Effect of long fasting on myocardial accumulation in 18F-fluorodeoxyglucose positron emission tomography after chemoradiotherapy for esophageal carcinoma

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ABSTRACT

This study sought to evaluate the effect of fasting time prior to 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) on myocardial accumulation of FDG in patients receiving radiotherapy for esophageal carcinoma, and the spatial relationship between the irradiated dose and myocardial accumulation of FDG. Forty-one patients with thoracic esophageal carcinoma received FDG-PET with <18-h (24 patients) or ≥18-h (17 patients) fasting status. Their myocardial accumulation patterns of FDG were categorized using the maximal standardized uptake value (SUVₘₐₓ) into three types: physiological, focal and no pathological accumulation. The incidence rates of each pattern were then compared using the Fisher's exact test between two types of fasting, ≥18-h and <18-h, prior to FDG-PET. Additionally, the left ventricle was defined using four subsites depending on the irradiated doses, and the SUVₘₐₓ values were compared among the subsites using the Kruskal–Wallis test. The incidence of the physiological accumulation pattern decreased significantly more in the ≥18-h fasting status group than in the <18-h fasting group (18% versus 71%, P = 0.002), and the focal accumulation of FDG was detected at a significantly higher rate (65% versus 13%, P = 0.001). The left ventricular subsites receiving the higher doses showed significantly higher SUVₘₐₓ values than did the subsites receiving the lower doses (P < 0.001). In conclusion, radiotherapy was associated with abnormal myocardial accumulation of FDG. Long fasting for 18 h or more prior to FDG-PET would be useful in detecting subsequent myocardial damage from chemoradiotherapy compared with <18-h fasting prior to FDG-PET.

Keywords: ¹⁸F-fluoro-deoxyglucose; myocardium; fasting; chemoradiotherapy; esophageal neoplasms

INTRODUCTION

Although the treatment of thoracic esophageal carcinoma with chemoradiotherapy can lead to increased long-term survival, radiation-induced cardiac toxicity remains a problem. Heart disease or pericarditis has been observed at the 5-year follow-up in 11.1–13.8% of patients receiving definitive chemoradiotherapy for thoracic esophageal carcinoma [1–3]. Radiation-induced cardiac toxicity was associated with the non-cancer-related deaths, but this may be prevented by early detection of or intervention for serious cardiac damage. Abnormal myocardial accumulation of ¹⁸F-fluorodeoxyglucose (FDG) in FDG-positron emission tomography (FDG-PET) can occur in a damaged myocardium. Several authors have described patients with cardiomyopathy and ischemic heart disease experiencing abnormal accumulation during imaging [4, 5], which had been intended to reflect
metabolic changes in the myocardium [6–9]. Another study reported similar findings in 20.3% of patients who had received chemoradiotherapy for esophageal carcinoma [10]. This possibly reflected myocardial damage due to the radiotherapy. Therefore, the presence of abnormal myocardial accumulation of FDG in FDG-PET would be useful for evaluating myocardial damage following chemoradiotherapy for thoracic esophageal carcinoma.

Two issues were unknown with regard to abnormal myocardial accumulation of FDG following chemoradiotherapy. The first issue was the influence of fasting time prior to FDG-PET. Often, FDG accumulates physiologically in the myocardium in a diffuse pattern, making it difficult to distinguish between abnormal and physiological myocardial accumulation. Long fasting, for at least 18 h prior to FDG-PET, has been reported as suppressing physiological myocardial accumulation of FDG in patients with cardiac sarcoidosis [11]. However, it has till now been unclear whether long fasting prior to FDG-PET is useful for detecting abnormal myocardial accumulation by suppressing physiological myocardial accumulation in the irradiated myocardium. The second issue was the spatial relationship between irradiation doses and myocardial accumulation of FDG; previous reports have mentioned only whether the abnormal myocardial accumulation of FDG existed after chemoradiotherapy [10].

The aim of this study was to compare the incidence rates of physiological myocardial accumulation of FDG between <18-h and ≥18-h fasting status, and to reveal the spatial relationships between the irradiated doses to the myocardium and myocardial accumulation of FDG in patients with esophageal carcinoma receiving chemoradiotherapy.

**MATERIALS AND METHODS**

**Eligibility**

Prior to treatment, all patients gave written informed consent for the use of their clinical data for research. This study was reviewed and approved by the Institutional Review Board at our institution on 30 September 2016. From January 2010 to January 2015, 128 patients received definitive chemoradiotherapy for esophageal squamous cell carcinoma at our institution, of which 41 consecutive patients were included. The eligibility criteria were as follows: (i) presence of clinical Stage I to IV carcinoma without distant organ metastasis [as defined by the Union for International Cancer Control (UICC) TNM Classification of Malignant Tumors, 7th edition], (ii) prescription of ≥50 Gy for all gross tumors, including the primary tumor and metastatic lymph nodes, (iii) concurrent administration of 5-fluorouracil plus or minus platinum, and (iv) FDG-PET performed after chemoradiotherapy.

This study collected the following information from patient medical records: fasting time prior to FDG-PET, age, gender, Eastern Cooperative Oncology Group (ECOG) performance status, tumor location, clinical stage of carcinoma (UICC TNM Classification of Malignant Tumors, 7th edition), details of radiotherapy and chemotherapy, interval between the initial day of chemoradiotherapy and the day of FDG-PET, hemoglobin A1c levels, history of smoking, heart disease, and hypertension, and imaging results of FDG-PET.

**Details of radiotherapy and chemotherapy**

Computed tomography (CT) simulation was performed with all patients in the supine position. Target volume delineation has been previously described [12], and treatment plans were created using the cone-down method. Initially, anterior–posterior plus parallel oblique radiation fields were used up to a total dose of 40–41.4 Gy with 1.8–2.0 Gy fractions per day, which included gross tumors and prophylactic regional mediastinal lymph nodes (Fig. 1A). Boost irradiation was then applied to gross tumors using three to four coplanar fields (Fig. 1B). The median total dosage was 60 Gy (range, 50.4–60.0 Gy), and doses were delivered 5 days per week by a linear accelerator using 6–15 MV photon beams. In addition, 5-fluorouracil plus or minus platinum was used concurrently during radiotherapy.

**Dose distribution**

Three types of dose calculation algorithms were used in the 41 consecutive patients for the monitor unit settings, along with updates of treatment planning systems and machine calibration as follows: the pencil beam convolution version 8.6.15 (n=15), the anisotropic analytical algorithm version 8.6.15 (n=10)/version 11.0.31 (n=2), and the Acuros XB version 11.0.31 (n=14). To evaluate the spatial relationships between irradiated doses to the myocardium and myocardial accumulation of FDG, this study adopted the monitor units used clinically for each patient and recreated the 3D dose distributions calculated by the Acuros XB version 11.0.31 with heterogeneity correction (Bathe Power Law method; Eclipse treatment planning system version 11.0.31, Varian Medical Systems, Palo Alto, California, USA). Re-planning CT simulation was performed for boost irradiation in four patients. To create the summed irradiation plan, the initial irradiation fields with the monitor units calculated in the initial irradiation plans were copied to the re-planning CT simulation images.

**Details of FDG-PET/CT**

Patients received FDG-PET after chemoradiotherapy during the follow-up period in the current study. The median time from the initial day of chemoradiotherapy to the day of FDG-PET was 11 months [interquartile range (IQR), 7–21 months]. Patients were instructed to fast for at least 4 h prior to FDG-PET. We recorded the time of the last intake of glucose containing foods or drinks prior to FDG-PET, and the time of the injection of FDG in all patients. We calculated the fasting time of each patient from those records. After that, we grouped the patients according to the two values of fasting times before FDG-PET, <18 h and ≥18 h.

Patients received intravenous administration of ~200 MBq (3.7 MBq/kg body weight) of FDG with the Discovery ST Elite PET/CT scanner (GE Healthcare, Waukesha, WI, USA). Plasma glucose levels of all patients were <150 mg/dL. About an hour after administration of the FDG, low-dose CT was initially performed for attenuation corrections with the following parameters: 40–60 mA, 120 kV, 0.6-s tube rotation, and 3.75-mm section thickness. The CT scans were acquired during shallow breathing, and whole-body PET scans were then obtained from the upper thighs to the skull. Data acquisition was performed for 2–3 min for each bed position.

Of the 41 patients, abnormal accumulations out of the myocardium were observed in 17 patients, 8 of which were due to recurrent disease and the remaining 9 were due to inflammation, such as pneumonia or esophagitis. However, they could be distinguished
from myocardial accumulations and did not affect the measurement of myocardial accumulations.

**Endpoint analysis**

This study divided the left ventricle into four subsites depending on the irradiated doses in the radiotherapy planning systems. First, we defined the left ventricular subsite out of irradiation fields as $V_{\text{out of fields}}$ and it received $<18$ Gy. Second, the left ventricular subsite receiving $\geq 18$ Gy and $<30$ Gy as $V_{\text{low}}$. The upper threshold of $V_{\text{low}}$ was adapted from the threshold of irreversible myocardial damage, which was identified at 30 Gy [13]. Third, the subsite receiving $>42$ Gy was defined as $V_{\text{high}}$, and it received boost irradiation doses. Finally, the residual subsite receiving $\geq 30$ Gy and $<42$ Gy was defined as $V_{\text{moderate}}$ (Fig. 1C and D).

We evaluated the myocardial accumulation of FDG using the following four steps and categorized the myocardial accumulation patterns of FDG into three types; physiological, focal, and no pathological myocardial accumulation (Fig. 2). Initially, we excluded physiological myocardial accumulation from further analysis, because it was impossible to evaluate the existence of focal myocardial accumulation due to its diffuse myocardial accumulation. The dose distributions of radiotherapy and the images from FDG-PET were fused using MIM Maestro version 6.5 (MIM Software, Cleveland, OH, USA). We then calculated the maximal standardized uptake value ($\text{SUV}_{\text{max}}$) in each of the four left ventricular subsites ($V_{\text{out of fields}}, V_{\text{low}}, V_{\text{moderate}}$ and $V_{\text{high}}$). Finally, we divided the FDG accumulation into the focal and no pathological myocardial accumulation patterns using the $\text{SUV}_{\text{max}}$ values of the four left ventricular subsites. The upper threshold of the $\text{SUV}_{\text{max}}$ value of the subite with no pathological myocardial accumulation of FDG was set as the 95th percentile value of the $\text{SUV}_{\text{max}}$ in the $V_{\text{out of fields}}$ subsite.

To evaluate the spatial relationships between the irradiated doses and myocardial accumulation of FDG, we compared the $\text{SUV}_{\text{max}}$ values in each of the four left ventricular subsites ($V_{\text{out of fields}}, V_{\text{low}}, V_{\text{moderate}}$ and $V_{\text{high}}$) in the patients without physiological myocardial accumulation of FDG. The board-certified nuclear medicine specialist and radiation oncologist in our author group determined the patterns of myocardial accumulation and calculated the $\text{SUV}_{\text{max}}$ values of the four left ventricular subsites.

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**Fig. 1.** Initial and boost radiation fields, dose distribution, and contours of four left ventricular subsites: $V_{\text{high}}, V_{\text{moderate}}, V_{\text{low}}$, and $V_{\text{out of fields}}$. The initial irradiation fields (A), which included gross tumors and prophylactic lymphatic lesions. Boost irradiation fields were applied to gross tumors (B). Sum of radiation dose distribution of initial fields and boost fields (C). The contours of the left ventricular subsites of $V_{\text{high}}, V_{\text{moderate}}, V_{\text{low}}$, and $V_{\text{out of fields}}$ (D). Magenta contour $= V_{\text{high}}$, green contour $= V_{\text{moderate}}$, blue contour $= V_{\text{low}}$, yellow contour $= V_{\text{out of fields}}$.
Statistical analysis
The differences in characteristics between the patients with <18-h and ≥18-h fasting times prior to FDG-PET were analyzed. The continuous factors (fasting time prior to FDG-PET, age, and interval between the initial day of chemoradiotherapy and FDG-PET) and the categorical factors (gender, performance status, tumor location, clinical stage, and history of diabetes, smoking, heart disease, and hypertension) were analyzed using the t-test and Fisher’s exact test, respectively.

To examine whether the ≥18-h fasting reduced the physiological myocardial accumulation of FDG, the incidence rates of the three types of myocardial accumulation of FDG were compared using the Fisher’s exact test between patients with <18-h and ≥18-h fasting times prior to FDG-PET. Then, to quantitatively investigate the spatial relationships between the irradiated dose to the myocardium and the myocardial accumulation of FDG, the median SUV\textsubscript{max} values of the subsites were analyzed among the patients using the Kruskal–Wallis test, with the exception of the physiological myocardial accumulation pattern of FDG. All statistical tests were two-sided using EZR version 1.35 (Saitama Medical Center, Jichi Medical University, Saitama, Japan) [14], which is a graphical user interface for R (R Foundation for Statistical Computing, Vienna, Austria, version 3.0.2), and a P value of <0.05 was considered to indicate statistical significance. More precisely, EZR is a modified version of R commander used to facilitate biostatistical evaluation.

RESULTS
The numbers of patients in the <18-h and ≥18-h fasting groups were 24 and 17, respectively. Differences in patient characteristics were not observed between the patients with the <18-h and ≥18-h fasting groups prior to FDG-PET, except for the fasting times (Table 1). The median fasting time before FDG-PET was significantly longer in patients with ≥18-h fasting than in those with <18-h fasting [18 h (IQR, 18, 18.5 h) vs 13.5 h (IQR, 7.5, 17 h)].

The incidence of the physiological myocardial accumulation pattern was lower in the ≥18-h fasting group than in the <18-h fasting group; the physiological myocardial accumulation pattern was observed in 17 of 24 patients (71%) in the <18-h fasting group and in 3 of 17 patients (18%) in the ≥18-h fasting group prior to FDG-PET, respectively. There was a significant difference in the incidence rates of the physiological myocardial accumulation pattern between the two types of fasting times (P = 0.002).

The incidence of the focal myocardial accumulation pattern was higher in the ≥18-h fasting group than in the <18-h fasting group; among 21 patients, excluding the physiological myocardial accumulation pattern of FDG, the median values of SUV\textsubscript{max} in each of the four left ventricular subsites are shown in Table 2, and the 95th percentile value of the SUV\textsubscript{max} of the V\textsubscript{out of field} was 3.07. Following the predefined criteria, the focal myocardial accumulation pattern of FDG was observed in 14 patients; 3 of 24 patients (13%) with <18-h fasting and 11 of 17 patients (65%) with ≥18-h fasting before FDG-PET, respectively. In addition, there was a significant difference...
in the incidence rates of the focal myocardial accumulation pattern between the two types of fasting times ($P = 0.001$).

Among these 21 patients, excluding the physiological myocardial accumulation pattern of FDG, the median value of the SUVmax increased depending on the irradiated doses. Figure 3 shows the representative fused images of the four left ventricular subsites and the focal myocardial accumulation of FDG in $V_{\text{high}}$. The numbers of the patients with a focal myocardial accumulation pattern of FDG in $V_{\text{out of fields}}, V_{\text{low}}, V_{\text{moderate}}$ and $V_{\text{high}}$ were 0, 4, 9 and 10, respectively. The SUVmax values differed significantly between each of the four left ventricular subsites ($P < 0.001$) (Table 2), and the post hoc analysis showed significant differences in SUVmax between $V_{\text{out of fields}}$ and $V_{\text{moderate}}$, $V_{\text{high}}$ ($P = 0.016$ and $< 0.001$, respectively).

### DISCUSSION

This study showed that ≥18-h fasting prior to FDG-PET decreased the physiological myocardial accumulation of FDG more than did <18-h fasting. Also, the focal myocardial accumulation pattern was increasingly detected with ≥18-h fasting prior to FDG-PET than with <18-h fasting. In addition, the dose–response relationship between the irradiated dose to the myocardium and the myocardial accumulation of FDG was observed.

No reports have evaluated the effect of fasting time prior to FDG-PET on myocardial accumulation in the irradiated myocardium. However, previous reports have evaluated the myocardial accumulation of FDG based on follow-up studies of FDG-PET.

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**Table 1. Patient characteristics**

| Parameters                                      | All patients ($n = 41$) | <18 h fasting before FDG-PET ($n = 24$) | ≥18 h fasting before FDG-PET ($n = 17$) | $P$ value |
|------------------------------------------------|-------------------------|------------------------------------------|----------------------------------------|---------|
| Median fasting hours before FDG-PET (IQR)       | 17.5 (13, 18)           | 13.5 (7.5, 17)                           | 18 (18, 18.5)                         | <0.001 |
| Median age (years) (IQR)                        | 66 (61, 72)             | 65 (63, 70)                              | 71 (60, 73)                           | 0.13    |
| Gender (male/female)                            | 35/6                    | 21/3                                     | 14/3                                  | 0.68    |
| ECOG performance status (0/1)                   | 28/13                   | 16/8                                     | 12/5                                  | 0.94    |
| Tumor location (Ut/Mt/Lt)                       | 5/23/13                 | 4/10/10                                  | 1/11/5                                | 0.36    |
| Clinical stage (I/II/III/IV)*                   | 7/6/17/11               | 3/2/12/7                                 | 4/4/5/4                               | 0.36    |
| Median months from the initial day of chemoradiotherapy to FDG-PET (IQR) | 11(7, 21)                | 15 (7, 28.5)                             | 9 (6, 13)                             | 0.19    |
| Total dose of radiation (Gy) (50.4/59.4/60)     | 12/1/28                 | 6/0/18                                   | 6/1/10                                | 0.38    |
| Hemoglobin A1c (>6.2 / ≥6.2 and <6.8 / ≥6.8)    | 38/2/1                  | 22/1/1                                   | 16/1/0                                | 0.68    |
| Brinkman index (0 / ≥0 and <1000 / ≥1000)       | 3/22/16                 | 3/14/7                                   | 1/8/8                                 | 0.52    |
| Heart disease (+/−)                             | 5/36                    | 2/22                                     | 3/14                                  | 0.63    |
| Hypertension (+/−)                              | 13/28                   | 9/15                                     | 4/13                                  | 0.50    |

$V_{\text{out of fields}}, V_{\text{low}}, V_{\text{moderate}}$ and $V_{\text{high}}$ = the left ventricular subsite receiving <18 Gy, ≥18 Gy and <30 Gy, ≥30 Gy and <42 Gy, and ≥42 Gy, respectively.

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**Table 2. SUVmax value in four left ventricular subsites**

| Subsite                | Median volume (cm³) (IQR) | Median SUVmax (IQR) | $P$ value |
|------------------------|---------------------------|---------------------|---------|
| Left ventricle         | 179.5 (161.5, 211.5)      | 1.85 (1.59, 2.17)   |         |
| $V_{\text{out of fields}}$ | 103.8 (86.1, 144.7)     | 2.23 (1.69, 2.65)   | 0.367   |
| $V_{\text{low}}$       | 19.2 (15.2, 30.8)         | 2.56 (1.84, 3.99)   | 0.016   |
| $V_{\text{moderate}}$  | 24.8 (21.2, 32.9)         | 3.95 (2.56, 4.78)   | <0.001  |
| $V_{\text{high}}$      | 6.6 (0, 33.5)             |                     |         |

SUVmax = maximal standardized uptake value, IQR = interquartile range, $V_{\text{out of fields}}, V_{\text{low}}, V_{\text{moderate}}$ and $V_{\text{high}}$ = the left ventricular subsite receiving <18 Gy, ≥18 Gy and <30 Gy, ≥30 Gy and <42 Gy, and ≥42 Gy, respectively.
images after radiotherapy for thoracic tumors [10, 15]. The reported fasting time before FDG-PET in these studies was 4–6 h, and those researchers were not able to exclude the physiological myocardial accumulation of FDG. They showed that 20.3–23.1% of the patients had abnormal myocardial accumulation after radiotherapy, and these results were compatible with those of the <18-h fasting group in the current study (Table 3).

The current study also showed that ≥18-h fasting prior to FDG-PET more significantly suppressed physiological myocardial accumulation of FDG in the irradiated myocardium than did <18-h fasting. In the non-irradiated myocardium, myocardial metabolism is controlled by blood glucose levels, insulin, and free fatty acid levels [16]. Under fasting status, blood insulin and glucose levels decrease, and free fatty acid levels increase. Then, the main myocardial metabolism becomes dependent on the free fatty acids rather than on glucose, which suppresses the physiological myocardial accumulation of FDG.

Notably, Manabe et al. reported that physiological myocardial accumulation was suppressed in patients with sarcoidosis by fasting over 18 h prior to FDG-PET [11]. As far as we are aware, the effect of long fasting on the physiological myocardial accumulation of FDG in the irradiated myocardium has not been reported. Although the biological mechanism involved in the physiological accumulation of FDG in the irradiated myocardium may not be same as for that of the non-irradiated myocardium, the current study showed that the physiological myocardial accumulation of FDG would be suppressed in the ≥18-h fasting group compared with the <18-h fasting group, even in the irradiated myocardium.

Suppression of the physiological myocardial accumulation of FDG appeared to detect the abnormal myocardial accumulation of FDG. In the patients suspected of having cardiac sarcoidosis, suppressing the physiological myocardial accumulation of FDG using 18-h fasting prior to FDG-PET reportedly led to the accurate diagnosis of cardiac sarcoidosis in these patients [11]. As for the case for the non-irradiated myocardium, long fasting was expected to be useful in detecting early myocardial damage before any symptom appears in the irradiated myocardium. Early detection of abnormal myocardial accumulation of FDG may be beneficial in screening for functional abnormality of the irradiated myocardium.

It has not been established what preparation prior to FDG-PET is the best for evaluating myocardial damage in the irradiated myocardium. Several types of preparations for detecting metabolic changes in the myocardium have been reported: oral glucose loading, hyperinsulinemic euglycemic clamp, and long fasting [17, 18]. Oral glucose loading prior to FDG-PET resulted in 20–25% unsatisfactory images. Hyperinsulinemic euglycemic clamp prior to FDG-PET was known to

![Fig. 3. Axial (A) and sagittal images (B) of fusion of the contours of the four left ventricular subsites and 18F-fluorodeoxyglucose positron emission tomography. Abnormal myocardial accumulation was observed in the V_high subsite. Magenta contour = V_high, green contour = V_moderate, blue contour = V_low and yellow contour = V_out of fields. V_high, V_moderate, V_low and V_out of fields = the left ventricular subsite receiving ≥42 Gy, ≥30 Gy and <42 Gy, ≥18 Gy and <30 Gy, and <18 Gy, respectively.](image)

| Primary site | Radiotherapy technique | Fasting time (h) | Median interval from initial day of chemoradiotherapy to FDG-PET (months) | Number of patients | Number of patients with abnormal myocardial accumulation |
|--------------|-----------------------|-----------------|-------------------------------------------------|--------------------|-----------------------------------------------|
| Evans et al. [15] | lung | SBRT | <6 | 11 | 39 | 9 |
| Jingu et al. [10] | esophagus | 3DCRT | <4 | 9.25 | 64 | 13 |
| Current study | esophagus | 3DCRT | <18 | 15 | 24 | 3 |
| | esophagus | 3DCRT | ≥18 | 9 | 17 | 11 |

FDG-PET = 18F-fluorodeoxyglucose positron emission tomography, SBRT = stereotactic body radiotherapy, 3DCRT = 3D conventional radiotherapy.
create better image quality than with long fasting. However, it includes rigorous procedures and a risk of causing hypoglycemia [19]. Long fasting prior to FDG-PET was considered minimally invasive and a feasible preparation. It would be useful for screening for abnormal myocardial accumulation in the follow-up FDG-PET after chemoradiotherapy for thoracic esophageal carcinoma.

The current study also demonstrated the dose–response relationship between the irradiated dose to the myocardium and myocardial accumulation of FDG. The threshold dose that caused irreversible histologic changes in the myocardium has been reported at 30 Gy [13], which seemed compatible with the occurrence of the focal myocardial accumulation; the current study showed that $V_{\text{moderate}}$ and $V_{\text{high}}$, which received $\geq30$ Gy, had significantly higher SUV$_{\text{max}}$ values than did $V_{\text{out of fields}}$. In addition, the correlation between the irradiated dose and the SUV$_{\text{max}}$ value in the irradiated myocardium would indicate the existence of radiation-induced myocardial damage.

An in vivo study showed that the abnormal myocardial accumulation of FDG in the irradiated myocardium corresponds to perivascular fibrosis and mitochondrial degeneration without inflammation [20]. Both perivascular fibrosis and mitochondrial degeneration affects the metabolism of glucose and free fatty acid [21, 22]. 123I-beta-methyl-iodophenyl pentadecanoic acid (BMIPP) accumulates in the myocardium where free fatty acids are metabolized in mitochondria, and the accumulation of BMIPP was suppressed in the higher dose–irradiated myocardium [23]. Its incidence rate was similar to that of the abnormal myocardial accumulation of FDG in $\geq18$h-fasting group in the current study. This result will support the hypothesis that high-dose irradiation to the myocardium caused perivascular fibrosis and mitochondrial degeneration, and affected myocardial metabolism of glucose and fatty acid. The abnormal myocardial accumulation of FDG possibly resulted from metabolic changes, rather than inflammation observed in radiation-induced pericarditis. Radiotherapy-induced inflammation, such as radiation pericarditis, is well known as late toxicity. The inflammation may relate to the abnormal myocardial accumulation of FDG, but we need to keep in mind that some metabolic changes have appeared to exist following radiotherapy for thoracic tumors.

The current study had several limitations. First, our institution did not routinely perform FDG-PET before chemoradiotherapy. Among the enrolled 41 patients in the current study, only four patients received FDG-PET before chemoradiotherapy. Thus, the current study could not evaluate the pre-treatment FDG-PET findings; the existence of the focal myocardial accumulation of FDG before chemoradiotherapy was not excluded. Incidental focal myocardial accumulation was reportedly observed in 16.0% before chemoradiotherapy was not excluded. Incidental focal myositis; the existence of the focal myocardial accumulation of FDG in the current study could not evaluate the pre-treatment FDG-PET data. Thus, the current study showed that 65% of patients received FDG-PET with $\geq18$h-fasting status had the focal myocardial accumulation pattern; however, none of them had any cardiac symptoms during follow-up. Moreover, the 5-year incidence rate of heart disease or pericardial effusion following chemoradiotherapy ranged from 11.1% to 13.8% [1–3]. Further follow-up is required to reveal the clinical significance of abnormal myocardial accumulation of FDG following chemoradiotherapy.

In conclusion, radiotherapy was associated with abnormal myocardial accumulation of FDG. Long fasting for $\geq18$h prior to FDG-PET would be useful in detecting subsequent myocardial damage from chemoradiotherapy compared with the $<18$h-fasting prior to FDG-PET.

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CONFLICT OF INTEREST
The authors have no conflicts of interest to disclose.

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