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Postoperative Changes in Splenic Volume after Spleen-preserving Distal Pancreatectomy with Conservation of the Splenic Artery and Vein, and after Digestive Tract and Breast Surgery

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ABSTRACT

Aim: There is a paucity of information about changes in splenic volume after surgery. The aim of this study was to investigate postoperative changes in splenic volume (SV) and the factors influencing SV after spleen-preserving distal pancreatectomy (SPDP) with conservation of the splenic artery and vein (CSAV), and after surgery of the digestive tract and breast.

Methods: We investigated 113 patients who underwent SPDP with CSAV (n=7), breast surgery (n=24), colorectal surgery (n=45), distal gastrectomy (n=27) and total gastrectomy (n=10). SV changes were determined for three years after surgery using volumetry based on computed tomographic imaging, and splenic vein diameter changes after SPDP with CSAV were also determined.

Results: Splenic vein diameter after SPDP with CSAV did not change during 3 years. SV did not change significantly during 3 years after SPDP with CSAV and distal gastrectomy. After breast and colorectal surgery, and total gastrectomy, SV was decreased.

Conclusions: Postoperative SV changes differed according to the type of surgery. SV did not change significantly during 3 years after SPDP with CSAV.

Key words: splenic volume, spleen-preserving distal pancreatectomy, SPDP, digestive surgery, breast surgery

Introduction

The spleen is the largest peripheral lymphoid organ and plays an important role in immune function¹⁾. Overwhelming post-splenectomy infection (OPSI) occurs in 3.2% of all splenectomized patients²⁾. A method of spleen-preserving distal pancreatectomy (SPDP) with conservation of the splenic artery and vein (CSAV) that emphasized the importance of splenic vein dissection from the pancreatic body to the tail was first reported by Kimura et al³⁾. Another way of preserving blood flow to the spleen in SPDP is preservation of the

short gastric and left gastroepiploic vessels with excision of the splenic vessels, which is called Warshaw's procedure⁴⁾. Warshaw's procedure is technically easier but recently the importance of preserving the splenic vessels in SPDP has been widely recognized⁵⁾.

Recently, it has been reported that a small spleen (<1.1 cm³/kg) in patients who do not undergo splenectomy is a risk factor for severe infection⁶⁾. Therefore, preservation of splenic function is very important in pancreatic surgery. No standard method for assessment of splenic function has yet been established, although some authors have proposed that the appearance of Howell-Jolly bodies

in peripheral blood, or measurement of splenic volume (SV), could be useful in this respect⁷⁾.

To date, few reports have documented changes in SV after pancreatic surgery, including SPDP with CSAV, and other forms of surgery.

The aim of the present study was to determine the changes in SV after SPDP with CSAV, and after digestive tract and breast surgery, using an image-processing workstation based on computed tomography (CT) imaging data, and to reveal the possible factors that influence postoperative changes in SV.

Materials and Methods

The present study was based on 129 patients who underwent surgery at Yamagata University Hospital between June 2006 and May 2008. Seven patients underwent SPDP with CSAV, 29 underwent breast surgery, 54 underwent colorectal surgery, 29 underwent distal gastrectomy and 10 underwent total gastrectomy. Patients who had conditions possibly influencing SV, such as liver cirrhosis (n=3), infections at the time of CT scan (n=2), postoperative hematological disorder (n=1), portal vein tumor thrombosis due to postoperative recurrence (n=1), and postoperative oxaliplatin chemotherapy (n=2) within 3 years after surgery were excluded. Patients who underwent surgery involving other intra-abdominal organs concomitantly or within 3 years after surgery were also excluded (n=7). Accordingly, we investigated a final total of 113 patients who underwent SPDP with CSAV (n=7), breast surgery (n=24), colorectal surgery (n=45), distal gastrectomy (n=27) and total gastrectomy (n=10).

We verified the preoperative and follow-up (1, 2 and 3 years after surgery) postcontrast CT images of all patients. Data pertaining to pre- and postoperative clinical characteristics [age at surgery, sex, preoperative body weight, BMI, SV and SV/BMI ratio, pre- and postoperative laboratory data such as white blood cell count, platelet count, red blood cell count, albumin, and C-reactive protein (CRP) level, surgical procedure, pathology, stage, adjuvant chemotherapy and

hormonal therapy, and postoperative body weight change] were collected retrospectively from the hospital charts. The staging of each cancer was defined in accordance with the 7th edition of the American Joint Committee on Cancer (AJCC) staging criteria⁸⁾.

SPDP with CSAV was performed for low-grade malignant lesions in the body or tail of the pancreas without obvious stromal invasion or lymph node metastasis, as judged based on imaging modalities and operative findings. For the other operations, the surgical procedures were selected based on tumor location, size, depth of invasion and lymph node metastasis, and regional lymph node dissections were performed for malignancy.

In the colorectal surgery, distal gastrectomy and total gastrectomy groups, patients with lymph node metastasis received adjuvant chemotherapy with oral fluoropyrimidine drugs for 1–2 years, depending on the situation.

Breast surgery patients received adjuvant chemotherapy for about 6 months after surgery depending on the situation. Female patients with estrogen receptor positive cancer received hormonal therapy with tamoxifen for 5 years and/or LH-RH agonist for 2 years if premenopausal, or with

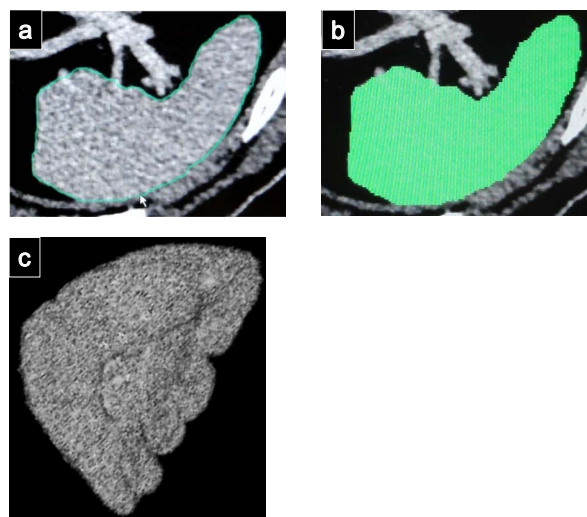


Fig 1. Splenic volume measurements

The spleen was outlined by manual contouring on a Zio workstation (a, b). 3-Dimensional computed tomography images of the spleen were constructed by volume rendering (c), and the value of SV was calculated automatically.

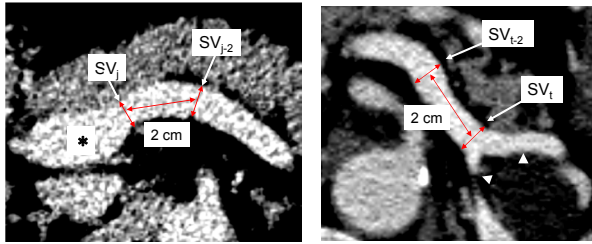


Fig 2. Splenic vein diameter measurements
 Splenic vein diameters were measured on axial images on the workstation at the following four points: junction of the splenic vein and portal vein (SV_j) ; 2 cm distal to the SV_j (SV_{j-2}) ; junction of the splenic vein branches at the splenic hilum (SV_t) ; 2 cm proximal to the SV_t (SV_{t-2}).

aromatase inhibitor for 5 years if postmenopausal. After adjuvant chemotherapy, patients with estrogen receptor-positive cancer sequentially received hormonal therapy. Postoperative radiotherapy (approximately 50 Gy to the whole breast and an additional 10 Gy for some patients) was performed for the remnant breast after breast-conserving surgery.

The study was approved by the hospital ethics committee.

Summary of surgical procedures

SPDP with CSAV was performed using Kimura's procedure³⁾. An important aspect of this method is dissection of the splenic vein from the pancreatic body to the tail after mobilization of the spleen and distal pancreas from the retroperitoneum³⁾. The left gastroepiploic and short gastric vessels were dissected in this cohort. Hand-assisted laparoscopic-SPDP with CSAV was performed using the method reported previously^{9),10)}. For distal gastrectomy, the left gastroepiploic vessels were dissected.

Splenic volume and splenic vein measurements

All CT imaging examinations were performed using multi-detector CT (MDCT) scanners (an Aquilion 64 [Toshiba Medical Systems, Tokyo, Japan] or a SOMATOM Sensation 32 [Siemens Medical Solutions, Forchheim, Germany]) with a 1-mm slice thickness in the equilibrium phase (120 seconds after initiation of IV contrast injection). SV values were calculated automatically on a Ziostation version 1.17 (Ziosoft Inc., Tokyo, Japan) using

manual contouring of the spleen.

Splenic vein diameters were measured on axial images on the workstation at the following four points (Fig. 2) : junction of the splenic vein and portal vein (SV_j) ; 2 cm distal to the SV_j (SV_{j-2}) ; junction of the splenic vein branches at the splenic hilum (SV_t) ; 2 cm proximal to the SV_t (SV_{t-2}).

Statistical analysis

Numerical data are expressed as mean \pm standard deviation. Statistical analysis for paired data was done using the Wilcoxon signed rank test. Categorical variables were analyzed using Fisher's exact test. Continuous variables were analyzed by Kruskal-Wallis test. Statistical analysis was performed using SAS version 9.4 (SAS Institute Inc., Cary, NC). Differences at $p < 0.05$ were considered statistically significant.

Results

Pre-and postoperative clinical characteristics of each surgical procedure

Table 1 summarizes the clinicopathological characteristics of the patients. The mean age of the patients overall at the time of surgery was 66.0 ± 11.8 years (range: 35-87). The preoperative mean SV for the patients overall was 117 ± 58 cm³ (range: 27-378 cm³).

Among the 113 patients, 107 (94.7%) had malignant disease. The pathological diagnoses in the patients who underwent SPDP with CSAV included intraductal papillary mucinous neoplasm (IPMN) with low- or intermediate-grade dysplasia (n=5), IPMN with an associated invasive carcinoma (n=1) and pancreatic neuroendocrine neoplasm (n=1).

One patient who underwent SPDP with CSAV received adjuvant chemotherapy with gemcitabine. Patients in the colorectal surgery group received oral fluoropyrimidine (n=17), and those in the distal gastrectomy (n=4) and total gastrectomy (n=2) groups received oral fluoropyrimidine. Patients in the breast surgery group received adjuvant hormonal therapy with LH-RH agonist (n=1), LH-RH agonist and tamoxifen (n=2), tamoxifen (n=6), and aromatase inhibitor (n=7). Recurrence within

Table 1. Clinicopathological characteristics of patients

| Variable | Total (n=113) | SPDP with CSAV (n=7) | Colorectal surgery (n=45) | Distal gastrectomy (n=27) | Total gastrectomy (n=10) | Breast surgery (n=24) | P value |
|---|-----------------------------|----------------------------|---------------------------------|---------------------------------|--------------------------------|--------------------------|---------|
| Age at surgery | 66.0 ± 11.8 | 67.1 ± 10.8 | 69.3 ± 9.6 | 68.1 ± 9.0 | 67.4 ± 15.0 | 57.3 ± 13.8 | 0.017 |
| Sex, male/ female | 65 (57.5 %)/ 48 (42.5 %) | 7 (100 %)/ 0 | 29 (64.4 %)/ 16 (35.6 %) | 21 (77.8 %)/ 6 (22.2 %) | 8 (80 %)/ 2 (20 %) | 0/ 24 (100 %) | <0.001 |
| Preoperative body weight (kg) | 58.9 ± 10.6 | 58.3 ± 6.7 | 59.2 ± 11.2 | 58.9 ± 10.6 | 63.4 ± 13.4 | 56.5 ± 9.3 | 0.545 |
| Preoperative BMI (kg/m ²) | 23.2 ± 3.4 | 21.7 ± 2.2 | 23.2 ± 3.4 | 22.9 ± 3.4 | 23.9 ± 3.7 | 23.8 ± 3.7 | 0.522 |
| Preoperative SV (cm ³) | 117 ± 58 | 131 ± 59 | 117 ± 61 | 103 ± 43 | 122 ± 63 | 128 ± 65 | 0.655 |
| Preoperative SV/BMI ratio | 5.0 ± 2.2 | 6.0 ± 2.4 | 5.0 ± 2.3 | 4.5 ± 1.7 | 5.2 ± 2.9 | 5.4 ± 2.4 | 0.514 |
| Preoperative laboratory data | | | | | | | |
| White blood cell count (/μl) | 5702 ± 1525 | 4634 ± 902 | 5764 ± 1275 | 5727 ± 1650 | 5476 ± 1338 | 5964 ± 1943 | 0.280 |
| Red blood cell count (×10 ³ /μl) | 424±54 | 424±49 | 424±56 | 428±48 | 438±62 | 417±56 | 0.913 |
| Platelet count (×10 ³ /μl) | 25.4 ± 7.3 | 19.6 ± 4.8 | 27.1 ± 7.9 | 25.2 ± 6.4 | 23.5 ± 7.5 | 25.2 ± 6.9 | 0.079 |
| Albumin (g/dl) | 4.1 ± 0.5 | 4.1 ± 0.2 | 3.9 ± 0.4 | 4.1 ± 0.5 | 4.3 ± 0.6 | 4.2 ± 0.6 | 0.207 |
| CRP (mg/dl) | 0.4 ± 0.8 | 0.3 ± 0.5 | 0.5 ± 1.0 | 0.4 ± 0.9 | 0.3 ± 0.4 | 0.3 ± 0.5 | 0.442 |
| Pathology and Stage | | | | | | | |
| Benign or stage 0/ I | 60 (53.1 %) | 7 (100 %) | 15 (33.3 %) | 21 (77.8 %) | 6 (60 %) | 11 (45.9 %) | <0.001 |
| Stage II/III | 53 (46.9 %) | 0 | 30 (66.7 %) | 6 (22.2 %) | 4 (40 %) | 13 (54.1 %) | |
| Adjuvant chemotherapy | 35 (30.9%) | 1 (14.3 %) | 17 (37.8 %) | 4 (14.8 %) | 2 (20 %) | 11 (45.9 %) | 0.085 |
| Adjuvant hormonal therapy | 16 (14.2 %) | 0 | 0 | 0 | 0 | 16 (66.7 %) | <0.001 |
| Radiation therapy | 9 (8 %) | 0 | 0 | 0 | 0 | 9 (37.5 %) | <0.001 |

Values are mean ± standard deviation or n (%)

SV splenic volume, SPDP spleen-preserving distal pancreatectomy, CSAV conservation of the splenic artery and vein

* (Preoperative value - mean BW from 1 to 3 years after surgery)/preoperative value×100 (%)

Table 2. Splenic vein diameter changes after spleen-preserving distal pancreatectomy with conservation of the splenic artery and vein

| | Preoperative value | 1 year after surgery | p value* | 2 years after surgery | p value* | 3 years after surgery | p value* |
|------------------------|-----------------------|-------------------------|----------|--------------------------|----------|--------------------------|----------|
| SV _j (mm) | 6.9 ± 1.7 | 7.8 ± 1.8 | 0.578 | 7.6 ± 1.6 | 0.469 | 7.8 ± 1.6 | 0.469 |
| SV _{j-2} (mm) | 8.2 ± 2.0 | 8.5 ± 3.0 | 0.563 | 8.8 ± 2.6 | 0.375 | 8.4 ± 2.1 | 0.344 |
| SV _{i-2} (mm) | 7.0 ± 1.7 | 7.3 ± 1.9 | 0.469 | 7.5 ± 1.4 | 0.219 | 7.3 ± 1.5 | 0.219 |
| SV _i (mm) | 7.0 ± 1.0 | 7.4 ± 1.1 | 0.563 | 7.6 ± 0.8 | 0.156 | 7.4 ± 0.8 | 0.203 |

Values are mean ± standard deviation

*Comparison between the preoperative splenic vein diameter and splenic vein diameter obtained after surgery by the use of Wilcoxon signed-rank test

3 years was observed in 1 of the 10 patients in the total gastrectomy group.

Postoperative changes in splenic vein diameter of SPDP with CSAV

Postoperative changes in splenic vein diameter after SPDP with CSAV are shown in Table 2. Splenic vein diameter after SPDP with CSAV was not change significantly during 3 years after surgery.

Postoperative changes in splenic volume

Postoperative changes in SV after each type of surgery are shown in Table 3 and Figure 3. SV after SPDP with CSAV and distal gastrectomy did not change significantly until 3 years after

surgery. SV after breast surgery was decreased significantly from 1 year after surgery in comparison with the preoperative SV (128 ± 65 vs. 116 ± 56 cm³, p<0.001). SV after total gastrectomy was decreased significantly from 2 years after surgery in comparison with the preoperative SV (122 ± 63 vs. 102 ± 38 cm³, p=0.020). In both the breast surgery and total gastrectomy groups, SV reached a plateau from 2 years after surgery. In the colorectal surgery group, SV was decreased significantly at 2 years after surgery in comparison with the preoperative SV (117 ± 61 vs. 111 ± 58 cm³, p=0.006). In the patients overall, SV was decreased significantly from 1 year after surgery (117 ± 58 vs. 113 ± 52 cm³, p=0.006), and reached a plateau from 2 years after surgery.

Postoperative changes in splenic volume

Table 3. Splenic volume change after surgery

| | preoperative | 1 year after surgery | 2 years after surgery | 3 years after surgery |
|--|---------------------|--------------------------|----------------------------|----------------------------|
| SPDP with CSAV (cm ³) (n=7) (%) ^a | 131 ± 59 (100 %) | 135 ± 55 (104 ± 4 %) | 133 ± 54 (102 ± 6 %) | 131 ± 49 (101 ± 6 %) |
| Colorectal surgery (cm ³) (n=45) (%) ^a | 117 ± 61 (100 %) | 114 ± 58 (98 ± 11 %) | 111 ± 58* (95 ± 13 %) | 112 ± 56 (98 ± 17 %) |
| Distal gastrectomy (cm ³) (n=27) (%) ^a | 103 ± 42 (100 %) | 105 ± 42 (103 ± 17 %) | 101 ± 38 (100 ± 20 %) | 100 ± 36 (99 ± 19 %) |
| Total gastrectomy (cm ³) (n=10) (%) ^a | 122 ± 63 (100 %) | 108 ± 44 (93 ± 13 %) | 102 ± 38* (89 ± 14 %) | 103 ± 42* (89 ± 17 %) |
| Breast surgery (cm ³) (n=24) (%) ^a | 128 ± 65 (100 %) | 116 ± 56* (92 ± 13 %) | 112 ± 56* (90 ± 15 %) | 112 ± 57* (90 ± 15 %) |
| Total (cm ³) (n=113) (%) ^a | 117 ± 58 (100 %) | 113 ± 52* (98 ± 13 %) | 109 ± 51* (94.0 ± 15 %) | 110 ± 51* (95.9 ± 17 %) |

Values are mean ± standard deviation

SPDP spleen-preserving distal pancreatectomy, CSAV conservation of the splenic artery and vein,

^a(splenic volume at each point/preoperative splenic volume)×100 (%)

*P<0.05; Comparison between the preoperative splenic volume and splenic volume obtained after surgery by the use of Wilcoxon signed-rank test

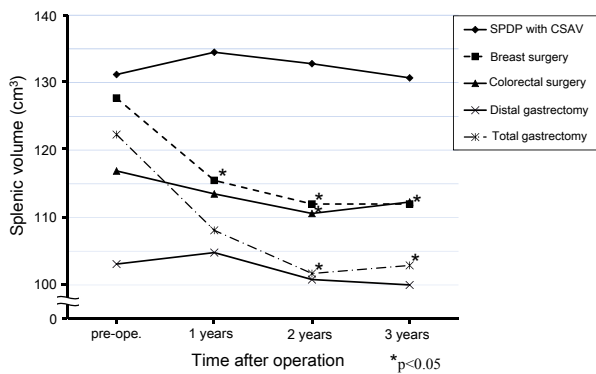


Fig 3. Postoperative changes in splenic volume after each type of surgery.

SPDP; spleen-preserving distal pancreatectomy, CSAV; conservation of the splenic artery and vein.

Discussion

Studies from Japanese institutions have reported the mean SV ranging from 112–127 cm³ ^{11),12)}. The preoperative mean SV in the present study population was 116 cm³, and thus within the reported range. The mean SV in studies from western countries is larger, ranging from 209–219 cm³ ^{13)–15)}. Several recent reports have documented changes in splenic volume (SV) in various conditions ^{11),16)–18)}. SV is affected by various factors; for example, in adults it is correlated with height¹³⁾, weight^{13),12)}, body mass index (BMI) and body surface area¹²⁾, and inversely related to age^{12),19)}. It is reported that SV is increased in the presence of higher portal venous

pressure²⁰⁾, infection²¹⁾, inflammatory, hematologic and metabolic disorders²²⁾, cytotoxic chemotherapy including oxaliplatin¹⁶⁾ and certain drugs²³⁾, whereas it is reduced by drugs²³⁾, decreased arterial flow to the spleen²⁴⁾, and radiation therapy¹⁸⁾.

In this study, SV did not change significantly after SPDP with CSAV. This may be because both blood flow from the splenic artery and venous return through the splenic vein may have been sufficiently preserved. Splenic volume reduction may be a risk factor for severe infection. Therefore, Kimura's procedure is excellent in terms of preservation of splenic function. It is reported that 32.4% (12/37) of patients who underwent Warshaw's procedure, which does not preserve the splenic vessels, had splenic enlargement of more than 20% compared to the preoperative value, at a follow-up CT 6 months after surgery²⁵⁾. In the present study, splenic enlargement exceeding 20% was not observed after SPDP with CSAV. However, in patients undergoing laparoscopic distal pancreatectomy, splenic enlargement of more than 20% compared to the preoperative SV was observed in 59% (10/17) of patients treated using Warshaw's method and 43% (3/7) of patients in whom the splenic vessels were preserved¹⁷⁾. Splenic venous occlusion after SPDP with CSAV has been described in some reports²⁶⁾, but in the present study no obvious splenic vein occlusion or stenosis was observed. Splenic vein patency may influence the postoperative SV. Careful

ligation and cutting of the splenic vein branches are required to avoid injury to the venous wall.

In relation to post-gastrectomy changes in SV, Oida et al.²⁷⁾ in an ultrasonographic study reported that the diameter of the spleen in terms of maximum bipolar diameter increased after DG and TG. In our present study, however, SV after DG did not change significantly until 3 years after surgery, and SV after TG were significantly decreased from 2 years after surgery in comparison with the preoperative value. Postoperative splenic enlargement of more than 20% relative to the preoperative volume was seen in 11% (3/27) of patients after DG, and in 10% (1/10) of patients after TG at any postoperative point. These results suggest that splenic enlargement after gastrectomy may not be a common phenomenon. In this study, SV after distal gastrectomy did not change significantly during 3 years after surgery, but SV after total gastrectomy was significantly decreased starting at 2 years after surgery compared with the preoperative value. Post-gastrectomy body weight loss is a common phenomenon²⁸⁾. Body weight change is one of the factors that influence SV^{12), 13)}. Therefore, the body weight loss may partially contribute to SV reduction after surgery in total gastrectomy. In distal gastrectomy, most of the venous outflow from the remnant stomach enters the splenic vein through the short gastric vein, and this increased flow in the splenic vein may cause relative congestion, which may prevent postoperative SV reduction.

In patients who underwent colorectal and breast surgery, which may not influence hemodynamics around the spleen, the mean SV after surgery was significantly decreased compared with the preoperative value. Aging is a factor that influences SV because the spleen becomes smaller with age^{12), 19)}. However, because there were no obvious decreases in SV between 2 and 3 years after surgery, the effects of aging on SV changes may have been limited. In patients with malignant tumors, the spleen is reported to be immunologically reactive against the tumor²⁹⁾, thus leading to an increase in SV^{29)–31)}.

In this series, adjuvant hormonal therapy with

tamoxifen and/or LH-RH agonist, or aromatase inhibitor, was performed for estrogen receptor-positive breast cancer. Tamoxifen is a selective estrogen receptor modulator. On the relationship between estrogen and SV, an animal study has demonstrated that estrogen caused an increase in the weight of the spleen³²⁾. In humans, estrogen receptor is present in many organs, including the spleen³³⁾, and modulation of estrogen receptor by tamoxifen or a decrease in the level of serum estrogen by treatment with LH-RH agonist or aromatase inhibitor may cause SV reduction.

In conclusion, SV did not change significantly after SPDP with CSAV. SPDP with CSAV may be a feasible method for appropriate cases. In this study, the pattern of postoperative change in the SV differs for each type of surgery and most patients showed a decrease in SV after surgery. Determining the specific mechanism of these changes in SV and its significance require further investigation.

Conflicts of interest Koji Tezuka and co-authors have no conflicts of interest.

Abbreviations: AJCC; American Joint Committee on Cancer, BMI; body mass index, CRP; C-reactive protein, CSAV; conservation of the splenic artery and vein, CT; computed tomography, IPMN; intraductal papillary mucinous neoplasm, OPSI; overwhelming post-splenectomy infection, SPDP; spleen-preserving distal pancreatectomy, SV; splenic volume.

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