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의학석사 학위논문

Effect of Supradiaphragmatic Lymph Node Metastasis Detected in 18F-FDG PET/CT on the Prognosis of Advanced-stage Epithelial Ovarian Cancer

진행성 상피성 난소암에서 18F-FDG PET/CT 상 발견된 횡경막 상부 임파선 전이의 예후에 대한 연구

2014 년 7 월

서울대학교 대학원

의학과 산부인과 전공

김 태 훈

A thesis of the Master's degree

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July 2014

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지도교수 송 용 상

이 논문을 의학석사 학위논문으로 제출함

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김 태 훈

김태훈의 의학석사 학위논문을 인준함

2014 년 07 월

위 원 장 (인)

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위 원 (인)

Abstract

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Introduction: In various study, supradiaphragmatic lymph node metastasis (SdLNM) was found to be the most common findings to classify FIGO stage III and IV disease in radiologic staging by PET/CT. Consequently, it is apparent that the use of PET/CT for diagnosing epithelial ovarian cancer (EOC) causes stage migration from stage III to stage IV and majority of the newly detected distant metastatic lesion is SdLNM. However, the prognostic impact of SdLNM detected by PET/CT has not been studied separately until today. Therefore I conducted retrospective study evaluating prognostic impact of SdLNM detected by PET/CT.

Methods: Seventy-five patients with advanced-stage EOC underwent PET/CT prior to treatment between 2003 and 2010. The patients were divided into three groups, as follows: PET stage III (n=45, group 1); PET stage IV by SdLNM alone (n=22, group 2); PET stage IV by SdLNM with other distant metastasis (n=8, group 3).

Results: Median age was 50 years, and the median duration of follow up was 46.6 months. Both overall survival (OS) and progression-free survival (PFS) were not poorer in group 2 than in group 1, whereas group 3 had worse OS when compared to group 1 (log rank, P =0.041) and group 2 (log rank, P <0.001). Multivariate analysis was conducted and included age, histology, grade, neoadjuvant chemotherapy and amount of intraperitoneal residual tumor. Whereas SdLNM with other distant metastasis was an independent prognostic factor for both OS (hazard

ratio [HR]: 3.4, 95% confidence interval [CI]: 1.03-11.15) and PFS (HR: 3.07, 95% CI: 1.12-8.43), SdLNM alone was not associated with poor prognosis.

Conclusions: Stage IV disease caused by SdLNM alone was not associated with poor survival unless accompanied by other distant metastasis. SdLNM alone should not be regarded as a poor prognostic factor when defining stage IV in advanced-stage EOC.

Key words: Ovarian cancer, staging, PET/CT, Supradiaphragmatic lymph node, prognosis, ^{18}F-FDG

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I. Introduction

Epithelial ovarian cancer (EOC) typically spreads throughout the peritoneal cavity, causing chronic bowel obstruction, which is the most common cause of death in EOC. Although intraperitoneal dissemination is considered the most common finding, EOC may also metastasize through lymphatic channels and hematogenously (1). Approximately 15% of patients with EOC are diagnosed as having International Federation of Gynecology and Obstetrics (FIGO) stage IV disease (2). The most common sites that cause upstaging of the disease to FIGO stage IV are intraparenchymal liver metastasis and malignant pleural effusion (3).

As a diagnostic work up for EOC, chest radiography should be performed to screen for pleural effusion, which should be pathologically proven by cytological examination. Additional imaging studies of the extra-abdominopelvic area are not mandatory for the diagnosis of EOC. However, when extra-abdominopelvic disease is suspected, any additional imaging modality can be used to detect distant metastasis (4). F-18-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) can detect various distant metastatic lesions, including metastasis to the liver parenchyma, lung, pleura, and supradiaphragmatic lymph nodes with improved sensitivity (5). Consequently, the use of PET/CT for diagnosing EOC leads to stage migration from stage III to stage IV due to the detection of metastatic lesions not visible using conventional imaging techniques (5, 6).

Supradiaphragmatic lymph nodes metastasis (SdLNM) in EOC was considered rare before PET/CT was introduced in the clinical setting (7). However, a recent study that evaluated the diagnostic accuracy of PET/CT in 95 prospectively enrolled patients with EOC reported that 16.5% had distant lymph node metastasis (5). They demonstrated that the most common finding in radiologic staging by PET/CT to classify stage III and IV disease was distant lymph node metastasis outside the pelvis and abdomen in which SdLNM comprised the majority of cases.

To date, few studies have evaluated the prognostic role of distant metastasis detected by PET/CT (6, 8, 9) and those that have done do not differentiate between SdLNM and other distant metastasis in the survival analysis. Thus, I investigated the prognostic significance of SdLNM detected by PET/CT in advanced-stage EOC.

II. Material and methods

II-1. Patients enrollment

Approval to conduct this study was obtained from our institutional review board. I identified 75 patients who underwent PET/CT as a diagnostic workup to evaluate the extent of the disease prior to treatment between June 2003 and December 2010. The inclusion criteria were as follows: (1) FIGO Stage IIIb–IV, (2) staging laparotomy for the purpose of maximal cytoreduction, (3) more than four cycles of adjuvant chemotherapy using carboplatin and taxanes, and (4) follow-up duration of more than three months. Patients that were treated with three to six cycles of neoadjuvant chemotherapy (NAC) before staging laparotomy were included in this study, while those with a previous diagnosis of another type of malignancy were excluded.

II-2. PET/CT imaging

Patients were evaluated using a dedicated PET/CT system (Gemini, Philips Medical Systems, Andover, MA, USA) prior to treatment and were instructed to fast for at least four hours before undergoing PET/CT. 125 ml of a barium sulfate solution (Readi-Cat [1.3% weight-volume barium sulfate suspension]; E-Z-EM, Westbury, NY, USA or EZCT [1.5% weight-volume barium sulfate suspension], Taejoon Pharm, Seoul, Korea) was administered orally one hour prior to imaging, following the method described in our previous study (10). PET/CT scans were obtained within one month (median, five days) of primary debulking surgery (PDS) or NAC.

Specialized nuclear medicine physicians evaluated the PET/CT images using all available clinical information. All PET/CT reports and images were reviewed by an experienced nuclear physician (Y.M.Y.) to ensure data consistency. A PET/CT-positive lymph node was defined as focal F-18-fluorodeoxyglucose (FDG) uptake above background. No specific standardized

uptake value was used when reading PET/CT, as in previous studies (9, 11). Physiologic uptake on PET/CT was excluded based on the comprehensive review of clinical information and the results of other imaging modalities, such as conventional CT. Size of SdLNMs were evaluated by using CT images.

II-3. Classification of patients by PET/CT staging

All distant metastatic lesions were identified using pretreatment PET/CT. Cytological evaluation was conducted if imaging studies showed pleural effusion. Distant metastasis detected by PET/CT presented two patterns: () SdLNM including cardiophrenic lymph nodes, internal mammary lymph nodes, mediastinal lymph nodes, and neck nodes and (2) other distant metastasis including intraparenchymal liver metastasis, lung metastasis, pleural metastasis, brain metastasis, and malignant pleural effusion. Based on PET/CT findings, the patients were divided into three groups: those with no evidence of distant metastasis (PET/CT Stage III, Group 1); those with SdLNM alone, without other distant metastasis (PET/CT Stage IV, Group 2); and those with SdLNM and other distant metastasis (PET/CT Stage IV, Group 3) (Fig. 1).

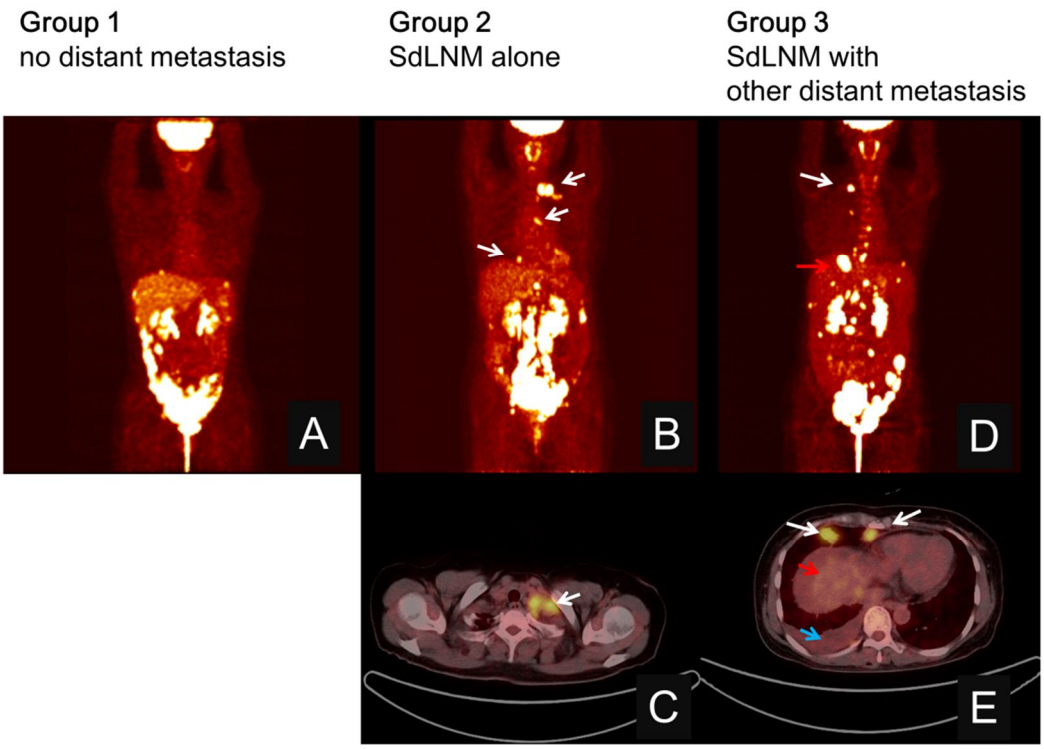
II-4. Optimal surgery

After staging laparotomy including maximal cytoreduction, the size and location of residual tumors were identified from the operation records. As PET/CT has high diagnostic value in detecting metastatic lymph nodes (12), it was necessary to decide whether the suspected metastatic lymph nodes on pretreatment PET/CT were considered when assessing the residual tumor status. To enable comparisons with other studies of residual tumor status, only surgically identified intraperitoneal residual tumors were considered when defining optimal surgery. Consequently, optimal intraperitoneal surgery indicated that the size of the residual tumors within the peritoneal cavity was 1 cm or less.

II-5. Statistical analysis

Various clinical and pathologic factors were compared using Fisher's exact test for categorical data and Student's t-test for continuous data. Recurrence was confirmed by biopsy or serial imaging studies. Progression-free survival (PFS) was defined as the time from the date of diagnosis to the date of histological and imaging evidence of recurrence. For overall survival (OS) analysis, information on date of death was obtained on January 15, 2013 from death certificates held at the Korea National Statistical Office. OS was defined as the time from the date of diagnosis to the date of death. Survival curves were estimated using the Kaplan–Meier method and differences between subgroups were compared using the log-rank test. The Cox proportional hazards model was used for multivariate comparison and the estimated hazard ratio (HR) and 95% confidence interval (CI) were calculated. A two-sided P value < 0.05 was considered statistically significant. SPSS ver. 19.0 (SPSS Inc., Chicago, IL) was used for the statistical analysis.

Fig. 1. (A, B, D) Maximum-intensity projection (MIP) anterior view. (C, E) Transaxial F-18-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) images of the supraclavicular region (C) and liver dome (E). A patient in Group 1 had no uptake in the supradiaphragmatic area or the liver parenchyma (A). A patient in Group 2 had intense uptake in multiple lymph nodes, including the retroperitoneal, cardiophrenic, parasternal, mediastinal, and supraclavicular lymph nodes (white arrows in B and C). A patient in Group 3 had intense uptake in the liver parenchyma (red arrows in D and E) and multiple lymph nodes, including the retroperitoneal, cardiophrenic, parasternal, mediastinal, and supraclavicular lymph nodes (white arrows in D and E). Pleural effusion is also depicted (blue arrow in E). SdLNM indicates supradiaphragmatic lymph node metastasis.



III. Results

III-1. Characteristics of study population

This study examined 75 patients that had undergone pretreatment PET/CT. The median age was 50 years (range, 33–76 years). 53 patients (70.7%) underwent PDS and 22 patients (29.3%) underwent three to six cycles of NAC followed by surgery. The median duration of follow-up was 46.6 months (range, 28.5–99.7 months). Optimal intraperitoneal surgery was completed in 58 cases (77.3%). All patients underwent adjuvant chemotherapy with carboplatin and taxane, with a mean of seven cycles (range, four to 12 cycles).

Pretreatment PET/CT identified 45 patients with PET/CT Stage III disease (Group 1) and 30 with PET/CT Stage IV disease (Groups 2 and 3). Of the 30 patients with PET/CT Stage IV disease, 22 patients presented with SdLNM alone (Group 2) and eight cases showed SdLNM with other distant metastasis (Group 3). The characteristics of the patients in Groups 1, 2, and 3 are summarized in Table 1. Patient age was significantly lower in Group 2 than Group 1 (median value, 49 vs. 52 years; $P = 0.024$) and NAC was conducted more often in Group 3 than in Group 1 (87.5% vs. 22.2%; $P = 0.001$). No patient with mucinous or clear cell histology presented with any distant metastasis. Intraperitoneal tumor status, rates of optimal intraperitoneal surgery and lymphadenectomy, and platinum resistance rates did not differ significantly between the groups. Of the patients who underwent lymphadenectomy, pathologically confirmed lymph node metastasis was more commonly observed in Group 2 than in Group 1 (86.7% vs. 51.5%; $P = 0.026$).

Table 2 depicts the characteristics of distant metastasis in 30 patients with PET/CT stage IV disease; the neck nodes were the most common distant metastatic lesion. In 20 patients, the SdLNMs were measured to be greater than 1cm on CT images. Neck node biopsy was performed in 9 of them, and all results showed positive tumor involvement.

III-2. Survival differences between groups defined by PET/CT staging

Figure 2 presents the PFS and OS curves for each group. There was no significant difference in PFS between Groups 1 and 2 (median value, 17.5 vs. 15.9 months; $P = 0.972$). Patients in Group 3 demonstrated shorter PFS than those in Group 1, but the difference was not statistically significant (median value, 11.5 vs. 17.5 months; $P = 0.06$). The OS curves differ significantly between the three groups: patients in Group 3 had worse OS when compared to those in Group 1 ($P = 0.041$) and Group 2 ($P < 0.001$). Interestingly, patients in Group 2 had better OS compared with those in Group 1 (log rank, $P = 0.032$).

To confirm the difference in prognosis of these groups, univariate and multivariate analyses were performed, taking into account age at diagnosis, histology, grade, NAC, and optimal intraperitoneal surgery (Table 3). In the multivariate analysis, mucinous or clear cell histology (hazard ratio (HR), 20; 95% confidence interval (CI), 4.56–87.55), non-optimal intraperitoneal surgery (HR, 3.44; 95% CI, 1.61–7.35), and SdLNM with other distant metastasis (HR, 3.07; 95% CI, 1.12–8.43) were independent predictors of recurrence, whereas SdLNM alone was not (HR, 1.05; 95% CI, 0.55–2.00). Regarding OS, age over 60, non-optimal intraperitoneal surgery, and SdLNM with other distant metastasis were statistically significant poor prognostic factors. However, SdLNM with other distant metastasis was the only independent prognostic factor for death in the multivariate analysis (HR, 3.40; 95% CI, 1.03–11.15).

Among 22 patients in group 2, histologic confirmation of SdLNM was achieved in 8 patients. 6 patients had continuously spreading retroperitoneal lymph node metastasis on PET/CT without peritoneal carcinomatosis and 7 patients remained alive at the time of this analysis, with a median follow-up duration of 45 months (range, 30–60 months). OS was not statistically different between patients with pathologically confirmed SdLNM and those without it (data not shown).

Table 1. Patient characteristics.

		PET/CT stage III	PET/CT stage IV	
	All	Group 1	Group 2	Group 3
Total	75	45	22	8
Age				
≤60	59 (78.7)	32 (71.1)	21 (95.5)	6 (75)
>60	16 (21.3)	13 (28.9)	1 (4.5)*	2 (25)
FIGO stage				
FIGO IIIB	9 (12)	9 (20)	0 (0)	0 (0)
FIGO IIIC	50 (66.7)	36 (80)	14 (63.6)	0 (0)
FIGO IV	16 (21.3)	0 (0)	8 (36.4)	8 (100)
Neoadjuvant chemotherapy				
no	53 (70.7)	35 (77.8)	17 (77.3)	1 (12.5)
yes	22 (29.3)	10 (22.2)	5 (22.7)	7 (87.5)*
Grade				
grade 1, 2 and unknown	19 (25.3)	12 (26.7)	5 (22.7)	2 (25)
grade 3	56 (74.7)	33 (73.3)	17 (77.3)	6 (75)
Histology				
Serous	65 (82.7)	36 (80)	20 (90.9)	6 (75)
Mucinous or clear cell histology	3 (4)	3 (6.7)	0 (0)	0 (0)
others	10 (13.3)	6 (13.3)	2 (9.1)	2 (25)
Intraperitoneal tumor status				
confined to pelvis	13 (17.3)	6 (13.3)	6 (27.3)	1 (12.5)
extrapelvic tumor	62 (82.7)	39 (86.7)	16 (72.7)	7 (87.5)
Intraperitoneal residual tumor				
optimal surgery	58 (77.3)	34 (75.6)	17 (77.3)	7 (87.5)
non-optimal surgery	17 (22.7)	11 (24.4)	5 (22.7)	1 (12.5)
Platinum resistance				
no	44 (58.7)	29 (64.4)	13 (59.1)	2 (25)
yes	31 (41.3)	16 (35.6)	9 (40.9)	6 (75)
Retroperitoneal lymphadenectomy				
no	22 (29.3)	12 (26.7)	7 (31.8)	3 (37.5)
yes	53 (70.7)	33 (73.3)	15 (68.2)	5 (62.5)
Pathologically positive lymph node				
no	21 (39.6)	16 (48.5)	2 (13.3)	3 (60)
yes	32 (60.4)	17 (51.5)	13 (86.7)*	2 (40)

FIGO indicates Fédération Internationale de Gynécologie et d'Obstétrique; PET/CT, F-18-fluorodeoxyglucose positron emission tomography/computed tomography

* The difference in comparison to group 1 was statistically significant ($P \leq 0.05$).

Table 2. Characteristics of distant metastasis in 30 patients with PET/CT stage IV.

Total	All	Group 2	Group 3
Number of patients with SdLNM	30	22	8
Size of SdLNM			
< 1cm	10	10	0
≥ 1cm	20	12	8
Patholgically confirmed SdLNM			
no	21	14	7
yes	9	8	1
Location of SdLNM			
Neck	18	13	5
Axilla	5	4	1
Parasternal	12	9	3
Mediastinum	13	8	5
Cardiophrenic	12	8	4
Other distant metastasis	8	0	8
Malignant pleural effusion	6	0	6
Liver parenchyma	2	0	2
Lung	1	0	1
Bone	2	0	2
Pleura	3	0	3

PET/CT indicates F-18-fluorodeoxyglucose positron emission tomography/computed tomography; SdLNM, supradiaphragmatic lymph node metastasis

Fig. 2. Progression-free (A) and overall (B) survival according to the pattern of distant metastasis.

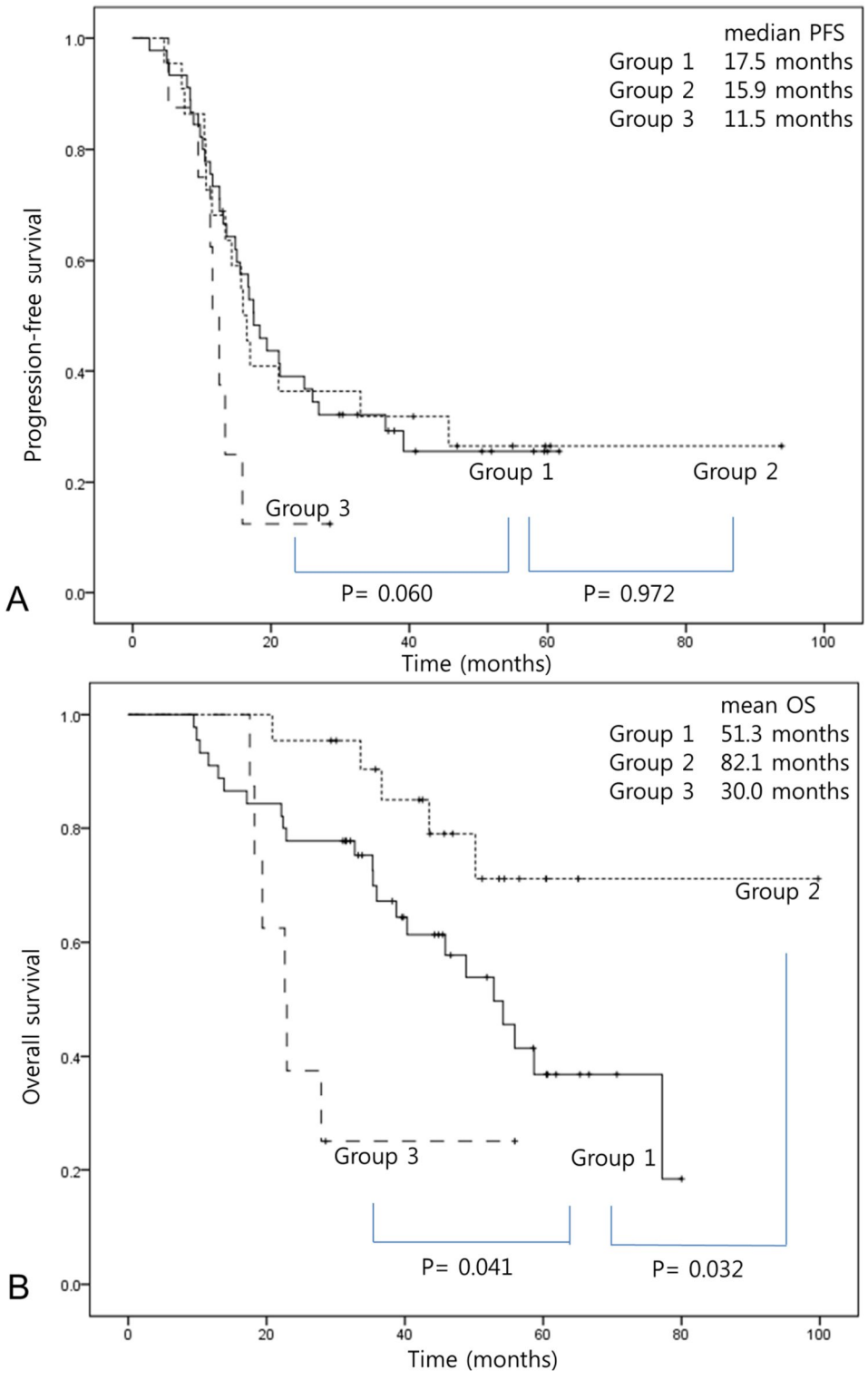


Table 3. Factors affecting pregression-free survival and overall survivals in study population.

Factor	Number	Progression-free survival				Overall survival			
		Univariate		Multivariate		Univariate		Multivariate	
		HR	95% CI.	HR	95% CI.	HR	95% CI.	HR	95% CI.
Age									
≤60	59	1.00	(reference)	1.00	(reference)	1.00	(reference)	1.00	(reference)
>60	16	1.66	0.88-3.11	1.22	0.54-2.76	2.12	1.04-4.29	2.24	0.78-6.44
Grade									
grade 1, 2 and unknown	19	1.00	(reference)	1.00	(reference)	1.00	(reference)	1.00	(reference)
grade 3	56	0.94	0.51-1.72	1.59	0.78-3.23	0.93	0.44-1.96	2.33	0.86-6.28
Histology									
Serous	62	1.00	(reference)	1.00	(reference)	1.00	(reference)	1.00	(reference)
Mucinous or clear cell histology	3	9.29	2.69-32.06	20.00	4.56-87.55	3.96	0.92-17.02	5.33	0.80-35.31
others	10	0.64	0.25-1.61	0.73	0.28-1.88	1.88	0.71-4.93	2.35	0.83-6.63
Neoadjuvant chemotherapy									
no	53	1.00	(reference)	1.00	(reference)	1.00	(reference)	1.00	(reference)
yes	22	1.11	0.62-1.97	1.01	0.49-2.05	1.24	0.59-2.63	0.96	0.35-2.56
Intraperitoneal residual tumor									
optimal surgery	58	1.00	(reference)	1.00	(reference)	1.00	(reference)	1.00	(reference)
non-optimal surgery	17	2.88	1.55-5.32	3.44	1.61-7.35	2.52	1.25-5.05	2.33	0.93-5.82
Distant metastasis lesion									
No	45	1.00	(reference)	1.00	(reference)	1.00	(reference)	1.00	(reference)
SdLNM alone	22	1.01	0.55-1.84	1.05	0.55-2.00	0.36	0.13-0.95	0.47	0.16-1.35
SdLNM with other distant metastasis	8	2.1	0.95-5.02	3.07	1.12-8.43	2.68	1.06-6.77	3.40	1.03-11.15

HR indicates harzard ratio; CI, confidence interval; SdLNM, supradiaphragmatic lymph node metastasis.

IV. Discussion

SdLNM in EOC was considered rare before PET/CT was introduced, as SdLNMs are difficult to access using conventional laparotomy and imaging study of extra-peritoneal area is not mandatory in staging of EOC. Although some investigators have suggested that it is possible to remove SdLNM without significant morbidity (13, 14), these types of advanced surgery are not commonly performed as they have not been found to have survival benefits. However, SdLNM has been reported to be the most common distant metastasis lesion in advanced-stage EOC, with an incidence of 30–66% in most studies using pretreatment PET/CT (6, 9, 11).

A small number of studies have evaluated the prognostic role of distant metastasis detected using PET/CT. In 2010, Risum et al. evaluated the prognostic role of PET/CT in 66 patients with advanced-stage EOC (64 cases of Stage III and two of Stage IV) and reported that the use of diagnostic PET/CT leads to stage migration, where 41% of cases (27 of 66) were diagnosed with PET/CT Stage IV (6). In 2012, the same authors published the largest prospective study evaluating the prognostic role of PET/CT in advanced-stage EOC (143 patients with Stage IIIC and 10 with Stage IV) (9). They evaluated 153 consecutive patients with preoperative PET/CT results that underwent primary debulking surgery. Of the 153 patients, 69 (45%) were diagnosed as PET/CT Stage IV. SdLNM was found in 45 patients and 16 patients had both SdLNM and other distant metastasis, such as parenchymal metastases or malignant pleural effusion. While PET/CT Stage IV remained a poor prognostic factor in a univariate analysis, the median difference in OS between PET/CT Stage III and Stage IV was just 1.5 months (28.6 vs. 27.1 months; $P = 0.01$) and this difference was not significant in a multivariate analysis. Although SdLNM was the most common distant metastatic lesion indicating PET/CT Stage IV, SdLNM was not considered separately from other distant metastasis in the survival analysis. It appears that the use of PET/CT in staging EOC compromises the discriminative value of staging and that SdLNM detected by PET/CT contributes to this reduced discrimination capability.

To date, only one study has attempted to evaluate the prognostic impact of SdLNM detected by PET/CT separately from other distant metastasis (8). However, this study did not evaluate all SdLNM lesions. To the best of our knowledge, our study is the first to evaluate every SdLNM in a survival analysis and to separate SdLNM from other sites of distant metastasis.

In Stage IV EOC, different sites of distant metastasis may reflect different tumor biology as opposed to more advanced disease at diagnosis, considering that the prognosis varies according to the site of distant metastasis (15, 16). In 2010, Wimberger et al. evaluated 573 patients with FIGO Stage IV disease that were included in multi-center prospective randomized Phase III trials (16). Complete cytoreduction, mucinous histological type, multiple sites of metastasis, and performance status were statistically significant independent prognostic variables for OS. While the median OS was 24.0 and 21.8 months in patients with malignant pleural effusion and intraparenchymal liver metastasis, respectively, patients with Stage IV disease indicated by other causes, including extra-abdominal lymph node metastasis, had a median OS of 33.7 months. In our study, the median OS of patients in Group 3 was 22.9 months, which is similar to the findings of these studies.

Lymphatic metastasis has received much attention due to its impact on prognosis, as well as the role of lymphadenectomy. It is apparent that patients with Stage IIIC EOC due only to positive nodes have a more favorable prognosis than other Stage IIIC patients (17-19). A similar concept can be applied to SdLNM. Cases of EOC showing supraclavicular lymph node involvement without peritoneal carcinomatosis have been reported (20). Moreover, in our study, of the nine patients with pathologically confirmed neck node metastasis, six had continuously spreading retroperitoneal lymph node metastasis on PET/CT without peritoneal carcinomatosis and seven remained alive at the time of this analysis, with a median follow-up duration of 45 months (range, 30–60 months). Interestingly, patients in Group 2 had better OS than those in Group 1 in the univariate analysis (Table 3). Although this result may seem paradoxical, it should be viewed as it is because the prognostic impact of SdLNM has not been evaluated separately to date. Moreover, the largest study that evaluated prognostic impact of distant

metastasis detected by PET/CT showed similar result with ours. In the study by Risum et al., 15 patients with neck metastasis on PET/CT had a median OS of 35.9 months, while the remaining 137 patients had a median OS of 26.9 months, although the difference was not statistically significant ($P = 0.07$) (9). From these findings, it can be inferred that there is a specific tumor biology favoring lymphatic spread and that this may be associated with a favorable prognosis. Further studies are warranted to identify the presence of these tumors.

In addition to SdLNM, malignant pleural effusion or parenchymal metastases such as pleura, lung, bone, and liver parenchyma were detected by PET/CT in eight patients. In contrast to patients with SdLNM alone, these patients had worse PFS and OS compared to those with PET/CT Stage III. Parenchymal metastasis is considered a result of hematogenous spread and may reflect different biologic behavior (16). PET/CT can detect various distant metastases with high sensitivity (5). However, it is inappropriate to classify every patient with SdLNM on PET/CT as Stage IV as, contrary to malignant pleural effusion and parenchymal metastases, SdLNM alone has not been shown to be a poor prognostic factor in advanced-stage EOC. I believe that SdLNM should not be considered a poor prognostic factor when defining Stage IV until its prognostic impact has been evaluated in a large-scale prospective study using PET/CT.

In multivariate model, debulking status was not a significant independent factor for OS (HR, 2.33; 95% CI, 0.93–5.82). Because optimal debulking status invariably has been demonstrated to be significant prognostic factor in EOC, I think that this result is an artifact due to the small number of patients in this study.

The main limitation of our study mainly is its retrospective nature and small number of patients. It is possible that a relatively greater number of patients that had an unusual disease spread pattern for EOC were included in the study population than could be expected in the general population of patients with EOC. Additionally, not all lymph nodes that were suspicious for metastasis on PET/CT were confirmed by pathologic review. However, PET/CT has been shown to be more accurate than CT or MRI especially in the detection of retroperitoneal lymph node metastasis (12). Although all PET/CT images were reviewed to exclude physiologic

uptake on PET/CT, it is still possible that physiologic uptake was considered as SdLNM. An attempt to biopsy each SdLNM detected by PET/CT can resolve these limitations. However, the patients in Group 2 with pathologically confirmed SdLNM showed excellent OS and there was no difference in OS between them and the patients in group 2 without pathologic confirmation, which means composition of group 2 is not heterogenous.

Based on our results, I conclude that SdLNM alone detected by PET/CT is not a poor prognostic factor unless accompanied by other distant metastasis, such as parenchymal metastasis or malignant pleural effusion. The presence of tumors favoring lymphatic spread can be identified by PET/CT and these tumors may have favorable biologic behavior. Large-scale prospective observational studies using pretreatment PET/CT are warranted to identify these tumors. In this regard, the spread pattern of distant metastasis assessed by PET/CT may be a prognostic marker in advanced-stage EOC.

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국 문 초 록

연구목적: 진행성 상피성 난소암에서 횡경막 상부 임파선 전이(supradiaphragmatic lymph node metastasis, SdLNM) 는 F-18-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) 를 통해 흔히 발견된다. SdLNM 은 PET/CT 를 통해 발견되는 원위 전이 중 가장 흔하며 이로 인하여 병기가 3 기에서 4 기로 변경된다. 진행성 상피성 난소암에서 PET/CT 상 발견된 SdLNM 의 예후에 대한 연구는 보고된 바가 없기에 의무기록을 이용한 후향적 연구를 진행하였다.

연구방법: 2003 년부터 2010 년까지 병기 III 기 또는 IV 기의 진행성 상피성 난소암으로 진단받은 환자 중 치료 시작 전 PET/CT 를 촬영하였으며 생존분석이 가능한 환자 75 명의 의무 기록을 검토하였다. PET/CT 결과를 토대로 병기설정을 하였을 때 PET 병기 3 기는 45 명 (그룹 1), PET 병기 4 기는 30 명이었다. PET 병기 4 기 환자 중 SdLNM 만으로 병기 IV 로 분류된 환자는 22 명 (그룹 2) 이었고 SdLNM 과 다른 원위 전이가 동반된 환자는 8 명 (그룹 3) 이었다. 세 그룹의 무병 생존과 전체 생존을 비교 분석하였다.

결과: 연구 대상 환자의 나이의 중앙값은 50 세 이었으며 경과 관찰 기간의 중앙값은 46.6 개월이었다. 53 명은 일차 종양 감출술을 시행 후 보조항암치료를 시행하였으며 22 명은 평균 3 회의 선행 항암치료를 시행 후 종양 감축술과 보조항암치료를 시행하였다. 그룹 1 과 비교하였을 때 그룹 2 의 무병 생존과 전체 생존은 차이가 없었다. 하지만 그룹 3 은 그룹 1 과 그룹 2 에 비하여 전체

생존이 짧았다. 나이, 조직학적 유형, 분화도, 선행 항암치료 여부, 수술 후 잔여 종양 크기 등을 보정한 콕스 회귀 분석을 시행하였다. SdLNM 과 다른 원위 전이가 동반되었을 경우 전체 생존과 무병 생존에 있어 독립적인 예후 인자이었으나 SdLNM 단독은 예후에 유의한 영향을 갖지 않았다.

결론: 다른 원위 전이 동반 없이 SdLNM 이 단독으로 존재하는 병기 4 기 환자는 병기 3 기 환자에 비해 나쁜 예후를 보이지 않았다. PET/CT 로 발견된 원위 전이는 그 분포에 따라 다른 예후를 보이므로 PET/CT 로 발견된 SdLNM 자체를 나쁜 예후 인자로 간주하는 것은 피해야 한다.

주요어: 난소암, PET/CT, 횡경막 상부 임파선, 예후, 18F-FDG

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