Modalities for Evaluating Chemotherapeutic Efficacy and Survival Time in Patients with Advanced Pancreatic Cancer: Comparison between FDG-PET, CT, and Serum Tumor Markers

Masaki Kuwatani1, Hiroshi Kawakami1, Kazunori Eto1, Shin Haba1, Tohru Shiga2, Nagara Tamaki2 and Masahiro Asaka1

Abstract

Objective It has recently been reported that 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) is useful for estimation of the chemotherapy effect. Thus, we examined the value of FDG-PET in assessing the efficacy of chemotherapy in advanced pancreatic cancer, and compared this modality with tumor markers (TMs) and CT.

Patients and Methods Nineteen patients with unresectable pancreatic adenocarcinoma were enrolled. All patients received chemotherapy with gemcitabine and S-1, an oral derivative of 5-fluorouracil, and underwent FDG-PET, CT, and serological examination for TMs before and after chemotherapy.

Results Standardized uptake value in FDG-PET before treatment and survival time were not correlated. A good prognosis was seen after 1 course of chemotherapy in patients whose tumors were in partial or complete remission as assessed by FDG-PET [median of survival time (MST), 12.5 months] or TMs (MST, 13.5 months), but not in CT responders (MST, 10.3 months). Furthermore, patient prognosis correlated with PET and TM assessment of the best tumor response through all courses. Namely, both PET and TM were useful for the prediction of survival or chemotherapy sensitivity of the patients.

Conclusion FDG-PET and TMs can each play an adjunct role to CT for estimating the effect of chemotherapy and predicting survival by distinguishing between responders and non-responders among patients with advanced pancreatic cancer.

Key words: FDG-PET, pancreatic cancer, tumor marker, computed tomography, predictor of survival

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Introduction

Pancreatic cancer is one of the most difficult diseases to detect and treat early in its progression. Although by worldwide consensus the best therapy for pancreatic cancer is surgical resection, unresectable cases have been treated with various methods, including chemotherapy (1), radiotherapy (2), chemoradiotherapy (3, 4) and immunotherapy (5, 6). Recently, studies have reported the effectiveness of chemotherapy with gemcitabine (GEM) alone or in combination with other drugs (7, 8). Although these treatments have improved performance status and survival, estimation of the therapeutic effect, especially at early stages of the disease, remains difficult. Computed tomography (CT) is the standard modality both for diagnosing pancreatic cancer and for estimating the effect of its treatment.

18F-fluorodeoxyglucose positron emission tomography (FDG-PET) has been used for systemic detection of small malignant lesions (9) and for estimation of glucose metabolism in a tumor (11). Some studies have demonstrated the usefulness of FDG-PET for predicting survival of patients.

1Department of Gastroenterology, Hokkaido University Graduate School of Medicine, Sapporo and 2Department of Nuclear Medicine, Hokkaido University Graduate School of Medicine, Sapporo

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Correspondence to Dr. Hiroshi Kawakami, hiropon@med.hokudai.ac.jp
with pancreatic cancer or for early estimation of the effects of chemotherapy (12) and radiotherapy (13). All of these studies illustrate the benefit of FDG-PET, however, this imaging modality is not necessarily useful in every situation.

The aim of this study was to clarify the effectiveness of FDG-PET in evaluating the response to therapeutic interventions, especially chemotherapy, for pancreatic cancer. We treated patients with unresectable pancreatic cancer using GEM and S-1, and we evaluated the tumor response to this chemotherapeutic regimen using FDG-PET, CT, and serum tumor markers (TMs).

**Patients and Methods**

**Patients**

The study population consisted of 19 patients with unresectable pancreatic cancer [stage III or IV according to the Union Internationale Contre le Cancer staging system (UICC-TNM), 6th edition], cytologically or pathologically diagnosed as adenocarcinoma. All subjects were treated at Hokkaido University Hospital between March 2004 and October 2007. Each individual underwent an FDG-PET scan, enhanced CT scan, and serological examinations for TMs sequentially within two weeks before the start of chemotherapy and one month afterwards. Ten patients also received an FDG-PET scan, in addition to CT and TMs, after every cycle of chemotherapy for 6 to 12 months. None of the patients had severe diabetes mellitus, which would strongly affect the results of FDG-PET. The duration of patient follow-up was 2.9-25 months after entry into the study (Table 1). All patients gave informed consent for receiving chemotherapy, FDG-PET scans, CT scans, and serological examinations.

**Treatment**

We administered GEM (800-1200 mg/m²) in a 30-min intravenous infusion on days 1 and 15 of each cycle. S-1, a combination of the oral fluorouracil prodrug tegafur with two modulators, 5-chloro-2,4-dihydroxypyridine and potassium oxonate, (60-80 mg/m²), was also administered orally twice daily for 14 consecutive days (from day 1 to day 14) followed by a 2-week break. This cycle was repeated every 28 days. Patients enrolled in the study received combination GEM and S-1 chemotherapy as their first regimen until either progression of the disease or unacceptable toxicity occurred. Patients in whom the first-line chemotherapy was discontinued received other chemotherapy or optimal supportive care.

**FDG-PET**

Whole-body ¹⁸F-FDG-PET imaging was performed with an ECAT EXACT 47 scanner (Siemens-CTI, Knoxville, Tenn.). This scanner provides 47 contiguous image planes with 3.375-mm plane spacing and an in-plane resolution of 6.6 mm.

Before the PET study, all of the patients fasted for at least 6 hours, and serum glucose levels were checked before administration of ¹⁸F-FDG. The dose of ¹⁸F-FDG was 4.5 MBq/kg for each patient.

Static emission scans were performed 60 minutes after ¹⁸F-FDG administration using the three-dimensional acquisition mode for a duration of 2 minutes per bed position. Thereafter, transmission scans using externally rotating germanium-68 rod sources were performed for attenuation correction. Attenuation-corrected data were reconstructed iteratively using an ordered subset expectation maximization algorithm. Image processing and reconstruction were performed on a SUN workstation.

The ¹⁸F-FDG uptake within lesions was quantified by determining the maximum activity within a spherical region of interest (ROI). The ROI was placed over the tumor in the slice that showed maximum FDG uptake in the baseline scan. In the second PET scan, the ROI was placed at the same position as in the baseline study using the anatomic landmarks of the transmission image as a reference. After correction for radioactive decay, the ROI was semiquantitatively analyzed by computing a standard uptake value (SUV) according to the following formula: Max SUV = maximum ROI activity (MBq/mL)/injected dose (MBq)/body weight (g).

**Evaluation of tumor response by CT**

Objective tumor responses were evaluated using contrast-enhanced CT scans according to the Response Evaluation Criteria in Solid Tumors (RECIST) criteria (14): complete response (CR), complete depletion of all lesions; partial response (PR), a 30% or greater reduction in the sum of the longest diameters of all measurable lesions; stable disease (SD), less than a 30% reduction or less than a 20% increase in the sum of the products of the longest diameters of all measurable lesions; and progressive disease (PD), an increase of 20% or more in the sum of the products of the longest diameters of all measurable lesions. A patient with a tumor whose response was visualized by CT as PR or CR was defined as a CT responder.

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**Table 1. Characteristics of 19 Patients**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>36-77 (median 59)</td>
</tr>
<tr>
<td>Male / Female</td>
<td>14 / 5</td>
</tr>
<tr>
<td>Location of the primary lesion</td>
<td>Ph / Pbt</td>
</tr>
<tr>
<td></td>
<td>9 / 10</td>
</tr>
<tr>
<td>Survival Time</td>
<td>2.9-25 months (median 11.5)</td>
</tr>
<tr>
<td>PET responder</td>
<td>11 / 19 cases (57.9%)</td>
</tr>
<tr>
<td>CT responder</td>
<td>5 / 19 cases (26.3%)</td>
</tr>
<tr>
<td>TM responder</td>
<td>9 / 19 cases (47.4%)</td>
</tr>
</tbody>
</table>

Ph: pancreas head, Pbt: pancreas body or tail.
a) Responder whose best tumor response was visualized by PET, CT or TM.
Survival curves for patients divided into three subgroups of UICC stage III, UICC stage IV. There was no significant difference between the two groups (log-rank test; p=0.59).

Evaluation of tumor response by FDG-PET

Objective tumor responses were also evaluated with FDG-PET scans according to modified European Organization for Research and Treatment of Cancer (EORTC) guidelines (15): CR, FDG uptake in all lesions comparable to background activity; PR, a 25% or greater decrease in the sum of SUV in all target lesions; SD, changes in the sum of SUV of less than 25% in all target lesions; and PD, an increase of 25% or more in the sum of SUV in all target lesions or the appearance of new abnormal uptake. A patient with tumor whose response was visualized by PET as PR or CR was defined as a PET responder.

Evaluation of tumor response by TMs

Objective tumor responses were also evaluated by TMs as follows: CR, normalization of all measured TMs (CA19-9: normal range, 0-37 U/mL; DU-PAN-2: 0-150 U/mL; Span-1: 0-30 U/mL); PR, a 50% or greater decrease in the values of TMs with initially elevated values; SD, changes in TM values of less than 50% in two of the three TMs listed above; PD, an increase of 50% or more in the value of at least one TM. A patient with tumor whose response was visualized by TM as PR or CR was defined as a TM responder.

Best tumor response

This was defined as the best tumor response through all courses (≥2 courses) as assessed by any of the three modalities (CT, PET and TMs), assuming the response was either PR or CR for each modality. For example, assuming the patient received four courses of chemotherapy, if the patient exhibited SD via PET after the 1st course, SD after the 2nd course, CR after the 3rd course, and PR after the 4th course, the best tumor response via PET throughout the four courses was CR, achieved after the 3rd course using PET.

Statistical analysis

Survival analysis was performed using the Kaplan-Meier method and the log-rank test. Categorical data were examined using the $\chi^2$ test. The test results were regarded as significant if p<0.05.

Results

Patient characteristics and survival

Characteristics of the 19 patients are shown in Table 1. Patient ages ranged from 36 to 77 years (median age, 59 years) and the ratio of males to females was 14/5. Survival time ranged from 2.9 to 25 months with a median survival time (MST) of 11.5 months (95% CI, 8.9-14.1). Good tumor response (PR or CR) through all courses (≥2 courses) was seen with PET in 11 cases (57.9%), CT in 5 cases (26.3%), and TMs in 9 cases (47.4%). Figure 1 shows patients’ survival curves divided into UICC stages III (n=6) and IV (n=13). MSTs were 10.6 months (95% CI, 8.6-12.6) in the stage III group and 12.5 months (95% CI, 5.8-19.2) in the stage IV group. There was no significant difference between the two groups (log-rank test; p=0.59).

FDG-PET, TM, and CT responses

Table 2 shows SUVs of the pancreatic lesions for all 19 patients enrolled in the study, as well as the results of chemotherapy as assessed using FDG-PET, CT, and serum TMs. The mean SUV for all of patients was 5.34 (range, 2.85-12.05). Only 4 cases (cases 1, 2, 6, and 15) showed concordance between the evaluations of all three modalities after 4 weeks (1 course), and only 5 cases (cases 1, 2, 3, 5, and 6) showed concordance between the evaluations of the best tumor response. After 1 course, evaluations by FDG-PET and TMs were consistent in 7 (39%) of the 18 evaluable cases, while evaluations by FDG-PET and CT were consistent in 9 (47%) out of the 19 evaluable cases (χ² test; p=0.85). Assessments of the best tumor response with FDG-PET and TMs were consistent in 9 (75%) of the 12 evaluable cases while those with FDG-PET and CT were consistent in 6 (46.7%) of the 13 evaluable cases (χ² test; p=0.23). Although no PET- and TM-complete responses (CR) were observed after the first 4 weeks of this study, two patients for whom the best tumor response was assessed by both PET-CR and TM-CR had survived for more than two years. Thus, although FDG-PET and TMs had limited value after 1 course of chemotherapy, they were useful in discerning the best tumor response for prediction of survival or the chemotherapy sensitivity of patients with advanced pancreatic cancer. With regard to estimation of poor prognosis, CT after 1 course of chemotherapy was most sensitive, as 4 CT-PD patients (cases 3, 8, 13, and 18) did not survive over 12 months.
Table 2. FDG-PET, TM and CT Responses and Survival Times

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age/Sex</th>
<th>Primary focus</th>
<th>UICC stage</th>
<th>SUV max of pancreatic lesion (CT)</th>
<th>ST (month)</th>
<th>Tumor response after 1 course PET</th>
<th>TM</th>
<th>CT</th>
<th>Best tumor response&lt;sup&gt;a&lt;/sup&gt; PET</th>
<th>TM</th>
<th>CT</th>
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</thead>
<tbody>
<tr>
<td>1</td>
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<td>Ph</td>
<td>III</td>
<td>10.70</td>
<td>9.8</td>
<td>PR</td>
<td>PR</td>
<td>PR</td>
<td>PR</td>
<td>PR</td>
<td>PR</td>
</tr>
<tr>
<td>2</td>
<td>56/M</td>
<td>Ph</td>
<td>III</td>
<td>3.45</td>
<td>8.9</td>
<td>SD</td>
<td>SD</td>
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<td>SD</td>
<td>SD</td>
<td>SD</td>
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<tr>
<td>3</td>
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<td>III</td>
<td>5.86</td>
<td>10.6</td>
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<td>SD</td>
<td>PD</td>
<td>PR</td>
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<td>4</td>
<td>75/F</td>
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<td>IV</td>
<td>4.20</td>
<td>15.9</td>
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<td>PR</td>
<td>SD</td>
<td>CR</td>
<td>CR</td>
<td>PR</td>
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<td>55/F</td>
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<td>2.85</td>
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<td>PD</td>
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</tr>
<tr>
<td>6</td>
<td>56/M</td>
<td>Pbt</td>
<td>IV</td>
<td>6.52</td>
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<td>SD</td>
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<td>SD</td>
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<tr>
<td>7</td>
<td>63/F</td>
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<td>10.8</td>
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<td>PD</td>
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<td>PR</td>
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<td>8</td>
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<tr>
<td>9</td>
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<tr>
<td>10</td>
<td>65/F</td>
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<td>PR</td>
<td>SD</td>
<td>CR</td>
<td>PR</td>
<td>SD</td>
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<tr>
<td>11</td>
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<td>SD</td>
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<td>SD</td>
<td>CR</td>
<td>CR</td>
<td>SD</td>
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<td>13</td>
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<td>IV</td>
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<td>4.8</td>
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<td>SD</td>
<td>PD</td>
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<td>-</td>
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<tr>
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<td>3.31</td>
<td>12.5</td>
<td>PR</td>
<td>PD</td>
<td>SD</td>
<td>PR</td>
<td>SD</td>
<td>SD</td>
</tr>
<tr>
<td>15</td>
<td>58/M</td>
<td>Ph</td>
<td>III</td>
<td>4.96</td>
<td>11.5</td>
<td>SD</td>
<td>SD</td>
<td>SD</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>16</td>
<td>44/M</td>
<td>Pbt</td>
<td>IV</td>
<td>3.02</td>
<td>13.0</td>
<td>PD</td>
<td>PR</td>
<td>SD</td>
<td>PD</td>
<td>PR</td>
<td>SD</td>
</tr>
<tr>
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<td>61/M</td>
<td>Pbt</td>
<td>IV</td>
<td>3.88</td>
<td>13.5</td>
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<td>PR</td>
<td>SD</td>
<td>PR</td>
<td>PR</td>
<td>SD</td>
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<tr>
<td>18</td>
<td>64/M</td>
<td>Pbt</td>
<td>IV</td>
<td>3.91</td>
<td>11.5</td>
<td>SD</td>
<td>w.n.l.</td>
<td>PD</td>
<td>SD</td>
<td>w.n.l.</td>
<td>SD</td>
</tr>
<tr>
<td>19</td>
<td>63/M</td>
<td>Pbt</td>
<td>IV</td>
<td>3.91</td>
<td>12.5</td>
<td>PR</td>
<td>PR</td>
<td>SD</td>
<td>-</td>
<td>PR</td>
<td>SD</td>
</tr>
</tbody>
</table>

<sup>a</sup> Estimation was done all through two or more courses. Space indicates no evaluation.


Characteristics of subgroups classified by survival times

We divided the 19 patients into two groups based on the survival time: patients who survived for 12 months or more (group ST ≥ 12: n = 8) and patients who survived for less than 12 months (group ST < 12: n = 11). The characteristics of the two groups are shown in Table 3. Age, location of pancreatic lesion, and gender did not differ significantly between the two groups. With regard to responders, the number of patients assessed by TMs who showed either PR or CR after 1 course (6/8: 75.0%) and for whom the best tumor response was identified by TMs (7/8: 87.5%) was significantly higher (p < 0.01 and p < 0.05, respectively) in group ST ≥ 12. The number of PET responders (patients whose best tumor response was visualized by PET) (6/6: 100%) was also higher in group ST ≥ 12, although this difference was not significant (p = 0.07). In indexes of the three modalities (FDG-PET, TM and CT), SUV of the pancreatic lesion alone showed a significant difference between the ST ≥ 12 and ST < 12 groups (p < 0.05). However, there was no significant difference between survival of the low SUV group (< 4.5) (n = 9, MST: 12.5 months) and that of the high SUV group (≥ 4.5) (n = 10, MST: 10.2 months) (Table 2).

There were four patients (cases 4, 10, 11, and 12) in this study who survived for more than 15 months (Table 2). All of them presented with PET-PR or TM-PR after 1 course (2 cases, PET-PR with TM-PR; 1 case, PET-PR; and 1 case, TM-PR). Both PET and TM assessed best tumor responses as CR, via PET in all patients and also via TM in 3. No patient who survived for fewer than 15 months exhibited PET-CR or TM-CR. In CT evaluation, all four cases presented with SD after 1 course; for two of those cases the best response was PR, while for the other two it was SD.

Survival times of subgroups classified by chemotherapy results

Figure 2 shows the survival curves of subgroups divided by tumor response after 1 course of chemotherapy. Although PET-PR and TM-PR groups presented with good prognosis [MST of PET responders, 12.5 months (95% CI, 10.1-14.9), MST of TM responders, 15.8 months (95% CI, 12.6-19.0)] (Fig. 2A, B), there was no significant difference between survival times of the subgroups. Moreover, the prognosis of the CT-PR group (MST, 10.3 months) was worse than that of the CT-SD group [MST, 15.8 months (95% CI, 9.6-22.0)].
Table 3. Characteristics of Patients Classified by Survival Time

<table>
<thead>
<tr>
<th></th>
<th>ST ≥ 12 (n=8)</th>
<th>ST &lt; 12 (n=11)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>62.6±10.4</td>
<td>56.7±9.0</td>
<td>0.20</td>
</tr>
<tr>
<td>Male/Female</td>
<td>5/3</td>
<td>9/2</td>
<td>0.60</td>
</tr>
<tr>
<td>Ph/Pbt</td>
<td>2/6</td>
<td>7/4</td>
<td>0.16</td>
</tr>
<tr>
<td>PET responder-1a)</td>
<td>5/8</td>
<td>4/11</td>
<td>0.37</td>
</tr>
<tr>
<td>TM responder-1a)</td>
<td>6/8</td>
<td>1/11</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CT responder-1a)</td>
<td>0/8</td>
<td>2/11</td>
<td>0.49</td>
</tr>
<tr>
<td>PET responder-B b)</td>
<td>6/6</td>
<td>3/7</td>
<td>0.07</td>
</tr>
<tr>
<td>TM responder-B b)</td>
<td>7/8</td>
<td>2/7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>CT responder-B b)</td>
<td>2/8</td>
<td>3/8</td>
<td>1</td>
</tr>
<tr>
<td>SUV of pancreatic lesion</td>
<td>4.04±0.70</td>
<td>6.29±2.96</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Size of primary lesion in CT (mm)</td>
<td>35.3±15.3</td>
<td>44.1±19.7</td>
<td>0.36</td>
</tr>
<tr>
<td>CA19-9</td>
<td>869±1364</td>
<td>581±628</td>
<td>0.54</td>
</tr>
</tbody>
</table>

(a) Responder-1 and (b) responder-B mean responder after 1 course of chemotherapy and that in the best tumor response, respectively.

Figure 2. Survival curves for patients categorized by modality [FDG-PET (A), TM (B) and CT (C)] and further grouped by PR, SD, and PD at four weeks (1 course) after the start of chemotherapy. No subgroup in any modality showed a significantly increased overall survival compared to other subgroups.

Changes of the values of each TM and SUV for TM responders

The changes of the values of TMs for all TM responders also indicated early decreases of the values within one (cases 1, 4, 12, 16, 17, 19) or two courses (cases 3, 11) (es-
Figure 3. Survival curves for patients categorized by modality [FDG-PET (A), TM (B) and CT (C)] and further grouped by best tumor response. PET responders (PR or CR) showed a significantly increased overall survival compared to PET nonresponders (log rank test; p<0.05) (A). TM responders (PR or CR) tended to have an increased overall survival compared to TM nonresponders (log-rank test; p=0.063) (B). No CT (C) subgroup showed an increased overall survival.

especially in CA19-9 and Span-1), which seemed to reflect the good responses of tumors to the chemotherapy as well as shown in the result of group ST/c033 in Table 3 (Fig. 4). Meanwhile, although the changes of SUVs for many TM responders also indicated an early decrease of that within one course (cases 1, 3, 4, 10, 11, 19), SUVs of two cases (cases 12 and 17) were reduced at late phase.

Presentation of cases

In case 12 (Fig. 5), FDG-PET before the start of chemotherapy showed FDG uptake (SUV=5.24) in the area of the pancreatic head (Fig. 5A). One course after that, FDG-PET revealed slight attenuation of uptake (SUV=4.79; PET-SD) (Fig. 5B). Depletion of the abnormal uptake (PET-CR) was achieved after six courses (Fig. 5C). Meanwhile, as shown in Fig. 5D, serum levels of CA19-9, Span-1, and DU-PAN-2 were markedly decreased after 1 course (TM-PR), followed by normalization (TM-CR). In this instance TMs were more useful in predicting survival than FDG-PET.

Discussion

The results of this study indicate that although FDG-PET is an important adjunct to TMs and CT for assessing treatment effect and predicting survival after chemotherapy in patients with advanced pancreatic cancer, it may be effectively replaced by TMs.

Pancreatic cancer is one of the most intractable malignancies and carries an extremely poor prognosis. Therefore, it is very important to distinguish between chemotherapy responders and nonresponders at an early stage so as to best determine treatment strategy. Previous studies indicated that the reduction or deletion of abnormal uptake of FDG within the first four weeks of starting chemotherapy correlated with effective chemotherapeutic results (12, 16). Thus, we compared FDG-PET to TMs and CT in terms of estimating the chemotherapeutic effects.

First, we investigated the association between survival and SUV of the pancreatic lesion. Although a previous study showed that the MST of a low SUV (<3.0) group was significantly longer (14 months) than that of a high SUV (≥3.0) group (5 months) (17), our data did not show a significant difference in survival between low and high SUV groups (Table 2). Our data therefore indicates that contrary to some previous studies (13, 17), SUV of the pancreatic lesion before treatment is not related to survival. This discrepancy may be due to differences in patient background: 7 stage III and 7 stage IV patients in the previous study (17) and 6 stage III and 13 stage IV patients in our study. One possible reason for the lack of association between SUV of
The pancreatic lesion and survival is that pancreatic cancer frequently metastasizes at an early stage without remarkable change to the primary lesion, and therefore causes early death of the host. Based on this hypothesis, considering the total SUVs of systemic lesions is critical when predicting survival.

Next, we compared FDG-PET with TMs and CT with regard to evaluating the efficacy of chemotherapy. Although CT is a standard modality for evaluating antitumor effects, CT cannot reflect tumor viability. FDG-PET achieves this goal by measuring glucose metabolism, while the TM method assesses the abnormal production of intra- or extracellular proteins of tumor cells.

According to Fig. 2, patient survival could not be as accurately predicted by FDG-PET as by CT and TMs after 1 course of chemotherapy. Some previous studies have indicated that after one cycle of therapy FDG-PET is a good predictor of survival of patients with malignancy (12, 16-20), while a few studies have shown that FDG-PET following therapy could not accurately predict survival (13). Given that Rigo et al (21) reported that FDG uptake correlates with tumor grade, one reason for this difference in the results may be that treatment and histology grades in each study were not identical between patients. In the present study, histology grades were not completely consistent, although the treatments were all the same. However, patients with tumors whose best response was visualized by PET as PR or CR had a significantly better prognosis (log-rank test, p<0.05) than did those with TM-PR or TM-CR evaluations (p=0.063), but this was not the case in CT (Fig. 3).

Some patients with advanced pancreatic cancer can show a response to chemotherapy without accompanying changes in the size of primary and metastatic lesions in CT. In such cases, FDG-PET and TMs appear to play important roles in discriminating chemotherapy responders from non-responders, as all patients in group ST≥12 in Table 3, as well as those whose best tumor response was discerned by PET or TM as PR or CR, showed SD by CT estimation after 1 course. Moreover, it is notable that when FDG-PET survival curves are divided by the best tumor response, results are very similar to those seen with TMs (Fig. 3) as well as the changes of the values of each TM and SUV for TM responders (Fig. 4). This may be caused by the similarity between FDG-PET and TMs, both of which reflect tumor cell activity or viability. Therefore, FDG-PET as a predictor of survival after chemotherapy may be replaced by TMs after considering cost versus performance, as many reports have indicated that TMs (CA19-9) are valid in predicting survival of patients with pancreatic cancer (22-27). However, since these studies rely on limited numbers of patients and use varying definitions of CA19-9 response, further studies in a large cohort and using combination of some...
TMs as the present study are needed. Although we started the present study expecting the apparent superiority of FDG-PET over TM and CT, the results did not indicate it as described above. Thus, we could not perform a larger large-scale study without limitation by small population size after considering cost versus performance. This small-scale study led to the different result of survival curves by subgroups of UICC stages III and IV (Fig. 1) from a previous report (28), while it also showed an importance of the best tumor response assessed by FDG-PET and TM.

Meanwhile, FDG-PET and TMs can each play an adjunctive role when, for example, the values of TMs are within normal limits (as in case 18) or carcinomatous ascites and effusion, which cannot be detected by FDG-PET, develop. Although CT was more sensitive than FDG-PET or TMs in predicting poor prognosis, as shown in Table 2, we think that this was due to the superior ability of CT to detect signs of metastasis such as carcinomatous ascites and small hepatic or mesenteric lesions.

We therefore suggest that FDG-PET should be used as an adjunct to TM and CT for estimating chemotherapeutic effects, especially when a new lesion evades CT detection despite normal or abruptly increased TMs.

In conclusion, FDG-PET and TMs can each supplement CT in estimating chemotherapeutic efficacy and predicting survival by identifying responders among patients with advanced pancreatic cancer.

References