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GYNECOLOGIC ONCOLOGY

Prognostic value of preoperative Ca125 and Tag72 serum levels and their correlation to disease relapse and survival in endometrial cancer

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Abstract
Objective To evaluate preoperative serum levels of Ca125 and Tag72–4 tumour markers and investigate if abnormal levels correlate to mortality and disease-free survival.
Method Retrospective observational study of a cohort of 282 women (mean age 62.3, SD 10.5 years) with primary endometrial cancer included all consecutive cases treated in a tertiary Gynaecological oncology Center. Excluded cases with other cancer or previous cancer treatment, major abdominal pathology or inflammation, endometriosis. Preoperative serum Tag72 and Ca125 levels were determined and evaluated in relation to disease-free survival (DFS) and disease-specific overall survival (DOS).
Results Raised Ca125 correlates to worse overall disease-specific survival (66.1 vs 87.8 months, $p = 0.021$) and Tag72 correlates to shorter disease-free survival (69.2 vs 67.3 months, $p = 0.021$) and higher recurrence rate (13.5 vs 6 %, $p = 0.021$). When both Ca125 and Tag72 are abnormal DFS and DOS are worse. 93.3 % (72.3 months) vs 82.4 %, (61.3 months) $p = 0.018$ and 96.3 % (74.8 months) vs 88.2 %, (65.9 months) $p = 0.021$, respectively.
Conclusion This study enhances the value of preoperative tumour markers and their prognostic value. Ca125 and Tag72 appear to be good predictors of poor prognosis in patients with endometrial cancer.

Keywords Endometrial cancer · Ca125 · Tag72 · Survival · Prognosis

Introduction

Endometrial cancer is the most common female genital tract cancer in western world [1], and the second commonest worldwide with an incidence of 287,000 new cases recorded for 2008, according to International Agency for Research on Cancer (IARC) [2]. Since 2008, incidence has a 21 % raise and mortality has doubled in the last two decades in USA [3]. Endometrial cancer is responsible for 74,000 deaths per year worldwide [4].

90 % of patients are over the age of 50 years old [5] and mainly postmenopausal. The higher incidence rate is identified among 60–79 years old. Mean age of diagnosis in United Kingdom is 63 years old [6]. Less of 20 % of cases are premenopausal and only 5 % are younger than 40 years old, accounting less than 2 cases per 100,000 women [7]. Survival is 90–95 % for stage I, 80 % for stage II, 55–75 % for stage III and 20 % for stage IV [8]. FIGO 2009 endometrial cancer staging classification reflects better prognosis and survival.

Prognosis is defined by the stage at disease, the histological type and grade of differentiation. Various tumour

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markers have been used to determine stage and prognosis for different cancers like for example Ca125 for ovarian cancer. This study aims to investigate the potential additional prognostic benefit of preoperative tumour markers (Ca125 and Tag72) in endometrial cancer.

Material and method

This is a retrospective, observational, non-interventional cohort study. We have included all patients diagnosed with primary endometrial cancer within the period May 2005–August 2012 at the EANP Metaxa Hospital. We have excluded all cases with a history of endometriosis, recent infection (temperature >38 °C within the previous 8 weeks) or abdominal surgery (laparoscopy or laparotomy for any reason), major intraperitoneal disease (Crohn disease, ulcerative colitis) and other cancer diagnosis, as these can increase tumour markers and especially Ca125 and would have act as confounding factor. In total we have studied 282 patients, which fulfilled inclusion and exclusion criteria. Patients diagnosed prior 2009, have been re-staged in accordance with FIGO 2009 staging classification for endometrial cancer by reviewing pathological reports.

Serous levels of tumour markers, Ca125 and Tag72 have been evaluated as part of the routine pre-operative assessment, occurred 1–6 days prior surgery. Normal levels of Ca125 and Tag72, have been established as <35 and <5 IU/ml, respectively.

Patients' demographics, family and personal history, stage and histopathology characteristics have been collated. Postoperative management and follow-up have been dictated by Gynaecological Oncology Multi Disciplinary Team meeting (MDT). Disease-free survival (DFS), recurrence rates and disease-specific overall survival (DOS) have been monitored by collecting data from hospital's records, electronic database and cross checking with personal telephone communication with every patient.

Statistical analysis

Data were anonymised and collected in Microsoft Office Excel 2007 spreadsheets. Descriptive statistics were used to analyse patients' characteristics. Proportional differences were evaluated using non-parametric tests (Chi-square, Mann–Whitney) for categorical variables and non-normal distributions and Student's t tests for mean differences of continuous variables and normally distributed data. Statistical analysis was performed with SPSS (version 22.0, Chicago IL). Descriptive statistics were used to analyse categorical and parametric variables. Mean values with standard deviation (SD) and standard error (SE) of mean with confidence interval (CI) of 95 % were calculated. For normal distributions t test used and for non-normal distributions, non-parametric tests (Kruskal–Wallis test) were used to compare median values and categorical characteristics among groups. Disease-free survival and disease-specific overall survival were assessed by Kaplan–Meier curves. Statistical significance has been evaluated at the level of 95 % ($p < 0.05$).

Results

Patients' demographics

282 white Caucasian patients have been studied with a mean age of 62.3 years old (62.3 ± SD 10.5 years). Only 27 patients (9.6 %) were under the age of 50 years old. Overall 86.5 % patients were postmenopausal and almost all of them, 84.8 % presented with postmenopausal bleeding. The rest 13.1 % of patients experienced perimenopausal irregular bleeding, and only 2.1 % was diagnosed through routine pelvic ultrasound scan and further investigations for incidental finding of endometrial thickening.

94.4 % of patients had at least one pregnancy and overall a mean of 3.2 pregnancies (SD 2.7 pregnancies). Almost half of them (46.7 %) had two children. Only 9.3 % were nulliparous. 18.3 % of cases had a positive family history with at least one first blood relative diagnosed with breast, colon and/or ovarian cancer.

45.7 % of patients were healthy with an anaesthetic score of ASA: 1 (American Society of Anesthesiology physical status scoring grade). A further 43.2 % had at least one mild systematic disease, well-controlled, mainly cardiovascular and/or diabetes mellitus type II. Finally rest 11.1 % suffered from a severe systematic disease with an ASA 3. 61 % of patients were obese with a body mass index (BMI) over 30 and 18.1 % (51/282 cases) morbidly obese (class II) with BMI over 35. Patients' demographics are summarised in Table 1.

Endometrial cancer characteristics

Endometrioid was the commonest histological type (79.3 %) followed by clear cell cancer (7.8 %) Less common were serous types (4.3 %), mucinous and adenosquamous (3.9 and 3.4 %, respectively). Only 17 % of tumors were well-differentiated (grade 1) and the rest 83 %, was moderately (grade 2) and poorly differentiated (grade 3), 54 and 29 %, respectively. Overall, 64.3 % of cases were Type I endometrial Cancer and 35.7 % were Type II. 19.3 % had been identified with positive peritoneal fluid/washings cytology. Almost half of the cases were stage Iα (51.9 %) and overall 78.4 % were stage I

Table 1 Patients' demographics and tumour characteristics

Patients' demographics *N*	282
Patients demographics	
Age (mean ± SD) years	62.3 ± 10.5
Age <50 years old	9.6 %
Parity ≥2	46.7 %
Post menopausal	86.5 %
BMI ≥ 30	61 %
ASA ≥ 2	54.3 %
FIGO 2009—stage	
I	78.4 %
II–IV	21.6 %
Type	
I	64.3 %
II	35.7 %
Grade of differentiation	
I–II	71 %
III	29 %
Peritoneal cytology	
Negative	80.7 %
Positive	19.3 %
Treatment received	
Surgery only	42.6 %
Radiotherapy	35.5 %
Radiotherapy + chemotherapy	12.8 %
Chemotherapy	4.6 %

disease. 8.6 % of cases were stage II at diagnosis and the rest 10.9 % and 2.2 % had stage III and IV disease. These results are summarized in Table 1.

Tumour markers

Mean value for Ca125 was 33.2 IU/ml, ranging from 0.3 to 745.5 IU/ml. Median was 13.2 IU/ml and 79.9 % of cases were normal (<35 IU/ml). Mean value for Tag72 was 4.1 IU/ml, ranging from 0.1 to 63.9 IU/ml. Median was 1.5 IU/ml and 78.4 % of cases were normal (<5 IU/ml). There was a linear correlation among tumour markers mean levels per stage. Correlation coefficient (ρ) was 0.27 and 0.32 for Ca125 and Tag72, respectively ($p < 0.001$).

Recurrence and survival

Disease-free survival (DFS), recurrence rate and disease-specific overall survival (DOS) have been monitored by collecting data from hospital's records, electronic database and cross checking with personal telephone communication with every patient.

56 out of 282 patients did not desired to participate on the follow-up monitoring of this study and they opted out on their first 3 month follow-up appointment. Remaining 226 patients have been followed up for at least 3 months and up to 91 months (overall a total of 7249 months), mean follow-up was 32.1 months (median 29 months). Standard follow-up was scheduled on 3 monthly intervals for the first 2 years and 6 monthly intervals for the following years. Recurrence has been verified after biopsy or imaging (CT and PET scan).

There were 16 cases with recurrent disease (7.07 %) irrespective stage with a mean age of 65.4 years old and they were all post-menopausal. 7 of them have been managed successfully and patients carried on with their follow-up and 9 died due to disease progression (3.98 %). Additionally, 6 patients (2.65 %) died from other causes (cardiovascular and heart disease, stroke, accident). Comparing pre-menopausal to post-menopausal women there was no statistical difference in disease-free survival and disease-specific overall survival, between these two groups ($p > 0.05$).

Investigating further the potential prognostic value of Ca125 and Tag72, patients were grouped according to their preoperative tumour markers value; normal versus abnormal irrespective stage of disease. Kaplan–Meier curves were plotted for disease-free survival and disease-specific overall survival, estimated in months following surgery.

We have further evaluated the combination of Ca125 and Tag72. We evaluated the group of patients with both tumour markers abnormal versus those with any other combination.

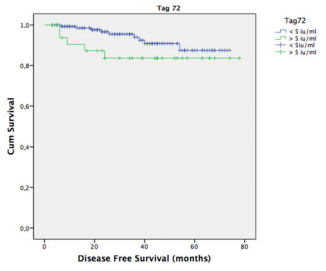
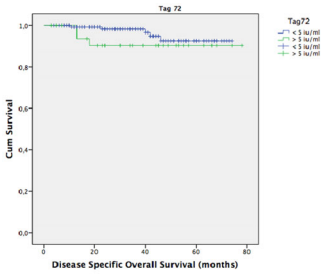
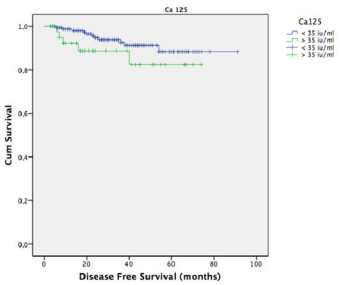
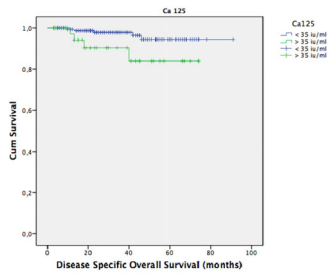
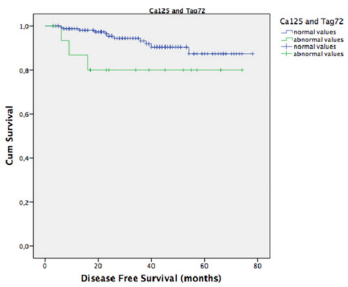
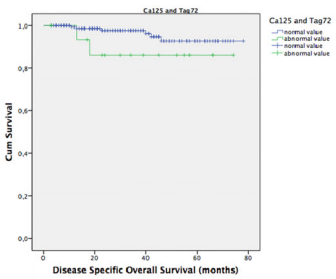
There were patients that decided to opt out from the follow-up part of the study, at the time of their first follow-up appointment, 3 months after their surgery, and these cases have been excluded from further analysis. Therefore, 226 patients were followed up for a total of 7249 months (range 3–91 months, mean 32.1 months, median 29 months).

Although in all occasions, curves were distinctive and not crossing, statistical significance ($p < 0.05$) was not proven in all of them.

Table 2 summarises our results. Pre-operative Ca125 correlates to disease-specific overall survival (DOS). Abnormal values (>35 IU/ml) are linked to a poorer prognosis, irrespective of stage of disease (66.1 vs 87.8 months, $p = 0.021$). Pre-operative Tag72 correlates to disease-free survival (DFS). Abnormal values (>5 IU/ml) are linked to a higher recurrent rate (13.5 vs 6 %, $p = 0.021$).

The combination of both tumour markers performs even better as a prognostic factor. When both tumour markers are abnormal, DFS was just 61.3 months, significantly shorter than 72.3 months, when tumour markers are within

Table 2 Mean disease-free survival, disease-specific overall survival and relevant rates (%) for patients with normal versus abnormal pre-operative tumour markers

	Disease Free Survival – DFS		Disease Specific Overall Survival – DOS	
				
Tag72	Normal vs Abnormal (p:0.021)		Normal vs Abnormal (p:0.060 NS)	
Rate (%)	94%	86.5%	96.7%	91.9%
Mean (months)	69.2	67.3	71.2	71.8
				
Ca125	Normal vs Abnormal (p:0.059 NS)		Normal vs Abnormal (p:0.021)	
Rate (%)	93.7%	89.1%	97.1%	91.3%
Mean (months)	84.1	64.6	87.8	66.1
				
Tag72 and Ca125	Normal vs Abnormal (p:0.018)		Normal vs Abnormal (p:0.044)	
Rate (%)	93.3%	82.4%	96.3%	88.2%
Mean (months)	72.3	61.3	74.8	65.9

NS non-significant

Table 3 Ca125 literature review

References	Years	*N* patients	Stage (extra uterine disease)	Lympnodal metastasis	Survival
Duk [10]	1986	121	✔	.	.
Patsner [11]	1988	89	✔	.	.
Soper [12]	1990	109	✔	.	.
Sood [13]	1997	210	✔	✔	✔
Cherchi [14]	1999	112	✔	.	.
Dotters [15]	2000	.	✔	✔	.
Ebina [16]	2002	180	✔	✔	.
Hsieh [17]	2002	124	✔	✔	.
Todo [18]	2003	214	✔	✔	.
Jhang [19]	2003	.	✔	✔	.
Santala [20]	2003	44	✔	.	✔
Powell [21]	2005	141	✔	✔	.
Chung [22]	2006	92	✔	✔	85.6 vs 60.0
Todo [23]	2007	211	✔	✔	.
Han [24]	2010	300	✔	✔	.
Kim [25]	2010	413	✔	.	✔
Lee [26]	2010	110	✔	✔	.
Sebastianelli [27]	2010	254	✔	✔	.
Yoon [28]	2010	131	✔	✔	.
Chen [29]	2011	120	✔	✔	95 vs 65 %
Goksedef [30]	2011	97	✔	✔	92 vs 70 %
Gupta [31]	2011	52	✔	✔	✔
Roelofsen [32]	2012	66	✔	.	HR = 3.12
Kang [33]	2012	360	✔	✔	.
Nicklin [34]	2012	657	✔	.	.
Yildiz [35]	2012	147	✔	✔	.
Antonsen [36]	2013	352	✔	✔	.
Saarelainen [37]	2013	98	✔	✔	.
Chao [38]	2013	757	✔	✔	HR = 2.34

✔ indicates correlation identified, *HR* hazard ratio, . non reported

Table 4 Tag72 literature review

References	Year	*N* patients	Stage (extra uterine disease)	Lymhpnode metastasis	Survival
Soper [12]	1990	109	✔	✔	.
Hareyama [39]	1996	72	✔	✔	.

✔ indicates correlation identified, . non reported

normal range ($p = 0.018$), and DOS was 65.9 vs 74.8 months ($p = 0.044$).

Discussion

Our cohort was random, from a non-selected population and had typical demographics and cancer characteristics, as observed in the literature. Obese, postmenopausal women with cardiovascular, metabolic and respiratory disease, presented with postmenopausal bleeding. Endometrial cancer cases were mainly type I and endometrioid was the most frequently observed histology. The majority of these patients have been diagnosed on an early stage (stage I) and recurrent rates and survival was comparable to published data.

In our study, we have observed a statistically significant correlation of preoperative tumour markers value (Ca125 and Tag72) and final postoperative stage. Furthermore, we have established the prognostic value of Ca125 and Tag72 to disease-free survival and disease-specific overall survival. This study reinforce the potential benefit of using preoperative tumour markers to risk assess patients with endometrial cancer.

Ca125 has been studied in the past as a prognostic factor to categorise patients into risk groups and guide further surgical management. Niloff at 1984 [9] published the first study that investigated the role of Ca125 into endometrial cancer and later Duk at 1986 [10] investigated the correlation of Ca125 to the stage of disease. Same year, Patsner and Mann evaluated Ca126 prognostic value to apparent early disease. They have established as normal values, those less than 35 IU/ml. In their study, abnormal Ca125 was related to advanced disease [11].

Since then, retrospective studies have been performed assessing Ca125 prognostic value. Table 3 summarises these published studies and their results correlating Ca125 to extrauterine disease and advanced stage. Very few of them have elaborated the correlation to survival.

All researchers agree that Ca125 correlates to endometrial cancer stage and abnormal, elevated preoperative values indicate advanced disease, extrauterine spread and lymph nodal metastasis. They all concluded that Ca125 could be used as an independent prognostic factor for lymph node involvement [19, 21, 33].

In our study, we have excluded patients that could have elevated Ca125 due to other disease like history of endometriosis, recent infection or abdominal surgery, major intraperitoneal disease (Crohn disease, ulcerative colitis) and other cancer diagnosis, in an attempt to minimise bias and confounding factors. Most researchers used a range (30–40 IU/ml) of Ca125 values as cut-off point for their studies. We have opted to maintain 35 IU/ml as cut-off point for normal values as this is the most commonly used [12, 14, 20, 21, 27, 28, 30, 33, 34].

LACE is a multi-centre study and the larger published cohort (657 patients) up to date. 30 IU/ml was the better performing cut-off point in distinguishing stage I disease to stage II–IV. This study has also identified Ca125 as a reliable prognostic factor and suggested that can be incorporated in risk prediction models for advanced stage disease as a valuable addition to the commonly used (histological type, grade of differentiation, tumour size and myometrial invasion) [34].

Researchers that have investigated Ca125 correlation to survival, either as disease-free survival or as disease-specific survival, agree with our results that abnormal elevated values are a negative prognostic factor irrespective stage [13, 20, 22, 25, 29–32, 38].

Tag72 has been investigated very little and these studies are quite dated (Table 4). Soper et al. [12] using 6 IU/ml as cut off point for their study, identified that 30 % of advanced disease cases had abnormal values, significantly higher to only 4 % of those with stage I disease. Unfortunately, they have had a quite high proportion of false positive results; therefore, they have failed to prove that the addition of Tag72 would have improved Ca125 prognostic value [12].

In 1996, Hareyama et al. [39] have studied Tag72 preoperative values in endometrial cancer patients and they have correlated values >4 IU/ml to increased depth of myometrial invasion, lymphovascular space invasion, lymph nodal and adnexal involvement.

In our cohort of 282 patients, Tag72 increased values correlated with statistical significance with advancing of disease stage. Additionally, Tag72 correlated to disease-free survival (DFS), nevertheless, stage (94.4 vs 89.4 %, p 0.021) implying that patients with abnormal preoperative Tag72 are more likely to relapse. Tag72 has also reinforced and improved Ca125 results when taking into account. Knowing that Tag72 is normal, for patients with abnormal Ca125, disease-specific overall survival (DOS) raises from 91.3 to 92.4 % with a mean of 72 compared to 66.1 months. In the contrary, when both tumour markers are abnormal, preoperatively, disease-specific overall survival (DOS) falls to 88.2 % with a mean of 65.9 months.

Conclusion

Literature review, has verified that over the last 25 years various researchers have been able to correlate abnormally raised preoperative Ca125 with extra uterine spread of endometrial cancer. Our study is in accordance with existing literature in this area and reinforces the additional potential use of tumour markers, which has not been utilised, up to now. Individualised surgical staging and treatment for endometrial cancer patients is key. There are challenges due to increased number of cases, patients' comorbidities and body habitus [40]. This study enhances the value of preoperative tumour markers and their prognostic value. Ca125 and Tag72 appear to be good predictors of poor prognosis in patients with endometrial cancer.

Conflict of interest All the authors declare that they have no conflict of interest.

References

1. Amant F, Moerman P, Neven P et al (2005) Endometrial cancer. Lancet 366:491–505

2. Ferlay J, Shin HR, Bray F et al (2010) Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer 127:2893–2917. doi:10.1002/ijc.25516
3. Sorosky JI (2012) Endometrial cancer. Obstet Gynecol 120(2 Pt 1):383–397
4. Ferlay J, Shin HR, Bray F (2010) GLOBOCAN 2008, Cancer Incidence and Mortality Worldwide. Lyon, France: International Agency for Research on Cancer: IARC Cancer Base No. 10
5. Sorosky JI (2008) Endometrial cancer. Obstet Gynecol 111(2 Pt 1):436–447
6. Colombo N, Preti E, Landoni F, Carinelli S, Colombo A, Marini C, Sessa C, ESMO Guidelines Working Group (2011) Endometrial cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 22(Suppl 6):vi35–vi39
7. Cancer Research UK. http://www.cancerresearchuk.org/cancer-info/cancerstats/types/uterus
8. Creasman WT, Odicino F, Maisonneuve P, Quinn MA, Beller U, Benedet JL, Heintz AP, Ngan HY, Pecorelli S (2006) Carcinoma of the corpus uteri. FIGO 26th Annual Report on the results of treatment in gynecological cancer. Int J Gynaecol Obstet 95(Suppl 1):S105–S143
9. Niloff JM, Klug TL, Schaetzl E, Zurawski VR Jr, Knapp RC, Bast RC Jr (1984) Elevation of serum CA125 in carcinomas of the fallopian tube, endometrium, and endocervix. Am J Obstet Gynecol 148:1057–1058
10. Duk JM, Aalders JG, Fleuren GJ, de Bruijn HW (1986) CA 125: a useful marker in endometrial carcinoma. Am J Obstet Gynecol 155:1097–1102
11. Patsner B, Mann WJ, Cohen H, Loesch M (1988) Predictive value of preoperative serum CA 125 levels in clinically localized and advanced endometrial carcinoma. Am J Obstet Gynecol 158:399–402
12. Soper JT, Berchuck A, Olt GJ, Soisson AP, Clarke-Pearson DL, Bast RC Jr (1990) Preoperative evaluation of serum CA 125, TAG 72, and CA 15-3 in patients with endometrial carcinoma. Am J Obstet Gynecol 163:1204–1209
13. Sood AK, Buller RE, Burger RA, Dawson JD, Sorosky JI, Berman M (1997) Value of preoperative CA 125 level in the management of uterine cancer and prediction of clinical outcome. Obstet Gynecol 90:441–447
14. Cherchi PL, Dessole S, Ruiu GA, Ambrosini G, Farina M, Capobianco G, Ambrosini A (1999) The value of serum CA 125 and association CA 125/CA 19-9 in endometrial carcinoma. Eur J Gynaecol Oncol 20(4):315–317
15. Dotters DJ, Preoperative CA (2000) 125 in endometrial cancer: is it useful? Am J Obstet Gynecol 182:1328–1334
16. Ebina Y, Sakuragi N, Hareyama H, Todo Y, Nomura E, Takeda M et al (2002) Para-aortic lymph node metastasis in relation to serum CA 125 levels and nuclear grade in endometrial carcinoma. Acta Obstet Gynecol Scand 81:458–465
17. Hsieh CH, ChangChien CC, Lin H, Huang EY, Huang CC, Lan KC et al (2002) Can a preoperative CA 125 level be a criterion for full pelvic lymphadenectomy in surgical staging of endometrial cancer? Gynecol Oncol 86:28–33
18. Todo Y, Sakuragi N, Nishida R, Yamada T, Ebina Y, Yamamoto R et al (2003) Combined use of magnetic resonance imaging, CA 125 assay, histologic type, and histologic grade in the prediction of lymph node metastasis in endometrial carcinoma. Am J Obstet Gynecol 188:1265–1272
19. Jhang H, Chuang L, Visintainer P, Ramaswamy G (2003) CA 125 levels in the preoperative assessment of advanced-stage uterine cancer. Am J Obstet Gynecol 188(5):1195–1197
20. Santala M, Talvensaari-Mattila A, Kauppila A (2003) Peritoneal cytology and preoperative serum CA 125 level are important prognostic indicators of overall survival in advanced endometrial cancer. Anticancer Res 23(3C):3097–3103
21. Powell JL, Hill KA, Shiro BC, Diehl SJ, Gajewski WH (2005) Preoperative serum CA-125 levels in treating endometrial cancer. J Reprod Med 50(8):585–590
22. Chung HH, Kim JW, Park NH, Song YS, Kang SB, Lee HP (2006) Use of preoperative serum CA-125 levels for prediction of lymph node metastasis and prognosis in endometrial cancer. Acta Obstet Gynecol Scand 85:1501–1505
23. Todo Y, Okamoto K, Hayashi M, Minobe S, Nomura E, Hareyama H, Takeda M, Ebina Y, Watari H, Sakuragi N (2007) A validation study of a scoring system to estimate the risk of lymph node metastasis for patients with endometrial cancer for tailoring the indication of lymphadenectomy. Gynecol Oncol 104(3):623–628
24. Han SS, Lee SH, Kim DH, Kim JW, Park NH, Kang SB et al (2010) Evaluation of preoperative criteria used to predict lymph node metastasis in endometrial cancer. Acta Obstet Gynecol Scand 89:168–174
25. Kim HS, Park CY, Lee JM, Lee JK, Cho CH, Kim SM et al (2010) Evaluation of serum CA-125 levels for preoperative counseling in endometrioid endometrial cancer: a multi-center study. Gynecol Oncol 118:283–288
26. Lee JY, Jung DC, Park SH, Lim MC, Seo SS, Park SY et al (2010) Preoperative prediction model of lymph node metastasis in endometrial cancer. Int J Gynecol Cancer 20:1350–1355
27. Sebastianelli A, Renaud MC, Grégoire J, Roy M, Plante M (2010) Preoperative CA 125 tumour marker in endometrial cancer: correlation with advanced stage disease. J Obstet Gynaecol Can 32(9):856–860
28. Yoon JH, Yoo SC, Kim WY, Chang SJ, Chang KH, Ryu HS (2010) Para-aortic lymphadenectomy in the management of preoperative grade 1 endometrial cancer confined to the uterine corpus. Ann Surg Oncol 17:3234–3240
29. Chen YL, Huang CY, Chien TY, Huang SH, Wu CJ, Ho CM (2011) Value of pre-operative serum CA125 level for prediction of prognosis in patients with endometrial cancer. Aust N Z J Obstet Gynaecol 51:397–402
30. Goksedef BP, Gorgen H, Baran SY, Api M, Cetin A (2011) Preoperative serum CA 125 level as a predictor for metastasis and survival in endometrioid endometrial cancer. J Obstet Gynaecol Can 33(8):844–850
31. Gupta D, Gunter MJ, Yang K, Lee S, Zuckerwise L, Chen LM, Goldberg GL, Huang GS (2011) Performance of serum CA125 as a prognostic biomarker in patients with uterine papillary serous carcinoma. Int J Gynecol Cancer 21(3):529–534
32. Roelofsen T, Mingels M, Hendriks JC, Samlal RA, Snijders MP, Aalders AL, Bulten J, van Ham MA, Massuger LF (2012) Preoperative CA-125 predicts extra-uterine disease and survival in uterine papillary serous carcinoma patients. Int J Biol Markers 27(3):e263–e271
33. Kang S, Kang WD, Chung HH, Jeong DH, Seo SS, Lee JM et al (2012) Preoperative identification of a low-risk group for lymph node metastasis in endometrial cancer: a Korean Gynecologic Oncology Group study. J Clin Oncol 30:1329–1334
34. Nicklin J, Janda M, Gebski V, Jobling T, Land R, Manolitsas T, McCartney A, Nascimento M, Perrin L, Baker JF, Obermair A, LACE Trial Investigators (2012) The utility of serum CA-125 in predicting extra-uterine disease in apparent early-stage endometrial cancer. Int J Cancer 131(4):885–890
35. Yildiz A, Yetimalar H, Kasap B, Aydin C, Tatar S, Soylu F, Yildiz FS (2012) Preoperative serum CA 125 level in the prediction of the stage of disease in endometrial carcinoma. Eur J Obstet Gynecol Reprod Biol 164(2):191–195
36. Antonsen SL, Høgdall E, Christensen IJ, Lydolph M, Tabor A, Loft Jakobsen A, Fagö-Olsen CL, Andersen ES, Jochumsen K, Høgdall C (2013) HE4 and CA125 levels in the preoperative assessment of endometrial cancer patients: a prospective

multicenter study (ENDOMET). Acta Obstet Gynecol Scand 92(11):1313–1322
37. Saarelainen SK, Peltonen N, Lehtimäki T, Perheentupa A, Vuento MH, Mäenpää JU (2013) Predictive value of serum human epididymis protein 4 and cancer antigen 125 concentrations in endometrial carcinoma. Am J Obstet Gynecol 209(2):142.e1–142.e6
38. Chao A, Tang YH, Lai CH, Chang CJ, Chang SC, Wu TI, Hsueh S, Wang CJ, Chou HH, Chang TC (2013) Potential of an age-stratified CA125 cut-off value to improve the prognostic classification of patients with endometrial cancer. Gynecol Oncol 129(3):500–504
39. Hareyama H, Sakuragi N, Makinoda S, Fujimoto S (1996) Serum and tissue measurements of CA72-4 in patients with endometrial carcinoma. J Clin Pathol 49(12):967–970
40. Neubauer NL, Lurain JR. (2011) The role of lymphadenectomy in surgical staging of endometrial cancer. Int J Surg Oncol 2011:814649