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Fusion Image of Positron Emission Tomography and Computed Tomography for the Diagnosis of Local Recurrence of Rectal Cancer

Hiroki Fukunaga, MD,[1] Mitsugu Sekimoto, MD, PhD,[1] Masataka Ikeda, MD, PhD,[1] Ichiro Higuchi, MD,[1] Masayoshi Yasui, MD,[1] Iwao Seshimo, MD,[1] Osamu Takayama, MD,[1] Hirofumi Yamamoto, MD, PhD,[1] Masayuki Ohue, MD, PhD,[1] Mitsuaki Tatsumi, MD, PhD,[2] Jun Hatazawa, MD, PhD,[2] Masakazu Ikenaga, MD, PhD,[3] Tsunehiko Nishimura, MD, PhD,[4] and Morito Monden, MD, PhD[1]

[1]Department of Surgery and Clinical Oncology (E2), Graduate School of Medicine, Osaka University, 2-2 Yamadaoka Suita, Kinetics (D9), Osaka 565-0871, Japan
[2] Department of Nuclear Medicine and Tracer Kinetics (D9), Graduate School of Medicine, Osaka University, 2-2 Yamadaoka, Suita, Osaka 565-0871, Japan
[3]Department of Surgery, Osaka National Hospital, 2-1-14 Hoenzaka, Chuo-ku, Osaka540-0006, Osaka, Japan
[4]Department of Radiology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, 465 Kajii, Kawaramachi-Hirokoji, Kamigyo, Kyoto 602-8566, Japan

Background: The aim of this study was to evaluate the clinical and therapeutic value of digital fusion image (FI) of positron emission tomography (PET) using ^{18}F-fluorodeoxy glucose and computed tomography (CT) in patients who were suspected of having a local recurrence of rectal cancer.

Methods:: Forty-two patients (32 men and 10 women; mean age, 61.4 years, range, 40–79 years) with a suspicion of local recurrence after curative resection of rectal cancer were prospectively recruited and underwent ^{18}F-fluorodeoxy glucose-PET and CT. The FI was reconstructed with a commercially available digital software program, T-B Fusion. Wilcoxon signed rank test was used to compare FI with CT alone or PET alone.

Results: FI yielded a correct diagnosis in 39 (93%) of 42 patients, whereas CT alone and PET alone did so in 33 (79%) and 37 (88%) patients, respectively. FI had better diagnostic accuracy than CT alone (P = .0138) and PET alone (P = .0156). Overall, FI altered patient management in 11 (26.2%) patients on the basis of additional information, including differentiation of the tumor from the postoperative scar in 6 patients, exact anatomical location in 3 patients, and both in 2 patients.

Conclusions: FI has a potential clinical value in the treatment of suspected local recurrence of rectal cancer.

Key Words: PET—CT—Fusion image—Local recurrence of rectal cancer.

Local recurrence of rectal cancer is still a critical issue in the management of primary advanced rectal cancer. It is reported that approximately one third of rectal cancer patients undergoing curative radical resection will develop local recurrence.[1] Local control and survival are possible for patients with isolated pelvic recurrence after extended radical operations, such as total pelvic exenteration and adjuvant chemotherapy. Wanebo et al.[2] reported that local recurrence of rectal cancer can be resected safely with

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Address correspondence and reprint requests to: Mitsugu Sekimoto, MD, PhD; E-mail: sekimoto@surg2.med.osaka-u.ac.jp.

an expectation of long-term survival of 33%. Suzuki et al.[3] reported that the 3-year survival rate for patients with curative R0 resection was 57%, but that for patients with R1 or R2 resection was only 26%. Therefore, early diagnosis of local recurrence is crucial to permit potentially curative reoperation.

In practice, however, many patients have tumors that require extended radical operations. Therefore, it is of clinical importance to differentiate recurrent tumor from postoperative scar after the diagnosis of local recurrence, for appropriate surgical planning. Conventional imaging modalities, including computed tomography (CT) and magnetic resonance imaging (MRI), are used to distinguish tumor from scar. However, CT is not specific for the detection of local recurrence, and its detection rate ranges from 69% to 95%.[4–6] Furthermore, MRI is another frequently used modality, but the ability of T2-weighted images to differentiate tumors from scar tissue is questionable.[7,8]

Positron emission tomography (PET) using ^{18}F-fluorodeoxy glucose (FDG) has emerged as a promising diagnostic modality in pelvic recurrence of rectal cancer; it detects the glycolytic activity of tumor cells.[9–11] FDG-PET can potentially improve patient selection for surgery and hence may have a positive effect on treatment outcome. However, FDG-PET provides imprecise information on the exact location of focal abnormalities. Thus, even if the results of PET and CT are visually correlated, the precise location of lesions is sometimes difficult to determine. In a preliminary report, we described the construction and superimposition of PET images on CT images and demonstrated the usefulness of this fusion image (FI) for the diagnosis and operational planning of local recurrence of rectal cancer.[12] The integrated PET/CT images have a promising value in the field of oncology.[13–15]

We recently developed software that can automatically generate a PET/CT FI. This study was conducted to determine the usefulness of FI for the detection of local recurrence of rectal cancer and to determine whether its use could influence surgical management.

PATIENTS AND METHODS

Study Population

Between April 2000 and May 2003, the Department of Surgery and Clinical Oncology, Graduate School of Medicine, Osaka University prospectively performed CT scanning and whole-body FDG-PET scanning in 44 consecutive patients with clinically suspected local recurrence of rectal cancer after curative resection. This study was approved by the institutional review board, and written informed consent was obtained before patients entered the study. Patients with underlying inflammatory bowel disease and diabetes were excluded because of potential diagnostic overlap with PET. In those 44 patients, 2 patients were excluded from the analysis; 1 had bladder cancer, and the other died during follow-up without confirmation of diagnosis. Thus, 42 patients (32 men and 10 women; mean age, 61.4 years; range, 40–79 years) were enrolled in this study. Of the 42 patients, 9 underwent surgery and were followed up in our department. The remaining patients underwent surgery and were followed up in other hospitals and then referred to our department for PET evaluation. Patients were referred because of CT/MRI findings suggestive of recurrence (n = 22), local symptoms (such as pain) suggestive of recurrence (n = 13), or increased levels of carcinoembryonic antigen (n = 7).

TABLE 1. *Characteristics of 42 patients*

Variable	Data
Age, y, mean (range)	61.4 (40–79)
Male/female	32/10
Primary operation	
Low anterior resection	16
Abdominoperineal resection	26
Final diagnosis	
Postoperative change	9
Local recurrence	33
Diagnosis confirmation	
C&R	20
Histological diagnosis	22
Surgical intervention	
None	24
Laparotomy	3
Tumor resection	7
TPE	8

C&R; clinical and radiological confirmation; TPE, total pelvic exenteration.

Follow-Up of Patients and Diagnosis Confirmation

Of 42 patients, pathologic confirmation was obtained by operation with curative intent in 17 patients and by biopsy specimens in 4 patients. The diagnosis of the other 21 patients was confirmed by clinical and radiological follow-up examinations (Table 1). The median follow-up period was 35.5 months (range, 12.5–45.2 months) for patients with a final diagnosis of postoperative change. The median time interval between the primary operation and the CT and PET scan was 24 months (range, 5–111.6 months).

Computed Tomography

All patients underwent CT of the abdomen and pelvis (Light Speed; General Electric, Milwaukee, WI) with intravenous administration of contrast material before PET studies (Omnipaque 300; Winthrop-Breon Laboratories, New York, NY). CT scans were obtained with 2.5-mm-thick axial planes in the upper portion of the abdomen and pelvis. The matrix size was 512 × 512, and the pixel size was .67 × .67 mm. Results of CT were reported by one senior radiologist with special interest in pelvic imaging who was blinded to the results of both PET and FI reading. Recurrence was evaluated, and the extent of pelvic recurrence was recorded when recurrence was suspected. The presence of other metastases was also recorded.

^{18}F-Fluorodeoxy Glucose Positron Emission Tomography

FDG-PET was performed with a PET scanner, the Headtome V (Shimadzu Co., Kyoto, Japan), which has 32 rings and simultaneously produces 63 slices, each 3.125 mm thick, along a 20-cm longitudinal field. The matrix size was 128 × 128, with a pixel size of 4 × 4 mm. After at least 4 hours of fasting, 370 MBq of FDG was administered intravenously. One hour later, transmission and emission images were obtained simultaneously. The bladder was continuously flushed via a triple-lumen catheter with 1000 mL of saline. PET scans were evaluated qualitatively by one nuclear physician and one surgeon familiar with the local recurrence of rectal cancer and pelvic anatomy without the knowledge of CT results. Recurrence was recorded. The PET images were retrospectively evaluated quantitatively by means of standard uptake value (SUV). A region of interest was placed over the most intense areas of FDG accumulation to minimize any partial volume effect. SUV was calculated as follows:

$$\text{SUV} = (\text{PET count} \times \text{calibration factor}) / (\text{injected dose/body weight})$$

Image Fusion Method

To enable digital fusion of the images, we used a commercially available digital software program (T-B Fusion; Shimadzu). The software automatically adjusted the pixel size. After the fusion area was selected manually on the transmission image according to the body shape, the fit image in the ordered area was registered according to the fusion algorithm based on minimizing the intensity difference on an image workstation. Then, automatically, the emission image corresponding to the transmission image was displayed transparently on the CT image. When necessary, fine adjustment was performed manually.

FI Readings

Two experienced oncologists with expertise in PET, but who were blinded to the clinical information and without knowledge of CT- and PET-alone results, evaluated all FIs independently. FIs were evaluated with five images. In these five images, FDG-PET images were superimposed on CT images with five grades of transparency: 0%, 25%, 50%, 75%, and 100%. To interpret the FI, sagittal, coronal, and transaxial images were prepared. When the diagnosis was different between the two observers, the final decision was determined after discussion.

Clinical Effect of FI Findings on Surgical Treatment and Management

Clinical management decisions were made first by one specialized surgeon on the basis of CT and PET findings. Afterward, the indication for surgical intervention was reconsidered by the surgeon with full knowledge of CT, PET, and FI. Changes in the therapeutic management before and after the results of the FI were compared, and the clinical usefulness of FI was evaluated.

Statistical Analysis

Statistical analysis was performed with SAS software, version 8.2 (SAS Institute, Cary, NC). To identify any improvements in the accuracy of the diagnosis of the local recurrence associated with the use of FI, the diagnosis of local recurrence by each imaging method was assessed by means of a score ranging from 0 to 3, as has been reported.[13] Briefly, score 0 indicates incorrect findings, score 1 represents equivocal but incorrect findings, score 2 indicates correct but equivocal findings, and score 3 indicates correct findings. Wilcoxon signed rank test was used to compare FI with the other imaging methods. Because score 0 and score 1 were both incorrect, we combined them in the analysis and assigned them a score of 0. To address the problem of multiple com-

TABLE 2. *Diagnostic accuracy of the imaging methods*

Imaging method	Classification correct (score of 3)	Classification correct but equivocal (score of 2)	Classification incorrect (score of 0 or 1)
CT alone	27 (64)	6 (14)	9 (21)
PET alone	31 (74)	6 (15)	5 (12)
Fusion image	35 (83)	4 (10)	3 (7)

CT, computed tomography; PET, positron emission tomography.
Data are number of patients (%).

parisons, Bonferroni's correction was applied, and *P* values < .025 were considered significant. All *P* values are two sided.

RESULTS

All 42 patients with presumed local recurrence of rectal cancer were imaged with conventional CT scans and PET scans, and FIs were reconstructed. Table 1 shows the patient characteristics, final diagnosis and confirmation of diagnosis, and treatment. Table 2 shows the diagnostic accuracy of the three imaging modalities. Thirty-three of 42 patients were classified correctly (scores 2 and 3) by CT alone, and 9 classifications were incorrect (scores 0 and 1). Of the nine cases classified incorrectly, seven patients had local recurrence. Of the seven patients who had local recurrence, CT alone could not detect the abnormality in four patients; it diagnosed postoperative change in two patients and abscess in one. In the other two patients who did not have local recurrence, CT alone diagnosed recurrence. Compared with CT alone, FI provided additional information in seven of nine patients who had been diagnosed incorrectly and led to the correct diagnosis. The additional information consisted of the exact location of local recurrence in five patients and of no tumor radionuclide uptake in two patients (Table 3). The exact location of recurrence included the presacral area in one patient, the rectal stump in one, and lateral pelvic lymph nodes in three. Three of those five patients underwent operation, and the other two patients received chemotherapy. In the two patients with no FDG uptake, CT raised suspicion of a local recurrence, but FI did not. Finally, two patients did not undergo operation because FI results were negative, and follow-up showed no progression of the lesions, thus making malignancy unlikely. However, FI could not diagnose local recurrence correctly in two patients because of small-volume disease and overlap with urinary tract activity. In those two patients, radiological follow-up confirmed local recurrence 4 and 12 months after the initial diagnosis.

Thirty-seven patients were classified correctly by PET alone, and five were classified incorrectly. All five patients had local recurrence, but radionuclide uptake was not detected in three patients, and tumor radionuclide uptake could not be differentiated from urinary tract activity in two patients. All nine patients without local recurrence were correctly diagnosed by PET alone (no false-positive cases). Compared with PET alone, FI provided information on the exact location of lesions in two of five patients who had been diagnosed incorrectly. In the other three patients, two could not be diagnosed correctly even with these three modalities. In the other patient (case 15), the initial CT showed a suspicion of local recurrence, whereas PET was negative. Surgery was postponed, but a CT taken 2 months later confirmed local recurrence by tumor growth, and the patient underwent operation. PET alone also detected extrapelvic disease in four patients: one patient with thyroid cancer, two patients with liver metastasis, and one patient with lung metastasis.

Finally, FI provided additional information on 8 (19%) of 42 patients over CT or PET alone positively for accurate diagnosis of local recurrence of rectal cancer. On the other hand, FI negatively affected the diagnosis in one patient. Overall, FI provided more accurate information on the diagnosis of local recurrence of rectal cancer than did the other two imaging modalities. Statistically significant improvement was observed with FI compared with CT alone ($P = .0138$) and PET alone ($P = .0156$).

Influence of FI on Therapeutic Management

Because FI can provide more precise information on the anatomical location of disease, the results of FI could potentially influence the therapeutic management of local recurrence. We had five such patients in this series. In those five patients, either CT alone or PET alone indicated local recurrence, but patients could not be candidates for radical operation if FI did not show the exact anatomical location of local recurrence. Four patients underwent total pelvic exenteration, and one patient underwent local tumor resection. Figure 1 shows patient 18, whose recurrent tumor was not detected by CT alone (Fig. 1A) but was clearly detected by FI (Fig. 1C). In Fig. 2, lateral pelvic lymph node metastasis was identified by FI and later resected (case 41), although CT alone could not detect the tumor and PET alone did not provide

TABLE 3. *Results of CT, PET, and FI for discrepant results*

Patient no.	Sex	Age (y)	Primary operation	Histology of primary tumor	CT score[a]	PET score[a]	FI score[a]	Final diagnosis	Diagnosis confirmation	Usefulness of FI	Reason for FI failure
9	M	60	APR	Mod	1	2	2	LR	H (laparotomy)	Exact location	
15	F	59	APR	Well	2	0	1	LR	H (TR)	–	Small-volume disease
18	M	65	LAR	Well	1	2	3	LR	H (TR)	Exact location	
21	F	40	APR	Muc	3	0	2	LR	H (TR)	Exact location	
25	M	73	LAR	Mod	1	3	3	PO	C&R	No FDG uptake[b]	
32	M	56	LAR	Mod	0	1	2	LR	C&R	Exact location	
33	M	48	APR	Mod	0	0	0	LR	C&R	–	Small-volume disease
35	M	55	APR	Well	1	0	0	LR	C&R	–	Urinary tract overlap
38	F	59	APR	Well	0	3	3	LR	C&R	Exact location	
41	F	57	APR	Mod	0	3	3	LR	H (TPE)	Exact location	
42	F	45	APR	Mod	0	3	3	PO	C&R	No FDG uptake[b]	

CT, computed tomography; PET, positron emission tomography; FI, PET-CT fusion image; APR, abdominoperineal resection; Mod, moderately differentiated; LR, local recurrence; H, histological diagnosis; Well, well differentiated; TR, tumor resection; LAR, low anterior resection; Muc, mucinous; PO, postoperative change; C&R, clinical and radiological confirmation; FDG, ^{18}F-fluorodeoxy glucose; TPE, total pelvic exenteration.

[a] Score 0, incorrect; score 1, equivocal but incorrect; score 2, correct but equivocal; score 3, correct.

[b] No FDG uptake was detected in the region suspected of having LR in the CT image.

sufficient information for surgical planning. FI is also useful for differentiating between physiological FDG uptake and tumor. Accumulation of FDG within the bladder and bowel (Figs. 1B and 2B) is easily discriminated in the FI (Figs. 1C and 2C).

Taken together, a clinical effect of FI findings on surgical treatment and management was evident in 11 (26.2%) patients. Three patients underwent radical operation after the precise anatomical location of the tumor was identified, and in six patients, the treatment was modified on the basis of correct diagnosis by FI. Two patients (patients 18 and 41) underwent surgery on the basis of both correct diagnosis and anatomical location with FI. In particular, the surgical plan was modified in 5 (27.8%) of 18 patients, who underwent operation because of the results of FI. However, we could not diagnose two patients correctly even with these three modalities because of small-volume disease and overlap with urinary tract uptake.

Quantitative Analysis of Suspected Local Recurrence of Rectal Cancer

Figure 3 shows the individual and median SUV of true-positive cases ($n = 28$), true-negative cases ($n = 9$), and false-negative cases ($n = 5$). The median SUV of true-positive cases was 3.93 (range, 2.02–8.17), and that of true-negative cases was 1.34 (range, .73–2.06). SUVs of false-negative cases fell well within the range between true-negative and -positive cases (median, 2.14; range, 1.8–2.64).

DISCUSSION

PET scanning is a useful imaging modality for the detection of local recurrence of rectal cancer, particularly because it distinguishes between recurrence and postoperative fibrosis.[9,16,17] Ito et al.[9] and Strauss et al.[17] reported its utility by semiquantitative analysis of FDG uptake. Keogan et al.[11] demonstrated the usefulness of visual correlation of PET and CT or MRI in detecting local recurrence of rectal cancer. The image fusion method, with more precise anatomical information on the PET image, was then introduced, and its utility in maxillofacial carcinoma and thoracic malignancies has been reported.[18,19] However, the usefulness of digital FI in the diagnosis of rectal cancer has not been studied. Our results with FI of PET and CT demonstrated that FI provided more accurate information on the diagnosis of local recurrence of rectal cancer than did the other two

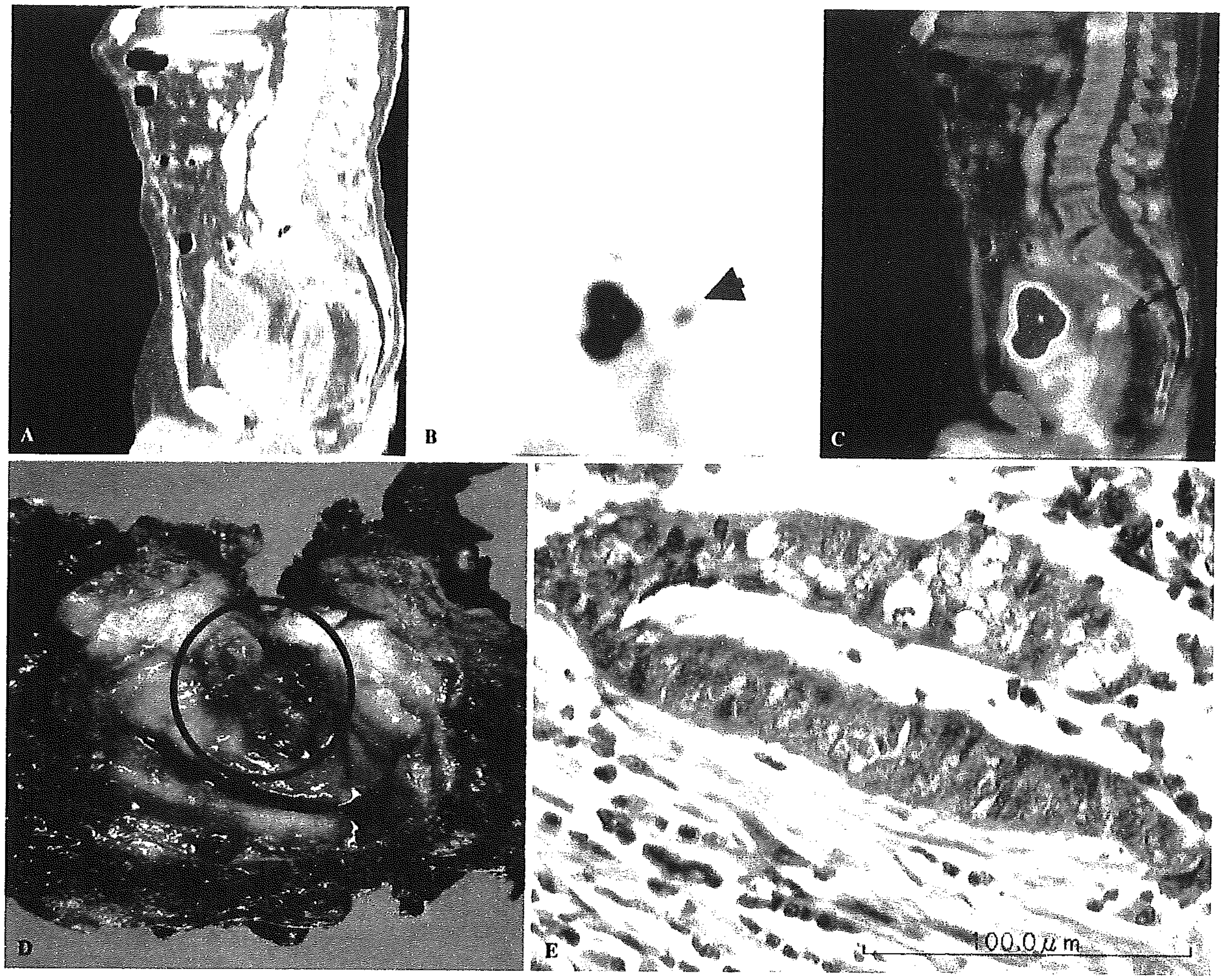

FIG. 1. A 65-year-old man (patient 18) with a history of low anterior resection with the Hartmann procedure, with recurrence at the rectal stump. (A) Sagittal computed tomography does not show tumor, and a differential diagnosis cannot be made. (B) Corresponding sagittal positron emission tomography image shows focal increase of ^{18}F-fluorodeoxy glucose uptake in the presacral area (*arrowhead*), suggesting tumor recurrence, but no precise anatomical information can be obtained. (C) Corresponding fusion image shows tumor recurrence at the rectal stump (*arrow*). (D) Resected specimen showing tumor recurrence (*red circle*). (E) Photomicrograph of the resected specimen confirms adenocarcinoma (stain, hematoxylin and eosin; original magnification, ×200).

imaging modalities. Statistically, a significant improvement was observed in comparison with both CT alone (P = .0138) and PET alone (P = .0156).

Recent development of inline PET/CT has improved diagnostic accuracy without visually correlating these two images by providing coregistered PET/CT images.[20] Significant improvement in diagnostic accuracy was found in the staging of non–small-cell lung cancer in comparison with visual correlation of PET and CT images.[13] Cohade et al.[21] demonstrated the superiority of PET/CT over PET alone in the evaluation of colorectal cancer. Although the inline PET/CT will be the standard of reference in oncological imaging in the near future, those scanners are still quite expensive and not frequently available. Therefore, the software-based image fusion technique used in our study may provide relevant information concerning diagnosis and treatment decision making in patients with suspected local recurrence of rectal cancer. It is less expensive and easier to use. Because the PET and CT images were taken separately, it is impossible to eliminate respiratory movement when they are registered. However, in the pelvic area, there are many landmarks for coregistering PET and CT images, and artifacts due to respiratory movement are negligible because local recurrence is a fixed tumor.

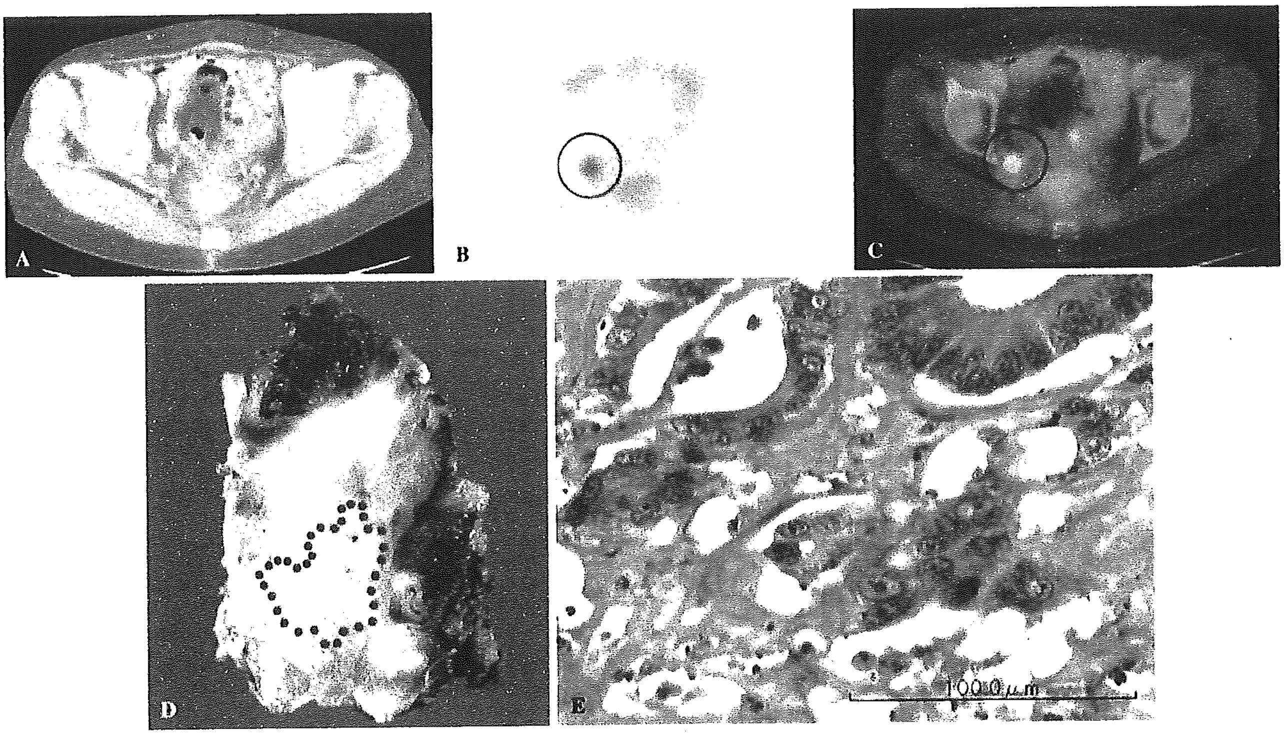

FIG. 2. A 57-year-old woman (patient 41) with a history of abdominoperineal resection, with recurrence at the lateral pelvic lymph node. **(A)** Transaxial computed tomography does not show any abnormalities. **(B)** Corresponding axial positron emission tomography image demonstrates increased metabolic activity in the right presacral area (*red circle*). **(C)** Transaxial fusion image reveals right lateral pelvic lymph node recurrence (*red circle*). **(D)** Resected specimen showing tumor recurrence (*area surrounded by red dots*). **(E)** Photomicrograph of the resected specimen confirms adenocarcinoma (stain, hematoxylin and eosin; original magnification, ×200).

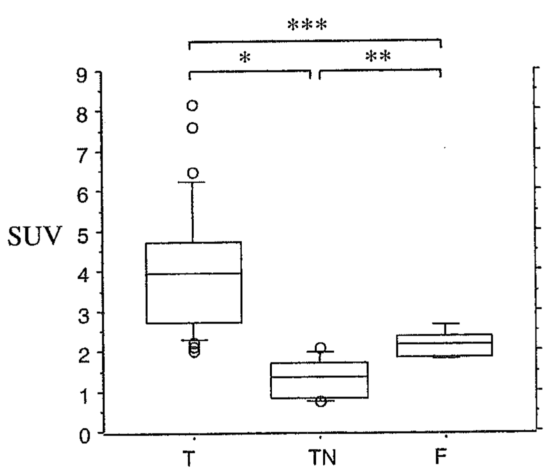

Fig. 3 Standard uptake value (SUV) of the region of interest in patients with suspected local recurrence of rectal cancer. Each bar represents the interquartile range, and the horizontal line within the bar represents the median value. To identify statistical difference among the three groups, the Kruskal-Wallis test was used. The Steel-Dwass test was then applied to compare between groups. **P* < .001; ***P* = .017; ****P* = .008. T, true positive; TN, true negative; F, false negative.

Local recurrence of rectal cancer is a complex disease. The treatment consists of surgery, radiotherapy, chemotherapy, or a combination of these.[22] Among these treatments, surgical resection remains the only potentially curative option in most patients.[2,3] It is therefore important to select favorable candidates for radical operation. Saito et al.[23] emphasized the importance of the pattern of recurrence, the area of invasion, and the presence of symptoms for successful curative operation. Wanebo et al.[2] reported that patients with previous anterior resections or preoperative carcinoembryonic antigen levels < 10 ng/mL had a favorable outcome. Taken together, it is apparent that patients with small tumors and adequate margins of resection have longer survival. In terms of early detection, PET is useful[24] and is also useful in terms of providing anatomical information when it is combined with CT.[20] In our series, in five patients (11.9%)—27.8% of patients who underwent curative resection—the treatment plan was altered on the basis of FI results; namely, the extent of tumor involvement was considered possible for curative resection on FI. This decision could not be made without FI. CT alone or PET alone is less powerful for the precise localization of recurrent tumors and their resectability.[25–27]

The clinical effect of FI on diagnosis or treatment decision making in this study was 26.2%. The frequency of patient management changes attributable to PET ranges from 20% to 61%.[27–32] Flamen et al.[32] reported that potential changes in therapeutic management were noted in 20% of their patients, and Kalff et al.[31] demonstrated that the frequency of change of patient management attributable to PET was 59% in their prospective study. In comparison with those studies, the clinical effect of FI on patient management in our study is comparable if the patient population is limited to local recurrence.

PET still has limitations. The detectability of tumor by PET depends on tumor size and uptake of FDG; therefore, PET scans cannot detect small-volume disease and underestimate the extent of lesions measuring <1 cm in diameter.[1,28] Bladder activity also remains a potential source of error in PET studies of the presacral area.[33] In our series, we had five (11.9%) false-negative cases by PET alone, and two were correctly diagnosed with FI by provision of additional anatomical information. However, the other three patients could not receive a correct diagnosis even with FI because of small-volume disease in two and overlap with urinary tract activity in one. Therefore, a correct diagnosis cannot be obtained in some patients even with this modality. Serial imaging studies and tumor markers are very important in patients who are highly suspected of having local recurrence but without confirmation.

In conclusion, combined morphological (CT) and functional (PET) imaging improves the diagnosis of local recurrence of rectal cancer and helps surgical management of this critical disease as an integral part of treatment decision making, even if each modality cannot provide sufficient information. FI allows selection of patients with a higher chance of cure while avoiding unnecessary operation on patients with diffuse disease and no chance for improvement of survival. Therefore, FIs have a potential clinical value in the treatment of suspected local recurrence of rectal cancer, and now we routinely perform FI on all patients being evaluated for local recurrence.

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High Incidence of Thrombosis of the Portal Venous System After Laparoscopic Splenectomy

A Prospective Study With Contrast-Enhanced CT Scan

Masataka Ikeda, MD, PhD, Mitsugu Sekimoto, MD, PhD,* Shuji Takiguchi, MD,* Masaru Kubota, MD,* Masakazu Ikenaga, MD, PhD,* Hirofumi Yamamoto, MD, PhD,* Yoshiyuki Fujiwara, MD, PhD,* Masayuki Ohue, MD, PhD,* Takushi Yasuda, MD, PhD,* Hiroshi Imamura, MD, PhD,† Masayuki Tatsuta, MD, PhD,† Masahiko Yano, MD, PhD,* Hiroshi Furukawa, MD, PhD,† and Morito Monden, MD, PhD**

Objective: The aims of this prospective study were to investigate the true incidence of portal or splenic vein thrombosis (PSVT) after elective laparoscopic splenectomy using contrast-enhanced computed tomography (CT) scan, and outcome of anticoagulant therapy for PSVT.

Summary Background Data: Although rare, thrombosis of the portal venous system is considered a possible cause of death after splenectomy. The reported incidence of ultrasonographically detected PSVT after elective open splenectomy ranges from 6.3% to 10%.

Methods: Twenty-two patients underwent laparoscopic splenectomy (LS group), and 21 patients underwent open splenectomy (OS group). Preoperative and postoperative helical CT with contrast were obtained in all patients, and the extent of thrombosis was investigated. Prothrombotic disorder was also determined.

Results: PSVT occurred in 12 (55%) patients of the LS group, but in only 4 (19%) of the OS group. The difference was significant ($P = 0.03$). Clinical symptoms appeared in 4 of the 12 LS patients. Thrombosis occurred in the intrahepatic portal vein (n = 9), extrahepatic portal vein (n = 2), mesenteric veins (n = 1), proximal splenic vein (n = 4), and distal splenic vein (n = 8). Prothrombotic disorder was diagnosed in 1 patient. Anticoagulant therapy was initiated once the diagnosis was established, and complete recanalization, except for distal splenic vein, was observed without any adverse event. Patients with splenomegaly were at high risk of PSVT.

Conclusions: PSVT is a more frequent complication of laparoscopic splenectomy than previously reported but can be treated safely following early detection by CT with contrast.

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From the *Department of Surgery and Clinical Oncology, Graduate School of Medicine, Osaka University, Suita, Japan; and †Department of Surgery, Sakai Municipal Hospital, Sakai, Japan.

Reprints: Masataka Ikeda, MD, PhD, Department of Surgery and Clinical Oncology (E2), Graduate School of Medicine, Osaka University, 2-2 Yamadaoka Suita, Osaka 565-0871, Japan. E-mail: mikeda@surg2.med.osaka-u.ac.jp.

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Thrombosis of the portal venous system has been reported as a possible cause of death after splenectomy. This complication was considered as an uncommon complication.[1] However, with the improvement in diagnostic modalities and the increased interest in this disease entity, it is becoming apparent that the incidence of portal or splenic vein thrombosis (PSVT) may be greater than clinically appreciated and may, at times, be asymptomatic.[2–6] Rattner et al[2] reported 6 patients in more than 1000 splenectomies, and recent reports on symptomatic PSVT demonstrated the incidence between 1.1% (4 of 350) and 8% (8 of 101).[5–7] However, since the above reports were all retrospective case log analyses, the actual incidence of PSVT after elective splenectomy has not been elucidated. In retrospective studies of postoperative imaging surveillance for detection of PSVT, Petit et al[3] reported 13 of 119 patients (10.9%) developed PSVT, 7 of whom were asymptomatic. Loring et al[8] reported 12 of 123 patients (9.8%) had PSVT, 3 of whom were asymptomatic.

To determine the true incidence of PSVT after splenectomy, prospective studies have been conducted with ultrasonography.[4,9,10] Skarsgard et al[9] presented one (6.3%) asymptomatic PSVT among 16 consecutive pediatric patients with hematologic diseases. Chaffanjon et al[4] reported one symptomatic and 3 asymptomatic PSVT (total 6.7%) in a prospective series of 60 consecutive splenectomies for hematologic disorders. Hassn et al[10] reported 5 patients (10%) with PSVT (one asymptomatic) in 50 elective splenectomy. Taken together, the incidence of postsplenectomy PSVT is about 5% to 10% according to these retrospective and prospective studies.

However, since these three prospective studies showed the incidence only after conventional open splenectomy (OS), the impact of laparoscopic splenectomy (LS) on the incidence of PSVT is still undetermined. Because LS is gaining wide acceptance as a safe, effective alternative to OS in the treatment of hematologic disorders,[11,12] it is important to determine the actual incidence of PSVT after LS. Only 2 of 545 patients with suspicious PSVT symptoms have been reported based on literature review of recent reports on the complications of LS, and these studies concluded that LS is safe and efficacious for benign and malignant hematologic diseases.[13–19] The symptoms in these reported patients were fever of unknown origin and intestinal infarction, but the diagnosis of PSVT was not made. In contrast, Winslow et al[6] emphasized that PSVT does occur after LS. To our knowledge, 6 cases with post-LS PSVT have been reported so far.[20–25]

The aim of this prospective study was to determine the actual incidence of PSVT after LS using contrast-enhanced computed tomography (CT) and to determine the treatment outcome of PSVT.

PATIENTS AND METHODS

Patient Eligibility and Population

Patients 18 years of age or older were enrolled in the study if they were scheduled for LS, hand-assisted LS (HALS), or OS. Before entry into the study, informed consent was obtained from all patients. Patients were excluded from the study if they had history of venous thromboembolism, had hypersensitivity to the intravenous contrast media, or had renal dysfunction. Between April 2001 and June 2003, 24 consecutive LS or HALS were performed at the Department of Surgery and Clinical Oncology, Osaka University Medical Hospital. Of these patients, 2 patients were excluded from this study because of hypersensitivity and renal dysfunction. Thus, 22 patients were entered into the study (LS group). HALS was performed in 3 patients with hypersplenism and lymphangioma, because of splenomegaly.

For comparison of OS versus LS, patients who elected to undergo OS were recruited to this study. During the same period, 19 patients with gastric cancer, 1 with rectal cancer, and 1 with ovarian cancer were recruited as open splenectomy group (OS group). The underlying diseases were gastric cancer (19 patients), splenic cyst, and metastatic splenic tumor originating from ovarian cancer. For the patients with gastric cancer, the indication for splenectomy was en bloc node dissection with total gastrectomy. Patients with pancreaticosplenectomy were not included in this study. One patient with splenic tumor underwent splenectomy for histologic diagnosis, and the operation was conducted during surgery for resection of rectal cancer. The diagnosis was a solitary splenic cyst. The other patient with metastatic splenic tumor underwent splenectomy in association with bilateral oophorectomy with radical lymph node dissection. Intermittent pneumatic foot pump was used for perioperative prophylaxis of deep venous thrombosis until full ambulation, but no anticoagulant was used for patients of both the LS and OS groups. Table 1 lists the clinical characteristics of our patients.

Operative Technique for Laparoscopic Splenectomy

After induction of general anesthesia, patients were placed in the right semilateral position. At the beginning of the procedure, patients were adjusted to a horizontal position by rotation of the table to the right side. The first trocar (12 mm) was inserted below the left costal margin, at the level of the midaxillary line, where the laparoscope would be placed. The abdomen was then insufflated (10–12 mm Hg) and three additional trocars were inserted under direct laparoscopic vision: 1) subxyphoid (5 mm); 2) subcostal left flank (5 mm); and 3) subcostal area between the first port and the left flank

TABLE 1. Patient Characteristics

	LS	OS	*P*
Total no. of patients	22	21	
Age (yr) (median, range)	50, 18–73	68, 45–79	< 0.0001
Sex (male:female)	3:19	16:4	< 0.0001
Type of disease			
Idiopathic thrombocytopenic purpura	13	0	
Malignant lymphoma	2	0	
Hypersplenism due to cirrhosis	2	0	
Autoimmune hemolytic anemia	1	0	
Splenic lymphangioma/hemangioma	2	0	
Evans syndrome	1	0	
Splenic cyst	1	1	
Gastric cancer	0	19	
Metastatic splenic tumor	0	1	
Operating time (min)			
Median	116	280	< 0.0001
Range	65–349	173–635	
Blood loss (mL)			
Median	40	1150	< 0.0001
Range	10–2200	260–3500	
Spleen weight (g)			
Median	145	—	
Range	11–2315	—	

port (12 mm). First, a thorough inspection of the abdomen for accessory spleen was made. The inferior pole of the spleen was mobilized by dissecting the splenocolic ligament. Short gastric vessels were then controlled with a harmonic scalpel and exposure of the splenic hilum was achieved. Once the anterior aspect of the hilum was exposed, the left gutter was dissected and the spleen was separated from the kidney and diaphragm. At this point, the spleen remains attached almost entirely by the vascular supply, and the gap between the splenic hilum and tail of the pancreas was enlarged. The splenic hilar vessels were divided with an endoscopic vascular stapler. Extraction of the spleen was accomplished by morcellation within EndoCatche II (USSC, Norwalk, CT). Special attention was paid to avoid splenic fracture and intraabdominal spillage of splenocytes to prevent the development of splenosis. For HALS, a skin incision for the hand insertion was made in the right subcostal area. The procedure for splenectomy was similar to that described for LS and the splenic hilar vessels were also divided with an endoscopic vascular stapler.

Operative Technique for Open Splenectomy

All OSs were performed through a midline incision. For patients with gastric cancer, since the indication of splenectomy was en bloc node dissection, the spleen was resected with the stomach without dissection of the gastrosplenic ligament. The vessels at splenic hilum were ligated and divided at the tail of the pancreas. For the patients with splenic tumor, only the spleen was excised, in addition to the rectal cancer or ovarian cancer operation. The procedure for the division of splenic hilum was similar to that used in patients with gastric cancer.

Detection and Diagnosis of PSVT Using Contrast-Enhanced CT

All patients underwent preoperative and postoperative helical CT. The diagnosis of PSVT was made by a radiologist and a surgeon based on the detection of unenhanced region in the dilated splenoportal system, where no abnormality was found in the preoperative CT. The extent of occlusion of the portal vein, splenic vein, and superior mesenteric vein was precisely defined. PSVT was divided according to the location of the thrombus. The inferior mesenteric vein (IMV) was identified, and thrombus formation in the splenic vein distal to the junction of IMV was diagnosed as distal splenic vein thrombosis (dSVT). Thrombi between the portal vein and IMV were diagnosed as proximal SVT (pSVT). In case of IMV directed towards the superior mesenteric vein (SMV), SVT was identified as dSVT. Portal vein thrombi were divided into intrahepatic and extrahepatic thrombosis (iPVT and ePVT, respectively). Portal vein branches involved with thrombus were also determined. Two patients in the LS group and 2 patients in the OS group developed only dSVT. Those 4 patients were not included among patients with PSVT because dSVT is resistant to anticoagulation, and no clinical sequelae were identified irrespective of treatment.

Laboratory Tests

Since prothrombotic disorders are commonly associated with PSVT,[26] blood samples were taken from all patients of the LS group, except 2 with liver cirrhosis and hypersplenism, to screen for thrombophilia, such as antithrombin III (AT-III) deficiency, protein C deficiency, protein S deficiency, and dysplasminogenemia. In addition, screening for antiphospholipid syndrome (lupus anticoagulant and β2 glycoprotein) was performed. Complete blood count, transaminases (AST, ALT), serum amylase, C-reactive protein (CRP), thrombin-AT-III complex (TAT), and D-dimer (DD) were examined perioperatively (before operation, on postoperative days 1, 2, 4 $\pm$ 1, and 7 $\pm$ 1).

Statistical Analysis

Continuous data are expressed as mean $\pm$ SD, unless specifically noted. Statistical analysis was performed using the χ^2 test or Fisher exact test for categorical data and Mann-Whitney U test for nonparametric data. Chronologic changes in the laboratory data were analyzed by analysis of variance for repeated measures. All statistical analyses were completed using StatView 5.0J (SAS Institute Inc., NC). A P value of <0.05 was considered significant.

RESULTS

Incidence of PSVT and Clinical Course After LS

Twelve (55%, 95% confidence interval, 32.2%–75.6%) of 22 patients who underwent postoperative CT (between 3 and 23 postoperative days [POD], median; 6.5 POD) developed PSVT after LS (Table 2). Specifically, 1 patient (case 2) had proximal and distal SVT, 4 patients (cases 1, 5, 10, and 12) developed iPVT and dSVT, 4 patients (cases 4, 7, 9, and 11) had iPVT alone, 1 patient (case 3) developed ePVT, SMVT, pSVT, and dSVT, 1 patient (case 6) had ePVT, pSVT, and dSVT, and 1 patient developed iPVT, pSVT, and dSVT (case 8). Figure 1 shows schematically the anatomic extension of the thrombus in each patient. The mean age of patients with and without PSVT was 44.0 years (17.8 years) and 48.2 years (19.2 years), respectively (Table 3). Nine of 13 patients with idiopathic thrombocytopenic purpura and 1 patient with splenic cyst did not develop PSVT, while all other patients developed PSVT. All 12 patients with PSVT received anticoagulant therapy (Table 2). Intravenous infusion or subcutaneous heparin was used for cases 1, 2, 4, and 5 (adjusted individually, aiming at 1.5- to 2-fold prolongation of the pretreatment activated partial thromboplastin time). All 12 patients received anticoagulant therapy with warfarin; the dose was adjusted to achieve an international normalized ratio (INR) between 1.5 and 2.0 until resolution of PSVT.

TABLE 2. Summary of CT Findings and Clinical Course for Patients With Post-LS PSVT

Case No./ Age (yr)/ Sex	Diagnosis	Spleen Weight (g)*	Symptoms	Site of Thrombosis					Anticoagulant Therapy (duration)	First CT (POD)	Second CT (POD)
				iPV†	ePV	SMV	pSV	dSV			
1/31/F	ITP	260	—	L,3,4	—	—	—	o	Yes (97)	4	84
2/50/F	Evans syndrome	300	Fever	—	—	—	o	o	Yes (65)	5	91
3/50/F	Hypersplenism	750	—	—	o	o	o	o	Yes (177)	6	97
4/48/M	Malignant lymphoma	214	—	A,7	—	—	—	—	Yes (51)	4	53
5/66/M	Malignant lymphoma	120	—	A,R,L	—	—	—	o	Yes (161)	4	161
6/67/F	Hypersplenism	334	Fever	—	o	—	o	o	Yes (98)	23	98
7/18/F	ITP	218	—	A,5,8,P,6.7	—	—	—	—	Yes (98)	8	107
8/25F	Splenic lymphangioma	2315	Abdominal pain, fever	8,6	—	—	o	o	Yes (87)	7	95
9/33/F	ITP	180	Abdominal pain, fever	A,5,8,P,6,7	—	—	—	—	Yes (87)	6	91
10/67/F	AIHA	98	—	R,P,5,8	—	—	—	o	Yes (91)	3	92
11/51/F	Hemangioma	180	—	8	—	—	—	—	Yes (85)	7	84
12/22/F	ITP	104	—	8	—	—	—	o	Yes (95)	4	94

iPV indicates intrahepatic portal vein; ePV, extrahepatic portal vein; SMV, superior mesenteric vein; pSV, proximal splenic vein; dSV, distal splenic vein; POD, postoperative day; ITP, idiopathic thrombocytopenic purpura; AIHA, autoimmune hemolytic anemia; L, left branch of portal vein; R, right branch of portal vein; A, anterior branch of portal vein; P, posterior branch of poral vein; o, patient developed thrombosis.

*Spleen weight was measured by pathologic specimen; only in case 7 was it estimated by volumetry based on thin slice CT.

†Values in the iPV column indicate branches of intrahepatic portal vein according to Couinaud's classification.

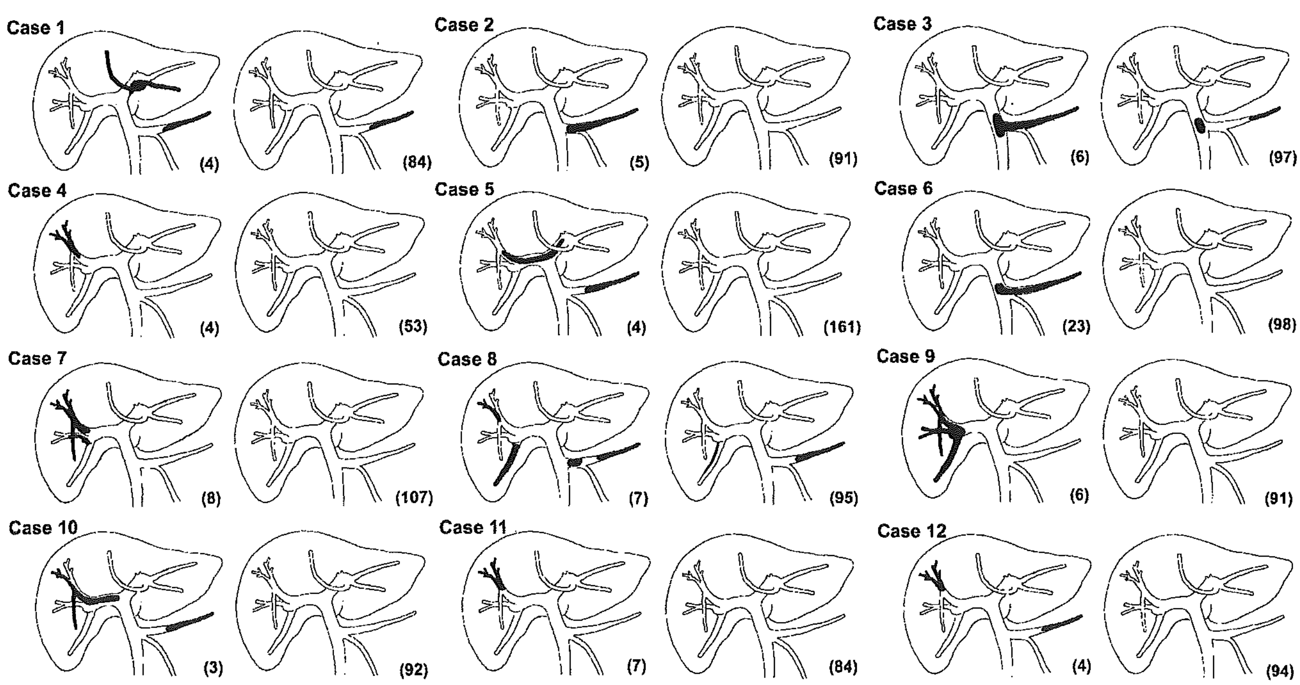

FIGURE 1. Schematic drawing of portal and splenic vein thrombosis (PSVT) after laparoscopic splenectomy (LS). Numbers in parentheses indicate days after operation.

TABLE 3. Comparison of Patient Populations

	Laparoscopic Splenectomy			Open Splenectomy		
	No PSVT	PSVT	*P*	No PSVT	PSVT	*P*
Age (yr) (mean ± SD)	48.2 ± 19.2	44.0 ± 17.8	0.60	68.4 ± 7.6	63.3 ± 13.1	0.31
Male/famale	1/9	2/10		14/3	2/2	
Indications for splenectomy						
Idiopathic thrombocytopenic purpura	9	4		—	—	
Malignant lymphoma	0	2		—	—	
Hypersplenism due to cirrhosis	0	2		—	—	
Autoimmune hemolytic anemia	0	1		—	—	
Splenic lymphangioma/hemangioma	0	2		—	—	
Splenic cyst	1	0		1	—	
Evans syndrome	—	1		—	—	
Gastric cancer	—	—		15	4	
Metastatic splenic tumor	—	—		1	—	

The median INR (interquartile range) of these patients before anticoagulation, 1 week, 2 weeks, 1 month, 2 months, and 3 months after the treatment was 1.09 (0.19), 1.56 (0.67), 1.72 (0.67), 1.52 (0.40), 1.57 (0.56), and 1.30 (0.32), respectively. There was no major or minor bleeding episode during warfarin treatment (median duration, 93 days).

Follow-up studies (performed between 53 and 161 POD; median, 93 POD) demonstrated complete resolution of PSVT in 9 of 12 patients and improvement in the other 3 patients. One patient (case 1) had only dSVT, and 1 patient (case 8) had iPVT and dSVT, and the other patient (case 3) had ePVT, SMVT, and dSVT. Case 3 received oral anticoagulant for 183 POD until complete resolution of both ePVT and SMVT. All pSVT and 8 of 9 iPVT showed complete resolution (Fig. 1). The resolution rate of dSVT, pSVT, and iPVT was 5 of 8 (62.5%), 4 of 4 (100%), and 8 of 9 (88.9%), respectively. Four patients (33.3%) had fever greater than 38°C, and 2 patients (16.7%) had abdominal pain postoperatively, but none had ascites or peritoneal edema. Eight patients (66.7%) were asymptomatic. Five patients had abnormal AST or ALT values after operation. Case 8 with marked splenomegaly had pancreatic injury, which needed 15-day drainage. The other patients with PSVT did not require treatment of major postoperative complications except anticoagulant therapy.

Incidence of PSVT and Clinical Course After OS

As shown in Table 1, patients who underwent OS were older, and their operative time and blood loss were significantly greater than those who had LS. Four (19%, 95% confidence interval, 5.4%–41.9%) of 21 patients who underwent postoperative CT (between 4 and 12 POD; median, 7 POD) developed PSVT after OS (Table 4), and all these 4 patients had gastric cancer. Specifically, 1 patient (case 1) had iPV alone, 2 patients (cases 2 and 3) had iPVT and dSVT, and the other patient (case 4) had ePVT, SMVT, pSVT, and dSVT. Figure 2 is a schematic drawing of the anatomic extension of thrombosis in each patient. Follow-up studies

TABLE 4. Summary of CT Findings and Clinical Course for Patients With Post-OS PSVT

Case No./ Age (yr)/ Sex	Diagnosis	Symptoms	Site of Thrombosis					Anticoagulant Therapy	First CT (POD)	Second CT (POD)
			iPV*	ePV	SMV	pSV	dSV			
1/47/M	Gastric cancer	Fever	5,8	—	—	—	—	No	6	120
2/79/F	Gastric cancer	—	3	—	—	—	o	No	6	244
3/65/F	Gastric cancer	Fever	4,8	—	—	—	o	No	6	—
4/62/M	Gastric cancer	Abdominal pain, fever	—	o	o	o	o	Yes	11	83

SMV, indicates superior mesenteric vein; pSV, proximal splenic vein; dSV, distal splenic vein; POD, postoperative day; o, patient developed thrombosis.
*Values in the iPV column indicate branches of intrahepatic portal vein according to Couinaud's classification.

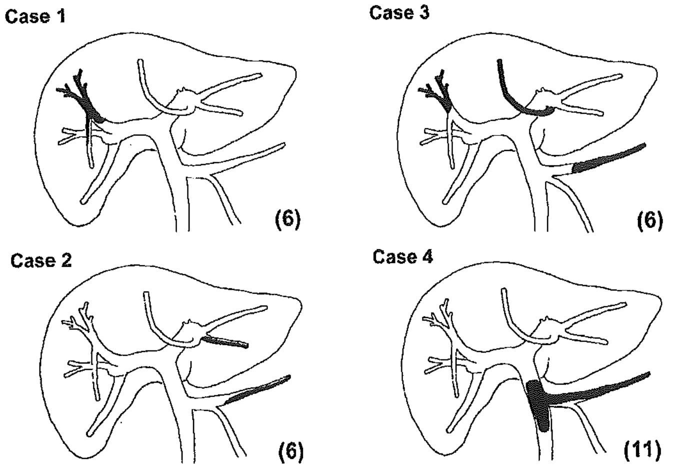

FIGURE 2. Schematic drawing of portal or splenic vein thrombosis (PSVT) after open splenectomy (OS). Numbers in parentheses indicate days after operation.

were performed in 3 patients on 83, 120, and 244 POD. These studies showed residual iPVT in case 1. In case 2, PSVT could not be evaluated because of multiple liver metastases. Anticoagulant therapy was administered for case 4, in the form of intravenous infusion or subcutaneous injection of heparin and warfarin. Three patients developed fever higher than 38°C, and 1 patient complained of abdominal pain postoperatively, but none had ascites or peritoneal edema. The incidence of PSVT after OS was significantly lower than that after LS ($P = 0.03$).

Incidence of Prothrombotic Disorders

Of 19 patients who participated in the screening for prothrombotic disorders, no dysplasminogenemia, AT-III, protein C, and protein S deficiencies were detected. Only 1 patient (case 2) who developed pSVT and dSVT had abnormal lupus anticoagulant, suggesting an association of antiphospholipid syndrome. Two patients with liver cirrhosis and hypersplenism who did not provide blood samples for screening for thrombophilia had PSVT. Nine of 12 patients with post-LS PSVT had no prothrombotic disorders, suggesting that PSVT can occur without primary deficiencies in natural coagulation inhibitors.

Factors Associated With PSVT

In an attempt to identify clinical and laboratory parameters that could predict the occurrence of postsplenectomy thrombosis, patients with PSVT were compared with those without such complication, with respect to age, sex, diagnosis, operation time, blood loss, splenic weight, preoperative and postoperative platelet count, white blood cell count, CRP, TAT, and DD. Age, sex, and diagnosis did not differ between the 2 groups (Table 3). Patients with PSVT had significantly heavier splenic weight (g) (median, 216 g; interquartile range, 167 g) than those without PSVT (median, 82 g; interquartile range, 67 g), suggesting that a large splenic mass is a possible risk factor for postsplenectomy PSVT, but we did not find difference in operation time (median, 124 minutes vs. 111 minutes) and blood loss (25 mL vs. 40 mL) between the two groups. Figure 3 shows serial changes in platelet count, white blood cell count, and CRP. Platelet count, white blood cell count, and CRP in patients with PSVT were greater than in those without PSVT, but the difference was not significant. We also did not find differences in preoperative and postoperative TAT and DD values.

DISCUSSION

In several prospective studies, the incidence of PSVT determined by ultrasonography ranged from 6.3% to 10%.[4,9,10] In the present study, the incidence of PSVT after

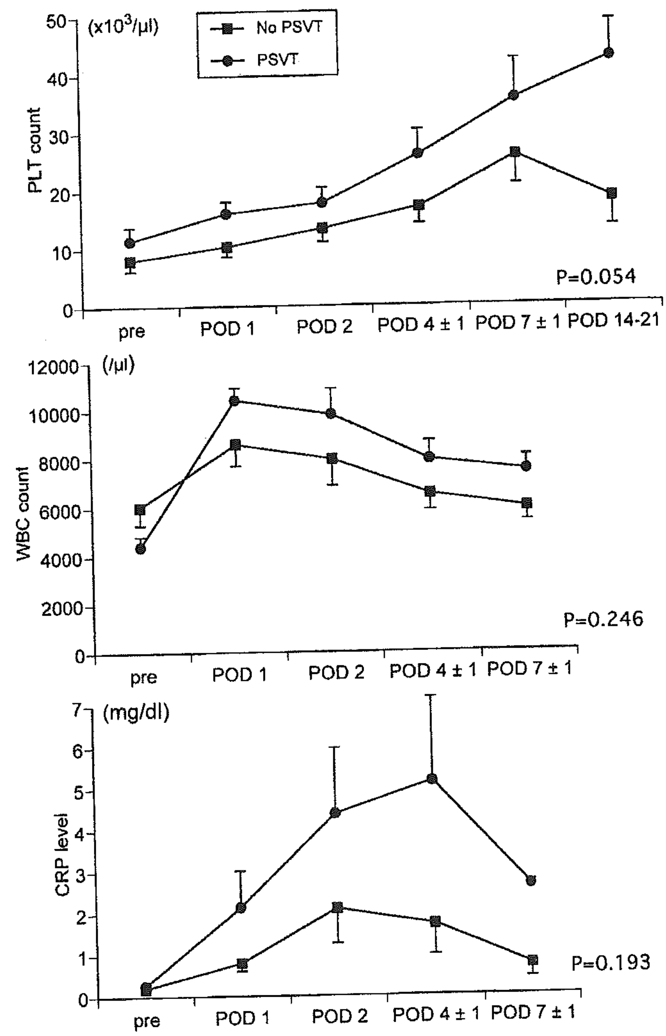

FIGURE 3. Sequential changes in preoperative and postoperative platelet counts, white blood cell counts, and C-reactive protein (CRP). Values are mean ± SEM.

elective laparoscopic splenectomy was 55% as determined by abdominal CT with intravenous contrast. The incidence was markedly higher than that reported in previous studies, and also significantly higher than that associated with open splenectomy, even though the patients in the OS group had known risk factors for thromboembolism, ie, old age and malignancy. The usefulness of CT for the diagnosis of PSVT after splenectomy has been emphasized previously.[2–4,6,8,27] In the presence of bowel distention or morbid obesity, ultrasonography is often limited in detecting thrombosis[3,4,8]; on the other hand, CT can provide objective images and exclude other intraabdominal complications.[6] CT is comparable to ultrasonography in evaluating portal veins.[28,29] Difference in the modality used to examine PSVT might explain the differences in the incidence of PSVT determined in the above previous studies and the present investigation. By using ultrasonography, Skarsgard et al[9] identified left portal vein thrombosis in asymptomatic patients, and Chaffanjon et al[4] diagnosed 3 cases of portal vein thrombosis of the main, right, and left branches, and one mesenteric thrombosis. Four other cases with PSVT were diagnosed by ultrasonography, with the thrombus in the main or major branches, not segmental branches,[20,24,25,30] suggesting that patients with only segmental portal vein thrombosis or distal splenic vein thrombosis cannot be diagnosed by ultrasonography. In our series, 5 patients (22.7%; cases 1, 3, 5, 6, and 10) had PSVT in major branches or the main portal vein, and the other 7 patients might have been diagnosed as normal by ultrasonography.

The fact that the date of onset of PSVT after splenectomy is unclear and we performed CT scanning once after splenectomy between 3 and 23 postoperative days might also influence the true incidence of PSVT. PSVT was diagnosed more than 1 year after splenectomy in some cases.[2,5] However, in most cases, PSVT was diagnosed on 2 to 22 days after open splenectomy,[2,5,6,9] and in patients with laparoscopic splenectomy the intervals between diagnosis and splenectomy were 4 to 14 days.[20–24] The date of postoperative CT scanning in our study is comparable to the reported dates of PSVT diagnosis, and Chaffanjon et al[4] demonstrated that no thrombus resolution was found until POD 30 by prospective study, suggesting that the incidence of PSVT is unlikely to be altered by performing CT once after splenectomy between 3 and 23 days postoperatively.

A number of investigators have recommended the use of postoperative prophylaxis such as heparin for high-risk patients.[6,9] It is possible that the lack of heparin use in our study might have contributed to the remarkably high incidence of PSVT. However, previous studies reported that 7 of 9 PSVT patients[5] and 5 of 8 patients[6] developed PSVT despite receiving prophylactic anticoagulation. Chaffanjon et al[4] reported that 6.7% developed PSVT even after using low molecular weight heparin, and Skarsgard et al[9] reported that 6.3% developed PSVT without any prophylaxis, suggesting that the role of prophylaxis remains uncertain. Our finding of the significantly higher incidence of PSVT in LS group compared with the OS group, even though both groups did not receive thrombosis prophylaxis implies that there must be some other factors that could contribute to the high incidence of PSVT in the LS group.

A possible reason for the high incidence of PSVT is the surgical technique itself. The 2 major differences in the operative technique between laparoscopic and open splenectomy in this study were pneumoperitoneum and ligation of splenic hilar vessels. In the OS group, splenic hilar vessels were ligated conventionally, while these vessels were divided with an endoscopic vascular stapler in the LS group. Previous studies showed that pneumoperitoneum may cause a hypercoagulable state during laparoscopic surgery.[31,32] Changes in intraabdominal pressure during splenectomy decrease portal vein blood flow and induce stasis.[33,34] Both stasis of venous flow and resulting congested coagulation factors may induce PSVT. Baixauli et al[35] reported PSVT after laparoscopic colectomy without known risk factor for venous thrombosis, and stressed the importance of pneumoperitoneum-induced changes in hemodynamic and coagulation states. In patients with splenomegaly, the large stump of splenic vein causes blood turbulence, which in turn can result in a local increase in coagulability and enhance thrombus formation.[2,6] In our series, spleen weight of patients with PSVT was significantly heavier than that of patients without PSVT, suggesting that spleen weight is a possible predictor of postoperative PSVT. Differences in the shape of the stump may also affect the hemodynamic and coagulation states. In the LS group, splenic hilar vessels were ligated extensively with endoscopic stapler, which results in a reduction of circulation around the ligated area, and may therefore enhance venous stasis at the very end of the stump.

Broe et al[36] demonstrated in a postmortem study that the thrombus originated in and extended from the distal splenic vein into the mesenteric and portal vein. This has been accepted as the key pathogenic event.[2] In our series, proximal propagation of thrombus was found in cases 2, 3 and 6; however, we also find 4 patients with isolated iPVT (cases 4, 7, 9, 11), and 5 patients with isolated iPVT and dSVT (cases 1, 5, 8, 10, 12). Majority of patients had right-side iPVT. Our speculation for the occurrence of iPVT is embolism of the thrombus originated in the distal splenic vein by the inferior mesenteric venous flow. Therefore, iPVT is likely to occur on the right side of the hepatic portal system because the right side of the portal venous flow is greater than the left one.

In this prospective study including preoperative and sequential postoperative imaging, routine postoperative CT imaging clearly demonstrated the occurrence of PSVT and the effect of anticoagulant therapy. Furthermore, initiation and termination of anticoagulant therapy were effectively performed based on CT images. Postoperative surveillance has been recommended for early diagnosis of PSVT, but its clinical use is still debatable.[3,8] Since the safety of LS has been well recognized in the clinical setting,[13–19] routine surveillance imaging for PSVT does not seem warranted. Postoperative surveillance must be confined to patients at high risk for PSVT, and anticoagulant therapy should be provided for patients with poor prognosis.

We found that spleen weight was a possible predictor of postoperative PSVT. Our results also showed that the frequency of PSVT was in part dependent on the underlying disease. All patients with hemolytic anemia, malignant lymphoma, lymphangioma, and hypersplenism developed PSVT, as has been reported previously.[5,6,37] Therefore, patients with splenomegaly, hemolytic anemia, malignant lymphoma, lymphangioma, and hypersplenism are at high risk of postsplenectomy PSVT and require close surveillance. In addition, for patients who develop leukocytosis, CRP elevation, and thrombocytosis during the postoperative period, they should be suspected of having PSVT and CT with contrast is recommended.

Loring et al[8] reported 2 cases with complete resolution and 1 case with partial resolution of 7 untreated PSVT patients, and Skarsgard et al[9] reported 2 cases with PSVT whose thrombosis resolved spontaneously without treatment. These 5 cases had SVT and iPVT without thrombus propagation into the SMV. On the other hand, in a disastrous case, autopsy revealed propagation of the thrombus from the remaining splenic vein into the SMV with resultant bowel infarction.[2,36] Involvement of SMV is associated with poor prognosis, while involvement of portal vein may be considered as a less serious condition. Gertsch et al[38] also reported poor prognosis with complete obstruction of SMV, and good prognosis with isolated portal vein thrombosis. Therefore, patients with SMVT should be treated without delay; however, whether all other patients not having SMVT require treatment should be determined.

The treatment used for PSVT in the present study was anticoagulation with heparin and/or warfarin. All 12 patients with PSVT received low-intensity warfarin therapy, which was designed to maintain INR between 1.5 and 2.0 for a median period of about 3 months. The usefulness of low-intensity warfarin therapy has been reported for the prevention of recurrent venous thromboembolism with low morbidity.[39] No thrombus progression was noted, and all portal, mesenteric, and proximal splenic vein thrombosis completely resolved within 6 months. One of the reasons for the effectiveness of low intensity warfarin therapy is the low incidence of prothrombotic disorders in our series. In contrast, a high prevalence of prothrombotic disorders, such as antiphospholipid syndrome, protein C, protein S, plasminogen, and antithrombin III deficiency, has been reported in patients with idiopathic PSVT (not after splenectomy).[26,40] For the latter group of patients, lifetime anticoagulation is often required.

CONCLUSION

We have demonstrated in the present study that PSVT is a common complication after laparoscopic splenectomy and can occur without any prothrombotic disorders. Especially, patients with splenomegaly were at high risk for PSVT. PSVT was safely treated by prompt anticoagulant therapy dependent on the CT results. Although our prospective study clearly demonstrated the usefulness of routine CT surveillance for the detection and treatment of PSVT, further studies are necessary to confirm the need for routine surveillance imaging, thrombotic prophylaxis, and treatment in the management of postsplenectomy PSVT.

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