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Glasgow prognostic score is a prognosis predictor for patients with endometrial cancer☆

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ABSTRACT

Objective: This study investigated whether the inflammation-based Glasgow prognostic score (GPS) predicted the prognosis of patients with endometrial cancer (EC) in terms of progression-free survival (PFS) and overall survival (OS).
Study design: Pretreatment GPS was examined to determine the correlations with recurrence and survival in 431 patients with EC. Statistical analyses were performed using the Mann–Whitney *U* test. PFS and OS were analyzed using the Kaplan–Meier method. Cox's proportional hazard regression was used for univariate and multivariate analyses.
Results: Median PFS and OS were 49.7 and 52.7 months, respectively. The follow-up range was 1 to 140 months. Kaplan–Meier analysis revealed that patients with EC cancer and high GPS (GPS 2) had a shorter PFS and OS than those with lower GPS (GPS 0 + 1) (PFS: $P < 0.001$; OS; $P < 0.001$). On multivariate analysis, GPS (GPS 2) was an independent predictor of both recurrence ($P < 0.001$) and survival ($P < 0.001$) for all cases of EC.
Conclusion: GPS can be useful as an indicator of poor prognosis in patients with EC.

1. Introduction

Endometrial carcinoma (EC) is the most common gynecologic malignancy in the United States, with an estimated 60,050 new cases diagnosed so far in 2016 [1]. In Japan, EC is currently the second most common gynecologic malignancy in women, with an estimated incidence in 2014 of 9673 new cases [2]. The overall survival (OS) rate of patients with EC is expected to be high because most patients have early-stage disease at the time of diagnosis [3,4]. However, the 5-year OS rate is around 80% for patients at any stage. Known prognostic factors for EC include stage, histology, myometrial invasion, cervical involvement and lymph node metastasis [5–9], but these parameters are not sufficient to accurately predict the prognosis of EC. A new approach for the pretreatment assessment of patients with EC is pivotal in improving outcomes.

Although serum CA125 levels have become a valuable tumor marker for the diagnosis of epithelial ovarian cancer and the detection of recurrence after primary treatment [10], its role as a useful tumor marker in EC is controversial. Several studies have reported that serum CA125 levels are important for the preoperative diagnosis and prediction of disease recurrence [11], and that their elevation is correlated with advanced-stage EC [12,13].

Inflammatory markers are important prognostic factors for survival in various cancer types. C-reactive protein (CRP) and albumin play prominent roles in tumor-related inflammation [14–16]. The Glasgow prognostic score (GPS) is based on the combination of CRP and albumin levels. Reportedly, inflammation-based prognostic scores, such as the GPS, are associated with survival in various cancers, including ovarian, lung, breast, esophagus, stomach, pancreas, kidney and colorectal cancers [17–24]. Thus far, GPS has not been shown to be a predictive factor for patients with EC. In this study, we investigated the correlation between pretreatment GPS and the prognosis of patients with EC.

☆ Condensation: Glasgow prognostic score is a prognosis predictor for patients with endometrial cancer.

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2. Materials and methods

2.1. Study population

In this retrospective study, we reviewed the medical records of 431 patients with EC who were treated at the Department of Obstetrics and Gynecology of Okayama University Hospital between January 2002 and December 2015. From the medical records, we extracted clinical and pathological data regarding pretreatment albumin, C-reactive protein (CRP), serum CA125, surgical International Federation of Gynecology and Obstetrics (FIGO) stage, histology, maximum tumor size, myometrial invasion, cervical invasion, lymphovascular space (LVS) involvement, peritoneal cytology, ovarian metastasis, lymph node metastasis, date of progression, date of last follow-up visit, and patient status at last visit. All patients were treated according to the Japan Society of Gynecologic Oncology clinical guidelines. Adjuvant chemotherapy was administered depending on risk factors (FIGO stage and histology), patient preference, and physician discretion. Chemotherapy consisted of paclitaxel (175 mg/m^2 infused over 3 h) and carboplatin (dose to achieve an area under the concentration-time curve of 5) for 3 to 6 cycles. All of the patients underwent a total abdominal hysterectomy, bilateral salpingo-oophorectomy and omentectomy with or without pelvic and/or para-aortic lymphadenectomy. Pelvic lymph node dissection included the right and left common iliac nodes, external and internal iliac nodes, as well as suprainguinal, obturator, sacral and parametrial nodal chains. Para-aortic lymph node dissection included the nodes located from the bifurcation of the aorta to the level of the renal vein.

2.2. Laboratory data collection

The serum albumin, CRP and CA125 levels of all subjects were recorded within 1 week before their treatments. Serum CA125 level was measured by electrochemiluminescence immunoassay (Modular Analysis E170, Roche Diagnostics, Tokyo, Japan). The cut-off value for the CA125 level was 35.0 U/ml. Levels of serum albumin and CRP were measured using latex nephelometry (LT Auto Wako, Osaka, Japan). The GPS was estimated as described previously [18]. Briefly, the high GPS group included patients with GPS 2: CRP levels >1.0 mg/dL and hypoalbuminemia (<3.5 g/dL). The low GPS group included patients with abnormal level of only one of these parameters (GPS 1) or no abnormalities (GPS 0).

2.3. Statistical analysis

Statistical analyses were performed using the Mann–Whitney *U* test for comparisons with controls. Progression-free survival (PFS) and OS of the groups were analyzed using the Kaplan–Meier method. Differences between the recurrence and survival curves were examined using the log-rank test. We performed univariate and multivariate analyses using Cox's proportional hazards model to determine which factors predicted PFS and OS after adjusting for effects of known prognostic factors. Analyses were performed using SPSS software version 20.0 (SPSS Inc., Chicago, IL, USA). A $P < 0.05$ was considered statistically significant.

3. Results

Patients were aged between 23 and 88 (mean: 58.0) years. Their mean pretreatment values were as follows: CRP, 0.1 (range: 0–15.23) mg/dl; albumin, 4.2 (2.1–5.2) g/dl; and CA125, 21.0 (3.5–1690.0) U/ml. Data on patients' FIGO stage, histology, maximum tumor size, myometrial invasion, cervical invasion, LVS involvement, peritoneal cytology, ovarian metastasis, lymph node metastasis, and CA125 are shown in Table 1.

We examined pretreatment GPS in patients with EC. P retreatment GPS was GPS 0 (CRP ≤ 1.0 mg/dL and albumin ≥3.5 g/dL) in 376 patients (87.2%), GPS 1 in 38 patients (8.8%) (CRP > 1.0 mg/dL and albumin ≥3.5 g/dL; 34 patients (7.9%), CRP ≤1.0 mg/dL and albumin <3.5 g/dL; 4 patients (0.9%)), and GPS 2 (CRP >1.0 mg/dL and albumin <3.5 g/dL) in 17 patients (4.0%) (Fig. 1A). We investigated whether pretreatment clinical characteristics were correlated with GPS and found that GPS was significantly associated with FIGO stage ($P = 0.001$), myometrial invasion ($P = 0.016$), cervical invasion ($P = 0.003$), LVS involvement ($P = 0.004$), lymph node metastasis ($P = 0.015$), and CA125 level ($P < 0.001$) of patients with EC (Mann–Whitney *U* test, $P < 0.05$; Table 2).

Patients had follow-up examinations approximately every 1 to 2 months for first 6 months, every 3 months for next 2 years, and every 6 months thereafter. For all patients, median PFS and OS were 49.7 and 52.7 months, respectively. The follow-up range was

Table 1
Patient and tumor characteristics.

Baseline characteristics		All patients
Age at diagnosis, y		Mean,58.0; range, 23–88
	Numbers	(%)
Stage		
I	309	71.7
II	36	8.3
III	51	11.8
IV	35	8.2
Histology		
Endometrioid adenocarcinoma G1	226	52.3
Endometrioid adenocarcinoma G2	96	22.2
Endometrioid adenocarcinoma G3	43	10
Clear cell carcinoma	4	0.9
Serous adenocarinoma	24	5.8
Mixed type carcinoma	6	1.3
Carcinosarcoma	27	6.4
Other carcinoma	5	1.1
Tumor maximum size		
≤4 cm	308	71.5
>4 cm	123	28.5
Myometrial invasion		
≤1/2	292	67.8
>1/2	139	32.2
Cervical invasion		
Absent	361	83.8
Present	70	16.2
LVS involvement		
Absent	357	82.8
Present	74	17.2
Peritoneal cytology		
Absent	359	83.3
Present	72	16.7
Ovarian metastasis		
Absent	399	92.6
Present	32	7.4
Lymph node metastasis		
Absent	378	87.7
Present	53	12.3
CA125		
≤35.0U/ml	292	67.8
>35.0 U/ml	139	32.2