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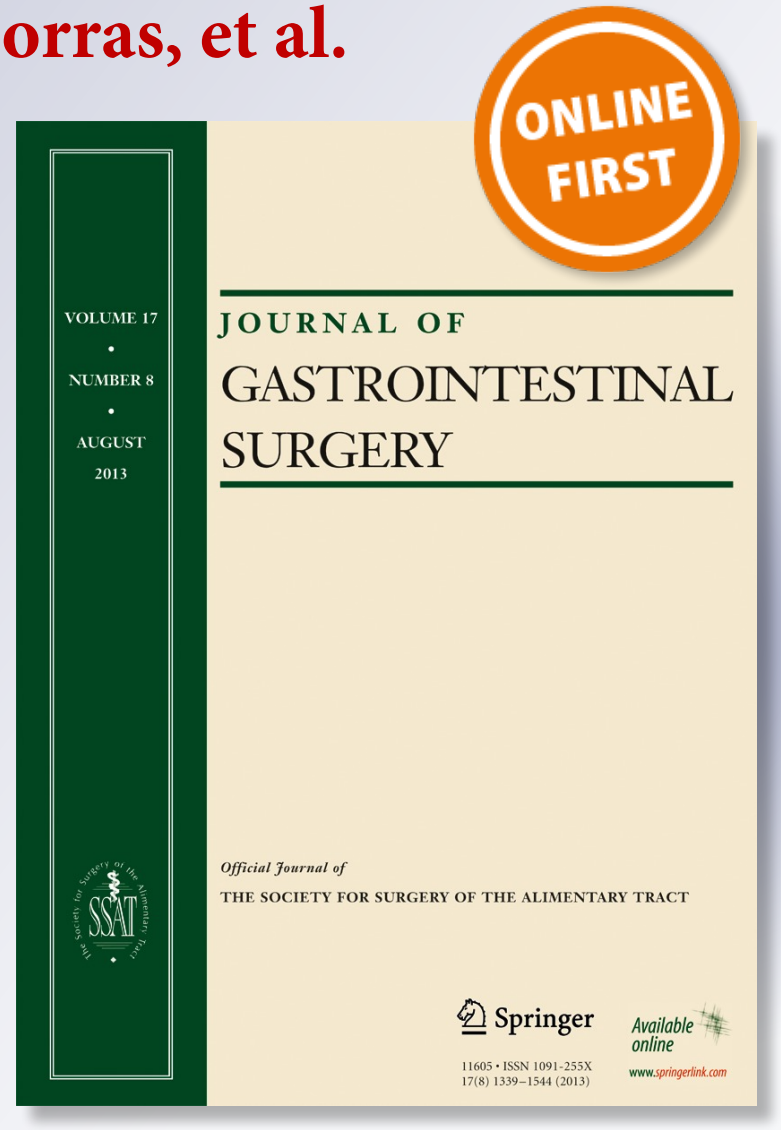

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ORIGINAL ARTICLE

Changes in Gastrosplenic Circulation and Splenic Function after Distal Pancreatectomy with Spleen Preservation and Splenic Vessel Excision

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Abstract
Introduction Distal pancreatectomy with spleen preservation and splenic vessel excision is a commonly used technique. However, it produces significant gastrosplenic circulation and splenic function changes.
Purpose The aim of this work was to determine the immediate consequences on gastrosplenic circulation, late consequences on splenic function, and development of varicose veins.
Methods Thirty-five patients with pancreatic tumors and anatomical feasibility were included. Preoperative splenic circulation was evaluated by dynamic contrast-enhanced computed tomography (CT) scans. Early splenic perfusion was assessed by CT 7 days after surgery and late changes in gastrosplenic circulation 6 months after surgery. Varicose veins were evaluated by CT and endoscopy 6 months after surgery. Pitted cells and Howell–Jolly bodies were used as markers of splenic function. Postoperatory findings included changes in splenic perfusion 7 days and 6 months after surgery, development of varicose veins on CT scans and endoscopy, and detection of markers of splenic hypofunction on blood smears.
Results and Conclusion Seven days after surgery, 63 % of patients had some degree of splenic hypoperfusion, and 6 months after surgery, 83 % of patients had normal perfusion. CT scans showed varices in 26 patients, and endoscopy revealed varicose veins in 11. Two patients experienced bleeding; markers of splenic hypofunction were found in 59 % of cases.

Keywords Pancreatectomy · Splenic preservation · Splenic vessel excision · Gastrosplenic circulation · Splenic hypofunction markers

Introduction

Traditionally, distal pancreatectomy included splenectomy to supposedly optimize oncologic outcomes. Spleen-preserving distal pancreatectomy, using a meticulous dissection to preserve the splenic vessels, was described in 1943 by Mallet-Guy and Vachon;[1] however, this technique is not always feasible, and it is contraindicated in malignant diseases. Distal pancreatectomy with spleen preservation and splenic vessels excision (DPSPSVE)[2] is another option for distal pancreatectomy with splenic preservation and the best suited for a laparoscopic approach. Nevertheless, this technique creates major changes in gastrosplenic circulation, which may lead to the development of gastric varices.[3–5]

This study is aimed at determining the immediate consequences of DPSPSVE on gastrosplenic circulation and its late consequences on splenic function as well as the late appearance of perigastric and submucose varicose veins.

Material and Methods

Study Design

This single-center prospective and observational study was performed at the Cosme Argerich Hospital, in Buenos Aires,

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Argentina, a tertiary care, university-affiliated public hospital, specialized in hepato-pancreato-biliary surgery. All procedures, including the patient's or responsible relative's written informed consent to be included in the study, were conducted in accordance with the recommendations of the Cosme Argerich Hospital's Ethics Committee. The study protocol was approved on May 19, 2004. There are no possible conflicts of interest declared.

Patients

All patients who had undergone DPSPSVE between May 1, 2004 and January 1, 2010 were included. Surgery was performed when the ligation of the splenic artery and vein near the splenic hilum preserving all short gastric vessels and the left gastroepiploic artery and vein was feasible. If not, left pancreatectomy with splenectomy was performed. No distal pancreatectomy with spleen preservation with splenic vessels preservation was performed. Laparoscopic or open approaches depended on tumor location and size.

Radiologic Preoperative Evaluation

Splenic circulation was investigated preoperatively with a dynamic contrast-enhanced computed tomography (CT) scan of the abdomen, focusing on the celiac axis, the superior mesenteric vessels, and the splenic parenchyma. All CT scans were performed on a Somaton helical scanner (Siemens). One hundred and fifty milliliters of nonionic contrast media was injected at a rate of 5 ml/s, using a power injector. Scans were obtained 20 and 80 s after the injection. Images were reconstructed every 3 mm for the arterial phase and every 5 mm for the portal venous phase. Splenic parenchyma perfusion, and arterial and venous gastric circulation were examined.

Postoperative Evaluation

Splenic Perfusion

To assess early splenic perfusion, a CT scan was performed 7 days after surgery with the same technique. Perfusion defects were defined as circumscribed hypodensities on the CT scan venous phase. Defects were classified by size in three grades: grade 0—normal perfusion; grade 1—perfusion defect less than 50 % of the total splenic volume (Fig. 1); grade 2—perfusion defect more than 50 % of the total splenic volume (Fig. 2). Spleen dimensions were also measured.

Late changes in gastrosplenic circulation were assessed 6 months later by a CT scan performed with the same technique. Perfusion defects were similarly graded as per the early scan.

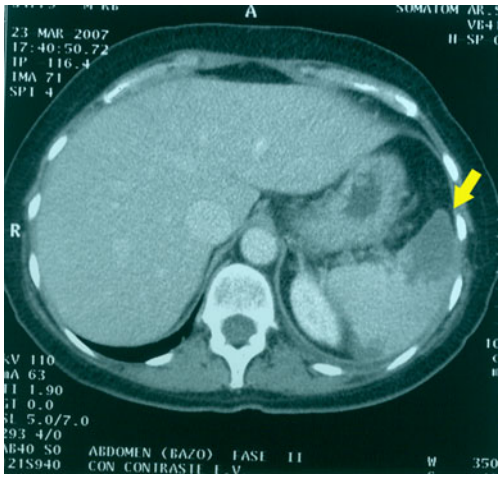

Fig. 1 Grade 1 perfusion defect of the spleen (*arrow*)

Gastric Varices

The presence of gastric varicose veins was assessed with CT scan and upper endoscopy 6 months after surgery. On CT scans, gastric varicose veins were diagnosed when tortuous vascular structures larger than 5 mm were identified.[6] Varices along the outside border of the gastric wall were defined as perigastric (Fig. 3a), and those within the wall were defined as submucosal (Fig. 3b). Varices were classified as short gastric, coronary, and gastroepiploic vein varices (Fig. 4).

Splenic Function

It has been shown that splenic function can be assessed by detecting Howell–Jolly bodies and pitted cells.[7] Howell–Jolly bodies are DNA remains of the erythrocyte stem cell nucleus. Usually, after leaving the bone marrow, the erythrocyte stem cell expels its nucleus. In some erythrocytes, nevertheless, a portion of the DNA remains. Usually, the spleen eliminates these erythrocytes from circulation. However, when the spleen is absent or has an impaired function, these erythrocytes, together with Howell–Jolly bodies, are kept in the blood. Howell–Jolly bodies in peripheral blood smears were detected with an optical microscope before surgery and 6 months after surgery.

Pitted cell detection, however, is a much more effective method of diagnosing splenic dysfunction. In patients with asplenia or hyposplenism, pits develop on the erythrocyte membrane and can be seen by immunofluorescence microscopy.[8] Detection of pits reflects the presence of low absorbance vacuoles lying beneath the red cell plasma membrane which, in the absence of a functioning spleen, are responsible for disposing of solid material from the erythrocyte.[9] The degree of splenic function is related to the number of pitted cells. The presence of 0 to 4 % pitted cells indicates normal splenic function; more

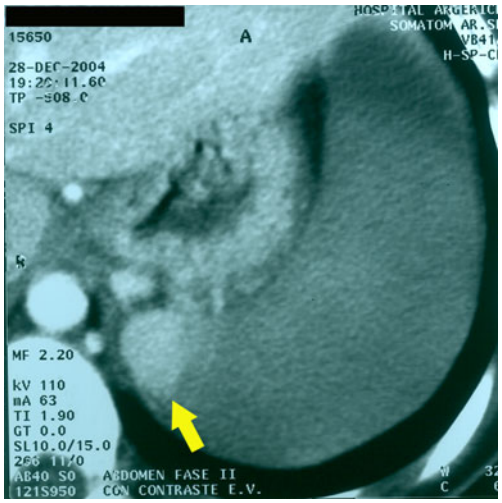

Fig. 2 Grade 2 perfusion defect. CT scan shows 95 % of hypoperfusion and a small area with normal perfusion (*arrow*)

than 4 % and less than 15 % means splenic hypofunction (Fig. 5) and more than 15 % denotes asplenia.[7] Development of pitted cells was investigated 6 months after surgery.

Complications

Pancreatic fistula was defined according to the international study group definition (ISGPF).[10] Pancreatic fistula definition is a drain output of any measurable volume of fluid on or after postoperative day 3 with amylase content greater than three times the serum amylase activity. Three different grades of pancreatic fistula (grades A, B, C) are defined according to the clinical impact on the patient's hospital course.

Results

During the study period, 83 distal pancreatectomies were performed; 36 underwent a DPSPSVE and the remaining 47 received left pancreatectomy with splenectomy. Open surgery was performed on 28 of DPSPSVE patients and laparoscopic surgery on eight.

In the 36 patients, 34 were women and two men; mean age was 43.35 years (range 19–74 years). The DPSPSVE average operative time was 134 min for open surgery and 190 min for laparoscopic surgery. Histopathological findings are listed in Table 1.

One patient was lost to follow-up and was excluded from the study. The remaining 35 patients were followed from 18 months to 6 years (average 3.7 years).

There was no operative mortality. Morbidity was 42.8 % and included pancreatic fistula (25.7 %), wound infection (8.6 %), pneumonia (5.7 %), and atelectasis (2.8 %). Nine patients had pancreatic fistula (25.7 %). Six of these patients (17.1 %) presented a grade A or B fistula and the remaining three (8.6 %) a grade C fistula which required, as sole treatment, a percutaneous drainage.

Radiologic Preoperative Evaluation

In the preoperative CT scan, all patients showed normal splenic perfusion. No splenic vein thrombosis or segmental portal hypertension was observed.

Splenic Perfusion

On the seventh postoperative day, 16 patients (46 %) showed signs of grade 1 perfusion defects; six (17 %) had a grade 2 perfusion defect and only 13 (37 %) exhibited normal spleen perfusion. Six months after surgery, 13 out of the 16 patients with grade 1 hypoperfusion, and three of the six patients with grade 2 hypoperfusion recovered normal splenic perfusion. In the remaining three grade 1 patients, perfusion defects remained unchanged. Meanwhile, in the remaining three grade 2 patients, perfusion defects changed to grade 1.

Presence of Varices

Varices were found on late CT scans in 26 out of 35 DPSPSVE patients. All of them had perigastric varices, and only 12 had submucosal varices. Varicose veins were located on the short vessels in 21 patients, on the coronary vein in 14 patients, and on the left gastroepiploic vein in 11 patients.

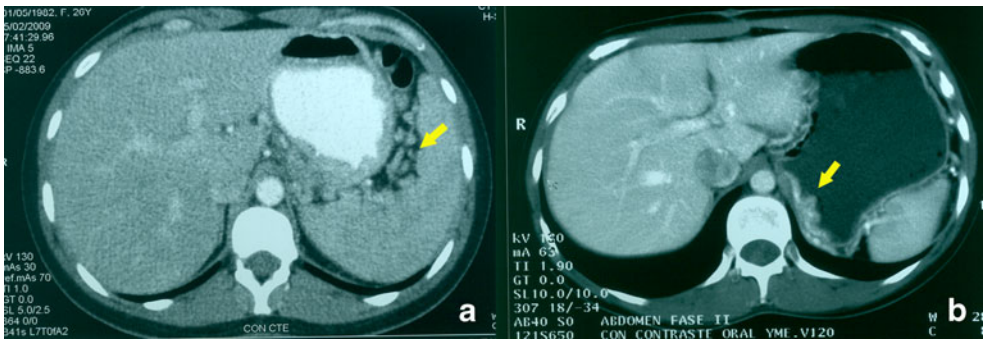

Fig. 3 **a** Perigastric varices (*arrow*); **b** submucosal varices (*arrow*)

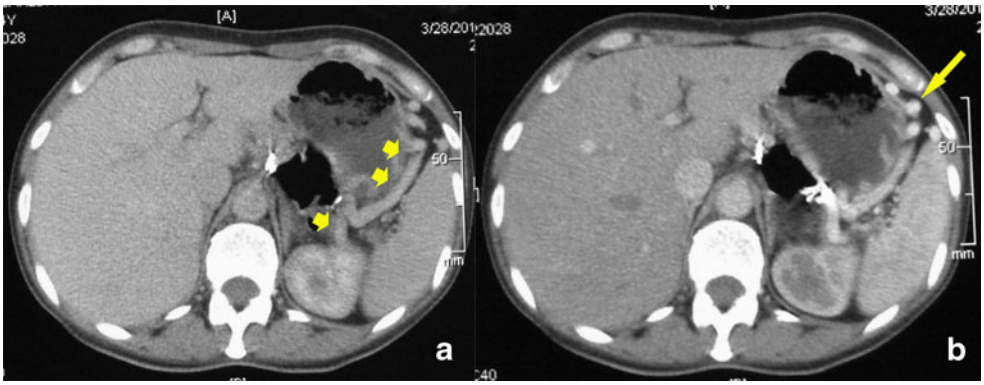

Fig. 4 **a** Gastroepiploic varices (*head arrows*); **b** short gastric varices (*arrow*)

Upper endoscopy studies showed gastric varices in 11 out of the 28 patients who consented to have the study performed. In seven patients who rejected endoscopy, a CT scan revealed perigastric varices. Out of the 11 patients with endoscopic varices, varices were identified by means of CT scans in eight of them; five had perigastric and submucosal varices and three had perigastric varices only.

Late gastric variceal bleeding occurred in two patients 3 and 4 years after surgery; both were treated endoscopically. One had a recurrent severe episode, and after effective endoscopic treatment, elective splenectomy was performed. Upper endoscopy performed 6 months after splenectomy showed complete disappearance of varices. The other patient experienced no additional events and has remained under control.

Splenic Function

Pitted cells and Howell–Jolly bodies were assessed in 27 out of 35 patients. Sixteen (59.2 %) showed splenic dysfunction, 13 (48.1 %) had hyposplenia, and three (11.1 %) had asplenia. Peripheral blood samples showed Howell–Jolly bodies in 13 patients (48 %) who also had pitted cells on blood smears. No Howell–Jolly bodies in peripheral blood samples were noted before surgery.

None of the patients developed late postsplenectomy complications during follow-up.

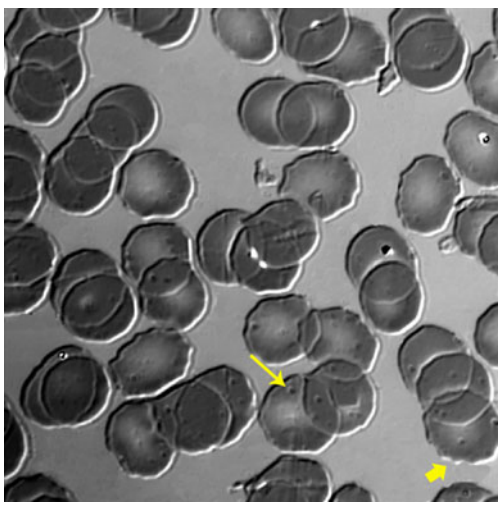

Fig. 5 Pitted cells (*arrows*) in a patient with hyposplenism

Discussion

This study showed that DPSPSVE produces gastrosplenic circulation changes, including early splenic hypoperfusion (although reversible in most patients in the long-term follow-up) and late development of gastric varices. It also revealed the appearance of indirect markers of splenic hypofunction on blood smears.

This is the first study designed to prospectively evaluate early changes of splenic perfusion in patients undergoing DPSPSVE. Seven days after surgery, 62.8 % of patients developed different grades of splenic hypoperfusion; however, symptoms were not observed, and normal splenic perfusion was re-established 6 months later in most cases. In contrast, other studies[11,12] have reported a 16.6 % incidence of signs secondary to splenic infarct or abscess and 1.9–11 % of patients required splenectomy.[13,14]

In previous studies,[4,5] the incidence of varices after DPSPSVE varied from 25 to 70 %. In the most recent study, Ferrone et al.[16] reviewed 158 patients, but only 125 were available for follow-up. Out of these 125 patients, CT scans

Table 1 Histopathology findings in 36 patients

Serous cystic neoplasia	14
Nonfunctioning neuroendocrine tumor	6
Solid pseudopapillary tumor	4
Mucinous cystic neoplasia	4
Insulinoma	2
Intraductal papillary mucinous neoplasm	2
Mucinous cystoadenocarcinoma	1
Pancreatic ductal adenocarcinoma	1
Hydatid cyst	1
Desmoid tumor	1

were obtained during surveillance in 65 (60 %) patients, and 16 (25 %) had perigastric varices. No submucosal varices were identified, and endoscopic studies were not performed. In our study, out of 11 patients with varices identified by endoscopy, only eight showed varices in the CT scan; out of them, five had submucosal and perigastric varices and the remaining three had only perigastric varices. It is apparent that the absence of endoscopic studies and retrospective assessment may lead to underestimate the incidence of varices.

The issue of splenic function after DPSPSVE had not been addressed before this study. Since preservation of splenic function is the main purpose of DPSPSVE, this is a key issue. Our study shows that 48 % of patients had pitted cells and Howell–Jolly bodies on blood smears 6 months after surgery, a finding that implies hyposplenia or asplenia. It is worth mentioning that none of the patients revealed Howell–Jolly bodies before surgery. Although these tests are useful to characterize spleen immunocompetence,[7] clinical signs of splenic dysfunction were not observed. However, since the frequency of late postsplenectomy complications in the adult population is low,[3,15] an accurate assessment would require a greater number of patients and a longer follow-up. An evaluation after several years may shed more light on this subject.

One drawback of this study is the limited follow-up. As the gastric plexus is an undesirable collateral pathway for splenic blood to the portal system, the long-term prognosis of gastric varices is still unknown. The spleen-preserving distal pancreatectomy with splenic vessel excision creates a new type of segmental portal hypertension since several of the naturally communicating venous channels disappear. The high venous pressure in gastric circulation may decrease when new effective collateral shunts develop, but this event is still uncertain.

The clinical significance of submucosal varices lies in the risk of bleeding.[4] Two (5.6 %) of our 35 patients had varicose venous bleeding, and one required splenectomy after a recurrent and severe episode. Miura et al.[5] reported one case (10 %) of variceal bleeding after a spleen-preserving pancreatectomy with splenic vessel ligation. That patient underwent a middle pancreatectomy with splenic vessel ligation, and although this procedure is not a DPSPSVE, the pathophysiology of the bleeding is the same. In this subset of patients with submucosal varices, we currently recommend an endoscopic study at 9-month intervals to control the size of the varices.

Conclusion

DPSPSVE produces gastrosplenic circulation changes. Upper endoscopy should be performed in all patients 6 months after surgery. Patients with an endoscopic diagnosis of varices are at risk of variceal bleeding, and a close follow-up is recommended. The significance of splenic hypofunction markers is still uncertain. A greater number of patients and a longer follow-up are needed to assess the usefulness of this technique.

Acknowledgments We want to acknowledge Dr Thomas J Howard for all his support.

Conflicts of Interest This is an observational study. There are no possible conflicts of interest declared.

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