade after curettage identified 65% of the patients who required a lymphadenectomy or sampling [6]. Our work (Kukura *et al.*, 1990) [7] presented a medium mature and immature grade of Stage I endometrial adenocarcinoma. Concentration of the CA-125 marker, with a cut-off value of 5 U/ml, was significantly higher when the tumor penetration exceeded one-third of the uterine wall. False-negative results were obtained in only two cases. Low serum CA-125 values though, pointed to a low malignant potential for Stage I and II endometrial adenocarcinoma. When the tumor metastasized outside the uterus, concentrations of the marker were considerably higher. Serum CA-125 was useful in identifying patients with possible occult metastatic disease in a group of women 45 years old or younger [8]. Cytokeratin and CA-125 were detected simultaneously on macrophages in lymph nodes, and could predict occult metastasis, which is a risk factor for recurrence in early-stage endometrial cancer [9]. Multivariate analysis of disease-free survival showed that the preoperative CA-125 level and pelvic lymph node metastasis were significant risk factors for recurrence [10]. Post-treatment elevation of CA-125 is a useful predictor for recurrence in patients with elevated pretreatment levels. The median lead-time between elevation of tumor markers and clinical evidence of recurrence was six months [11]. During the follow-up the combined use of CA-125 and CA-19-9 markers permitted a high sensitivity (83.3%), with only 12.8% false positive cases to predict recurrences [12]. Other nonivasive methods have also been employed in diagnosis, most commonly transvaginal sonography (TVS), computed tomography (CT) and magnetic resonance imaging (MRI). The sensitivity of TVS was significantly higher than CA-125 in predicting myometrial invasion of endometrial cancer. No differences were found in terms of specificity [13]. Helical CT has a sensitivity of 83% and a specificity of 42% for the detection of deep myometrial invasion. These results compare poorly with those of MRI which demonstrate a sensitivity of 92% and a specificity of 90% [14].

Hysteroscopy demonstrates high diagnostic accuracy for endometrial cancer with a sensitivity of 93.10% and specificity of 99.96%. When hysteroscopy was associated with endometrial biopsy it showed a sensitivity of 96.55% and a specificity of 100% [15].

All these methods can be used in planning an adequate surgical procedure and postoperative radiotherapy.

## Conclusion

Determination of tumor markers appears to be quite important in endometrial carcinoma. Concentrations of CA-125 in patient sera may indicate the level of malignant potential and thus help in choosing an appropriate therapeutic procedure.

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