# Changes in serum CA-125 levels after laparotomy?

R. Atmaca<sup>1</sup>, M.D., Assist. Prof.; O. Balat<sup>2</sup>, M.D., Assoc. Prof.; M. Cekmen<sup>3</sup>, M.D., Assist. Prof.; M.G. Ugur<sup>2</sup>, M.D., Resident; A.I. Kutlar<sup>2</sup>, M.D., Assoc. Prof.; F. Aksoy<sup>2</sup>, M.D., Resident

> Department of Obstetrics and Gynecology, Faculty of Medicine, Inonu University, Malatya <sup>2</sup>Department of Obstetrics and Gynecology, Faculty of Medicine, Gaziantep University, Gaziantep <sup>3</sup>Department of Biochemistry, Faculty of Medicine, Kocaeli University, Kocaeli <sup>4</sup>Department of Public Health, Faculty of Medicine, Gaziantep University, Gaziantep (Turkey)

## Summary

There is no adequate data in the medical literature defining serum CA-125 levels after laparotomy. Therefore we designed this prospective study to evaluate the effects of laparotomy for hysterectomy on serum CA-125 levels. Ninety-four women (mean age 44.6 ± 6.9 years) were included in the study between January, 2001 and April, 2003. Hysterectomies were performed in patients with chronic pelvic pain, dysfunctional uterine bleeding and myoma uteri. Mean serum CA-125 levels of the patients before and after laparotomy were  $16.29 \pm 8.11$  U/ml and  $16.37 \pm 8.05$  U/ml, respectively. The change in serum CA-125 levels prior to the operation was statistically insignificant when compared with the levels obtained at 24 hours after laparotomy (p > 0.05). We found that laparotomy for hysterectomy did not change the levels of CA-125 at the 24th hour after the operation, indicating either serum CA-125 levels are not correlated, at least within 24 hours, with peritoneal irritation or peritoneal irritation was minimal or absent in our operations.

Key words: Laparotomy; Hysterectomy, CA-125.

#### Introduction

The cancer antigen 125 (CA-125) is expressed in amnion and its derivatives of fetal coelomic epithelia such as Mullerian epithelia, peritoneum, pleura and pericardium, and in many adult tissues such as the epithelium of the fallopian tubes, endometrium, endocervix, pleura and peritoneum [1]. Increased levels of CA-125 may accompany many clinical conditions such as ovarian carcinoma, pregnancy, endometriosis, pelvic inflammatory disease, non-malignant ovarian cysts and ovarian hyperstimulation [2-5]. Although the structure of CA-125 is well defined [6], its physiological role is still unclear. CA-125 has been suggested to play a role as a lubricant in preventing adhesion of membranes [7]. In case of trauma, disruption of tissues such as the peritoneum, pleura, fallopian tubes or endometrium, results in increased CA-125 levels in circulation [7].

Hysterectomy is one of the most frequently performed major operations of obstetrics and gynecology all over the world [8, 9] and laparotomy is the most preferred route for this operation [10].

The exact physiological role of CA-125 is not well defined and if laparotomy leads to an increase in CA-125 levels, it may have unwanted effects in terms of undefined function of CA-125 in the human body.

Also, CA-125 measurements are mandatory in the follow-up of patients treated for ovarian carcinoma and any reason that changes CA-125 levels must be known and cautiously interpreted in such patients.

There is no adequate data in the medical literature defining serum CA-125 levels after laparotomy. Therefore we designed this prospective study to evaluate the effects of laparotomy on serum CA-125 levels.

Revised manuscript accepted for publication April 5, 2004

#### **Patients and Methods**

Study participants

In this study, a cut-off value for CA-125 was accepted as 35 U/ml and patients that were to undergo laparotomy with serum CA-125 levels below cut-off values were enrolled in the study. Ninety-four women (mean age  $44.6 \pm 6.9$  years) were included in the study between January, 2001 and April, 2003. Laparotomies were performed in patients with chronic pelvic pain, dysfunctional uterine bleeding and myoma uteri (Table 1). Serum CA-125 levels were evaluated 24 hours before and after laparotomy.

## CA-125 Measurement

CA-125 was determined by Immulite OM-MA, Diagnostic Products Corporation (DPC, Gwynedd, U.K.) which was a solid-phase, chemiluminescent enzyme immunometric assay. It was used with the Immulite DPC automated analyzer.

# Statistical Analysis

Statistical analysis was done by SPSS statistical software. Data are presented as the means-standard deviations. The statistical significance of change in serum CA-125 values was analyzed by the paired-samples test. A p value of < 0.05 was accepted as statistically significant.

## Results

Of 94 patients, 38 underwent abdominal hysterectomy for dysfunctional uterine bleeding, 43 for myoma uteri and 13 for chronic pelvic pain. There were no complications during the laparotomy procedures.

Mean serum CA-125 levels of the patients, before and after laparotomy, were  $16.29 \pm 8.11$  U/ml and  $16.37 \pm$ 8.05 U/ml, respectively. The change in serum CA-125 levels prior to laparotomy was statistically insignificant when compared with the levels obtained 24 hours after the operation (p > 0.05).

Table 1. — *Indications of hysterectomy and serum CA-125 levels.* 

	No. of patients	CA-125 level (U/ml)	
		Before laparotomy	After laparotomy
Chronic pelvic pain	13	$21.10 \pm 7.41$	21.27 ± 7.55
Dysfunctional uterine			
bleeding	38	$11.42 \pm 7.61$	$11.55 \pm 7.54$
Myoma uteri	43	$15.52 \pm 8.66$	$15.64 \pm 8.73$
All patients	94	$16.29 \pm 8.11$	$16.37 \pm 8.05$

## Discussion

The CA-125 tumor marker is a cell surface antigen derived from the surface coelemic epithelium, including the mucosa of the entire female genital tract and the germinal epithelium of the ovaries. Peritoneally derived CA-125 contributes significantly to circulating CA-125 concentrations and thus in case of irritation of the peritoneum serum CA-125 levels are thought to be increased [11].

It is already known that a number of conditions lead to increased serum levels of CA-125. The main clinical importance of CA-125 is its role in both diagnosis and follow-up of ovarian malignancies. Besides this clinical implication, many other pathologic states in obstetrics and gynecology are believed to have some degree of relation with CA-125 and measurement of its level may have a clinical role in both diagnosis and prognosis [12, 13].

Minimization of serosal injury is the basis of modern surgical principles since during pelvic and abdominal surgeries, whether performed by laparotomy or laparoscopy, any surgical injury to the peritoneum causes an immediate release of inflammatory substances which will then promote adhesion formation [14]. During trauma to the peritoneum it is likely that CA-125 antigens, which were present in the epithelium of the peritoneum, are released and their levels in circulation are increased. Therefore, one can speculate that measuring CA-125 levels could become an indicator of this peritoneal irritation. Although many conditions that lead to an increase in serum CA-125 levels are defined, data in the medical literature explaining serum CA-125 levels after laparotomy are unsatisfactory. In this study we have investigated the effect of laparotomy on serum CA-125 levels. In order to demonstrate peritoneal irritation in terms of CA-125 levels, the relationship between serum CA-125 levels and peritoneal irritation with laparotomy for abdominal hysterectomy was evaluated. We found that laparotomy did not change the levels of CA-125 at the 24th hour after laparoscopy thus expressing either that serum CA-125 levels are not correlated, at least within 24 hours, with peritoneal irritation or that peritoneal irritation was minimal or absent in our operations.

Although CA-125 is the one of the most commonly studied compounds, its biological function has not been fully elucidated. A number of studies have pointed out several properties of CA-125 related to its function such as adhesion prevention of membranes [7], immune suppression during pregnancy in order to protect the embryo from maternal immune rejection [15], an immunomodulatory effect in ovarian cancer [15], and enhancing the invasiveness of benign endometrial cells which may be an etiological role in endometriosis [16]. Laparotomy did not cause

an increase in CA-125 levels in our study, thus when the unknown functions of CA-125 are considered, potential undesired effects related to CA-125 seem to be prevented.

In conclusion, although CA-125 is widely used in detection and follow-up of ovarian carcinomas, serum CA-125 levels are increased in many other clinical conditions. The peritoneum is a major source of the CA-125 antigen and irritation and trauma to the peritoneum during surgical operations may cause elevated serum CA-125 levels. However, our results failed to show an increase in CA-125 levels after laparotomy, suggesting that trauma or irritation of the peritoneum was minimal.

## References

- [1] Kabawat S., Bast R.C., Bhan A.K., Welch W.R., Knapp R.C., Colvin R.B.: "Tissue distribution of a coelomic epithelium-related antigen recognized by monoclonal antibody CA-125". *Int. J. Gynecol. Pathol.*, 1983, 2, 275.
- [2] Halila H., Stenman U.H., Seppala M.: "Ovarian cancer antigen CA-125 levels in pelvic inflammatory disease and pregnancy". *Cancer*, 1986, 57, 1327.
- [3] Barbieri R.L., Niloff J.M., Bast R.C. Jr., Schaetzl E., Kistner R.W., Knapp R.C.: "Elevated serum concentrations of CA-125 in patients with advanced endometriosis". *Fertil. Steril.*, 1986, 45, 630.
- [4] Niloff J.M., Knapp R.C., Schaetzl E., Reynolds C., Bast J.M. Jr.: "CA-125 antigen levels in obstetric and gynecologic patients". Obstet. Gynecol., 1984, 64, 703.
- [5] Jager W., Diedrich K., Wildt L.: "Elevated levels of CA-125 in serum of patients suffering from ovarian hyperstimulation syndrome". Fertil. Steril., 1987, 48 (4), 675.
- [6] O'Brien T.J., Beard J.B., Underwood L.J., Shigemasa K.: "The CA-125 gene: a newly discovered extension of the glycosylated Nterminal domain doubles the size of this extracellular superstructure". *Tumour Biol.*, 2002, 23 (3), 154.
- [7] Hardardottir H., Parmley T.H. 2<sup>nd</sup>, Quirk J.G. Jr., Sanders M.M., Miller F.C., O'Brien T.J.: "Distribution of CA-125 in embryonic tissues and adult derivatives of the fetal periderm". *Am. J. Obstet. Gynecol.*, 1990, 163, 1925.
- [8] Davies A., Hart R., Magos A., Hadad E., Morris R.: "Hysterectomy: surgical route and complications". Eur. J. Obstet. Gynecol. Reprod. Biol., 2002, 104, 148.
- [9] Sills E.S., Saini J., Steiner C.A., McGee M. 3<sup>rd</sup>, Gretz H.F. 3<sup>rd</sup>: "Abdominal hysterectomy practice patterns in the United States". Int. J. Gynaecol. Obstet., 1998, 63, 277.
- [10] Farquhar C.M., Steiner C.A.: "Hysterectomy rates in the United States 1990-1997". Obstet. Gynecol., 2002, 99, 229.
- [11] O'Brien T.J., Hardin J.W., Bannon G.A., Norris J.S., Quirk J.G. Jr.: "CA-125 antigen in human amniotic fluid and fetal membranes". Am. J. Obstet. Gynecol., 1986, 155, 50.
- [12] Schmidt T., Rein D.T., Foth D., Eibach H.W., Kurbacher C.M., Mallmann P. et al.: "Prognostic value of repeated serum CA-125 measurements in first trimester pregnancy". Eur. J. Obstet. Gynecol. Reprod. Biol., 2001, 97 (2), 168.
- [13] Predanic M.: "Differentiating tubal abortion from viable ectopic pregnancy with serum CA-125 and beta-human chorionic gonadotropin determinations". Fertil Steril., 2000, 73 (3), 522.
- [14] Tsimoyiannis E.C., Tsimoyiannis J.C., Sarros C.J., Akalestos G.C., Moutesidou K.J., Lekkas E.T. et al.: "The role of oxygenderived free radicals in peritoneal adhesion formation induced by ileal ischaemia/reperfusion". Acta Chir. Scand., 1989, 155, 171.
- [15] Kui Wong N., Easton R.L., Panico M., Sutton-Smith M., Morrison J.C., Lattanzio F.A. et al.: "Characterization of the oligosaccharides associated with the human ovarian tumor marker CA-125". J. Biol. Chem., 2003, 278 (31), 28619.
- [16] Gaetje R., Winnekendonk D.W., Scharl A., Kaufmann M.: "Ovarian cancer antigen CA-125 enhances the invasiveness of the endometriotic cell line EEC 145". J. Soc. Gynecol. Investig., 1999, 6 (5), 278.

Address reprint requests to: R. ATMACA, M.D. Turgut Ozal Medical Center Department of Obstetrics and Gynecology Malatya (Turkey)