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# Prognostic value of FDG-PET in patients with ovarian carcinoma following surgical treatment

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***Objective:*** To determine the prognostic value of FDG-PET after surgical resection in patients with ovarian carcinoma, we compared the results of FDG-PET and serum CA-125 level and prognosis of patients. ***Methods:*** Eighteen patients underwent a total of 32 FDG-PET examinations following surgery for ovarian carcinoma from October 2001 to December 2002 at our hospital (median follow-up period, 31 months). Age of the patients at the time of the initial FDG-PET examination ranged from 31 to 73 years (mean 52 years) and the period from surgery to the initial FDG-PET examination ranged from 5 to 109 months (mean 30 months). Serum CA-125 levels were determined on the occasion of each FDG-PET examination. Recurrent tumors were treated with surgery in 5 cases, radiotherapy in 2 cases, and chemotherapy in 9 cases. ***Results:*** The initial FDG-PET examinations revealed that 13 cases had positive and 5 cases had negative findings, which included 2 false positive cases. The survival rate for all patients at 1 year and 2 years after the initial examination was 82% and 63%, respectively. Two-year survival rates in patients with positive and negative FDG-PET findings were 51% and 83%, respectively, and the difference was not statistically significant ($p = 0.19$). Furthermore, 4 patients with normal CA-125 levels and 14 patients with elevated CA-125 levels showed 2-year survival rates of 100% and 51%, respectively, and they were not significantly different ($p = 0.11$). For all 32 examinations, the 2-year survival rates for patients with normal CA-125 levels (100%) were significantly higher ($p = 0.025$) than that for patients with elevated CA-125 levels (47%), however there was no significant difference ($p = 0.20$) between FDG-PET positive cases (53%) and negative cases (83%). ***Conclusion:*** The prognosis of patients with positive FDG-PET findings was less favorable than that of patients with negative findings. However, over the mean extended observation period of about 2.5 years, no significant difference in the prognosis of patients was observed between the two groups. The results of the present study indicate that elevated serum CA-125 levels may be more useful for evaluating the prognosis of ovarian cancer during the post-operative follow-up than FDG-PET findings.

**Key words:** ovarian carcinoma, FDG-PET, CA-125, survival

## INTRODUCTION

THE USEFULNESS of positron emission tomography with 2-[$^{18}$F]fluoro-2-deoxy-D-glucose (FDG-PET) examinations to detect recurrent ovarian cancer has been reported.[1–4] Zimny et al. showed that FDG-PET was a relevant diagnostic tool to detect recurrent ovarian cancer in patients with an elevated Cancer Antigen (CA)-125 level.[5] Yen et al. showed that the diagnostic accuracy of FDG-PET,

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**Table 1** Relationship between results of FDG-PET and serum CA-125 at initial examination

| | | CA-125* | |
|---|---|---|---|
| | | Elevated | Not elevated |
| FDG-PET | Positive | 11 | 1 |
| | Negative | 3 | 3 |

*16 U/m*l* or higher, or more than double of the postoperative lowest level, is defined to be elevated.

**Table 2** Relationship between results of FDG-PET and serum CA-125 for all examination

| | | CA-125* | |
|---|---|---|---|
| | | Elevated | Not elevated |
| FDG-PET | Positive | 13 | 7 |
| | Negative | 5 | 7 |

*16 U/m*l* or higher, or more than double of the postoperative lowest level, is defined to be elevated.

serum CA-125, and CT/MRI examinations were 91.7%, 83.3%, and 66.7%, respectively, and indicated that FDG-PET was more useful than serum CA-125 and CT/MRI.[2] However, the relationship between FDG-PET results and the prognosis of patients has not been determined. In order to elucidate the value of FDG-PET in predicting the prognosis of patients with ovarian cancer after surgical resection, we compared the prognostic value of FDG-PET and serum CA-125 level.

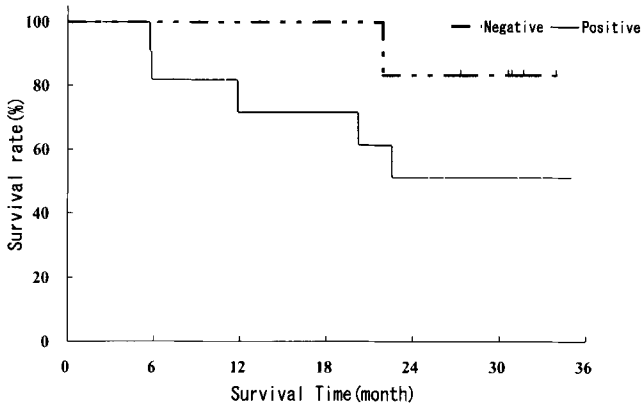


**Fig. 1** Survival by initial FDG-PET findings.

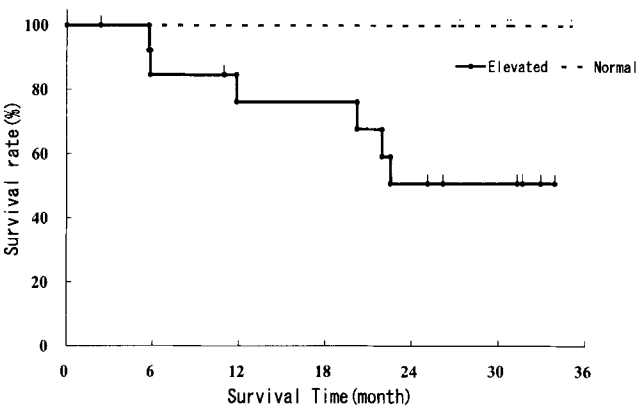


**Fig. 2** Survival by initial CA-125 levels.

## MATERIALS AND METHODS

*Patients*

The study included 18 patients with ovarian cancer who underwent FDG-PET examinations and measurements of serum CA-125 following surgery in the 15-month period from October 2001 to December 2002. Five patients underwent multiple examinations, and thus a total of 32 examinations were performed. The age of the patients at the initial FDG-PET examination ranged from 31 to 73 years (mean 52 years) and the period from surgery to the initial FDG-PET examination ranged from 5 to 109 months (mean 30 months).

*FDG-PET findings*

FDG-PET study was performed with PET scanner SET2400W (Shimadzu Corporation, Kyoto, Japan) at Gunma University Hospital or POSICAM-HZL (Positron Corporation, Houston, USA) at Nishidai Clinic. Whole-body image acquisition was initiated 50 minutes after the injection of 5–6 MBq/kg of FDG. A total of 5–6 bed positions from head to thigh were imaged with an acquisition time of 8 minutes per position. Patients were fasted for at least 5 hours before FDG was injected and were asked to void just before the scan to minimize the tracer accumulation in the urinary bladder. All FDG-PET images were interpreted independently by two experienced radiologists. CT and MRI examinations were performed at Toranomon Hospital and interpreted independently by two experienced radiologists. Discrepancies between readers were resolved by consensus.

*CA-125 levels*

Measurement of serum CA-125 was performed at the time of each FDG-PET examination. A level of 16 U/m*l* or higher, or more than double of the postoperative lowest level, was considered to be abnormally elevated. At the initial FDG-PET examination, 14 cases were abnormal and 4 were within normal limits. Of a total of 32 examinations, 18 examinations were classified as abnormal and 14 examinations were normal. Furthermore, CA-125 was measured in 13 of 18 patients at the time of the first treatment, and all the 13 patients showed an abnormal CA-125 level.

*Follow-up and treatment*

Follow-up examinations were carried out in the Department of Radiation Oncology and Nuclear Medicine and/

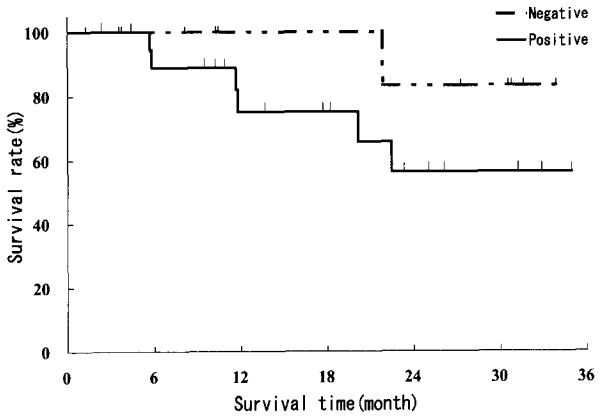


**Fig. 3** Survival by all FDG-PET findings.

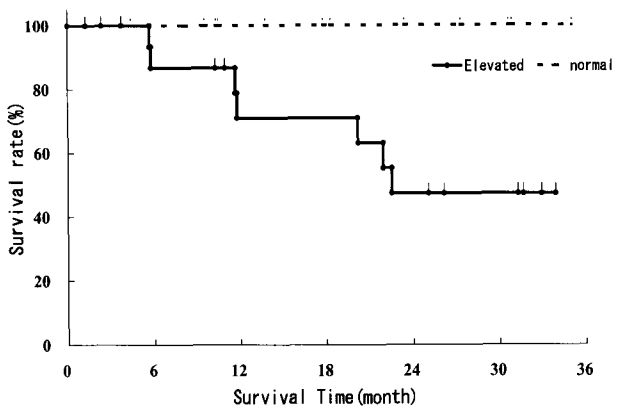


**Fig. 4** Survival by all CA-125 levels.

or Department of Obstetrics and Gynecology at Toranomon Hospital. Median follow-up period was 31 months (2–35 months).

Four patients did not receive treatment in the follow-up period. The other 14 patients received treatment; 5 with surgery, 2 with radiotherapy, and 11 with chemotherapy. Two patients received only optimal supportive care.

## RESULTS

At the initial FDG-PET examination, 14 patients showed positive uptake of FDG in the tumor, whereas 4 were negative. Among 14 patients with positive findings, there were two false positive cases, one with an atypical mycobacteriosis and one with physiological FDG uptake in the colon. These 2 false-positive cases showed no recurrence during the post-surgical course of observation. Therefore, our final analysis was performed with 12 positive cases and 6 negative cases (Table 1). As a result, 20 out of 32 FDG-PET examinations were positive and 12 examinations were negative (Table 2).

The survival rates for all patients at 1 year and 2 years after the initial FDG-PET examination were 82% and 63%, respectively. In patients with positive FDG-PET findings, the 2-year survival rate was 51%, whereas, in cases with negative FDG-PET was 83%, and they were not significantly different ($p = 0.19$) (Fig. 1). Moreover, for those patients with high CA-125 levels at the initial examination, the 2-year survival rate was 51%, while it was 100% with normal CA-125 levels, and there was no significant difference between them ($p = 0.11$) (Fig. 2).

As for all 32 examinations, including those during the extended follow-up period, the 2-year survival rate was 53% for patients with positive FDG-PET findings and 83% for those with negative findings ($p = 0.20$) (Fig. 3). Although all patients with normal CA-125 levels survived up to 35 months, those with elevated CA-125 levels had a survival rate of 47% at 2 years after the initial examination, and there was a significant difference ($p = 0.025$) between these two groups (Fig. 4).

## DISCUSSION

A few reports have suggested that FDG-PET is useful for evaluating the prognosis of ovarian cancer. Kim et al. reported that no differences in the progression-free and disease-free survival were observed between the group of patients for whom FDG-PET was performed following cyto-reductive surgery with adjuvant chemotherapy and the group of patients for whom second look surgery was performed.[6] To our knowledge there has been no report that compared the FDG-PET findings and survival of patients after surgical treatment of ovarian cancer.

In the present study, we performed FDG-PET following surgery for ovarian cancer to determine the relationship between the FDG-PET findings and survival. The results indicated that the FDG-PET findings did not seem to be a definitive predictor of survival as compared with serum CA-125 level. However, as shown in Figures 1 and 3, the prognosis was less favorable in cases with positive FDG-PET findings. In contrast, CA-125 level might be more useful as a significant prognostic indicator. It is notable that the prognosis is favorable when CA-125 is not elevated. Therefore, we conclude that an elevation in CA-125 might be more relevant than the FDG-PET findings to the prognosis of patients with ovarian cancer following surgical treatment.

There are a number of reports showing the relationship between the elevation of CA-125 levels and early detection of recurrence after treatment of ovarian cancer. As for cancer recurrence, many studies have shown that CA-125 levels are elevated prior to the manifestation of clinical symptoms or the detection of recurrence by diagnostic imaging such as CT. However, it remains controversial whether treatment should be started after suspecting recurrence only on the basis of elevated CA-125 levels.[7,8] Phase III randomized study of the benefit of early chemotherapy based on CA-125 level only versus delayed chemotherapy based on conventional clinical indicators is now under investigation by European Organization for

Research and Treatment of Cancer (called OV05 by MRC).

Histology, grading, and successful surgical treatment have been considered as prognostic factors for ovarian cancer. Recently, Gronlund et al. reported that CA-125 is a better prognostic tool than CT which is used for the Response Evaluation Criteria in Solid Tumor (RECIST) in second-line treatment with topotecan or paclitaxel plus carboplatin.[9] Makar et al. reported that histologic type and serum CA-125 at relapse were independent prognostic factors for further survival. They found that 25 patients with CA-125 ≤35 U/m*l* had a longer survival after diagnosis of recurrence than 110 patients with CA-125 >35.[10] On the other hand, Gadducci et al. reported that CA-125 level at relapse (at any cut-off value; 35, 76, 178, 339 U/m*l*) was not related to survival.[11]

FDG-PET has, as an imaging tool, a unique value to detect the site of recurrence that could not be visualized by the measurement of tumor markers, and aids in the local treatment. FDG-PET could detect recurrent foci in cases with negative results of tumor marker.[12]

There are some limitations that have to be mentioned about the present study. The population of the study is small. Only 5 patients were FDG-PET negative because the study was not a prospective randomized trial. The follow-up period (median, 31 months) may not be sufficiently long to show a difference in the survival rate between the two groups with FDG-PET positive and negative status. Effectiveness of the chemotherapy may also be one of the factors that make the difference in survival less than that of other cancers that are resistant to chemotherapy.[13] Accuracy of detecting recurrence is not considered in the present study, because the aim of the study is to compare the abnormal results of FDG-PET with the prognosis of patients.

In conclusion, the prognosis of patients with positive FDG-PET findings tended to be less favorable; however, no significant difference in the prognosis was observed between FDG-PET positive and negative cases over the median follow-up period of 31 months. The serum CA-125 level may be more valuable tool to evaluate the prognosis of ovarian cancer after operation as compared with FDG-PET. Further study with increased number of patients with longer follow-up period should be performed to support the findings of the present study.

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