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ORIGINAL ARTICLE

Distal pancreatectomy for pancreatic neoplasia: is splenectomy really necessary? A bicentric retrospective analysis of surgical specimens

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Abstract

Background: While distal pancreatectomy with splenectomy (DPS) is the reference treatment for pancreatic body and tail neoplasia, oncological benefits of splenectomy have never been demonstrated. Involvement of spleen, splenic hilum and lymph nodes (LN) was therefore assessed on DPS specimens.

Methods: All DPS pancreatic neoplasia specimens obtained in 2 Brussels University Hospitals over 15 years (2004–2018) were reviewed retrospectively, using both preoperative radiological imaging and postoperative pathological analyses of splenic parenchyma, hilar tissue and LN.

Results: The total of 130 DPS specimens included 85 adenocarcinomas, 37 neuroendocrine neoplasms and 8 other carcinomas. Tumours involved the pancreatic body without tail invasion for 59 specimens (B, Body group), and the pancreatic tail with/without body for 71 (T, Tail group). At pathology, direct splenic and/or hilar involvement was observed in 13 T specimens (13/71, 18.3%), but in none belonging to the Body group. The observed numbers of splenic hilar LN (only reported in 49/130 patients) were low, only one T adenocarcinoma had positive splenic LN in addition to direct splenic involvement.

Conclusion: Splenectomy remains justified during pancreatectomy for neoplasia involving the pancreatic tail, but in case of pancreatic body tumours, its benefits should be questioned in the light of absent splenic LN/parenchymal involvement.

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Introduction

Distal pancreatectomy (DP) with splenectomy (DPS) is considered as the reference treatment for pancreatic body and/or tail malignancies. The arguments used to associate spleen resection to simple DP are a better chance of negative surgical margin, an enlarged lymphadenectomy, and an easier and faster technique in case of open approach.[1] Traditionally, the spleen was also simultaneously resected due to technical difficulties emerging from the close anatomical relationships between the pancreas and the splenic vessels posteriorly, and the splenic hilum distally. However, thanks to improvements in surgical techniques including laparoscopic surgery, the feasibility and safety of spleen preservation during DP is currently widely recognised and demonstrated, even when it is necessary to remove the splenic vessels.[2,3] Advantages of spleen preservation during DP are fewer infectious complications, less intraoperative blood loss, a lower overall morbidity rate, and fewer subphrenic abscesses compared to DPS.[4]

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However, the oncological benefits of splenectomy during DP for left-sided pancreatic cancer have yet to be demonstrated, to our knowledge, despite it currently being performed globally. For optimal oncological staging, the consensus is that a lymphadenectomy must be performed, requiring therefore the splenic vessels resection as well as an enlarged posterior surgical margin. In a recent French study reassessing DPS cancer specimens, only 60% were observed to contain lymph nodes (LN) in the splenic hilum, and none was tumour-positive.[5] Direct involvement of the splenic parenchyma or hilum was only observed in 8% of their DPS specimens, which were all obtained from tumours located in the pancreatic tail.

Given these interesting results, we sought to confront these observations by studying the large cohort of patients treated by DPS for pancreatic cancer in 2 Brussels academic centres. The study aimed to assess any involvement of the spleen (parenchyma, hilar LN) on pathological DPS specimens obtained from patients treated for pancreatic malignancy over the past 15 years, and to compare body and tail pancreatic tumours.

Material and methods

All patients undergoing DP associated with splenectomy over the last 15 years, in 2 tertiary centres (Cliniques Universitaires Saint-Luc and Hôpital Universitaire Erasme, Brussels, Belgium) were retrospectively reviewed. The study was approved by the ethical committee of both institutions and was performed in accordance with the Declaration of Helsinki. The analysis was focused on patients operated for pancreatic malignancy, including exocrine carcinoma and neuroendocrine neoplasm. Surgical procedures were performed according to the multidisciplinary oncological board decision. Patients' data were collected in a retrospective database including demographics, preoperative assessment, intraoperative data and histopathological results.

Tumour diagnosis and work-up were routinely assessed by thoraco-abdominal contrast-enhanced computed tomodensitometry (CT) and/or abdominal magnetic resonance imaging (MRI), frequently completed by endoscopic ultrasonography (EUS) with fine needle aspiration/biopsy (FNA/B), cytological examination and isotopic scintigraphy. The lesion location was specified as being within the body and/or tail of the pancreas, along with its anatomical relationship with the spleen. The boundary between the pancreatic body and tail was defined as being where the splenic artery runs from the posterior to the anterior part of the pancreas.[6] Tumours involving only the pancreatic body were classified as belonging to the "Body Group" (B), without any involvement of the pancreatic tail, while tumours invading the tail (with or without involving the pancreatic body) constituted the "Tail Group" (T).

DPS included an *en bloc* resection of the spleen, the left part of the pancreas and the regional lymph nodes including splenic hilum (station 10), splenic artery (station 11) and inferior border of the pancreatic body (station 18), according to the Japanese Pancreas Society nomenclature.[7] An additional LN picking was performed at the coeliac trunk or common hepatic artery in case of suspect adenopathy (enlarged LN, stations 8 and 9).

Histopathological evaluation included pancreas length, lesion size, tumour type and differentiation, peripancreatic adipose tissue invasion, splenic hilum and parenchyma invasion, perineural/microvascular/lymphatic invasion, LN involvement and surgical margin status. Mapping of LN was performed by the pathologist: LN from stations 11 and 18 were considered as peripancreatic LN, and station 10 LN were defined as splenic hilum LN when they were specifically found on the specimen. Tumours were graded according to the 8th edition of the tumour-node-metastasis (TNM) by the American Joint Committee on Cancer (AJCC)/Union for International Cancer Control (UICC).[8] Resection was considered as R0 when the surgical margin measured $\geq$1 mm (on pancreatic transection, vascular and posterior margins). This was a protocol based analysis and pathological reports were performed by different pathologists over time but with the same pathology training in each hospital.

Statistical analysis

Quantitative data were expressed as median values ± interquartile range (SD/IQR) or upper and lower quartiles (Q1 – Q3), and qualitative data as frequency and percentages. Student's t test was used for continuous variables and chi-square for categorical variables. Two-sided $p \leq 0.05$ was considered statistically significant.

Results

Between January 2004 and February 2019, a total of 130 patients underwent a surgical resection (DPS) for pancreatic neoplasia, including 85 adenocarcinomas, 37 neuroendocrine neoplasms and 8 other rare exocrine carcinomas. Demographic and clinical characteristics of the 63 men and 67 women, with a median age of 64 ± 18 years, can be found in Table 1. Preoperative work-up included abdominal CT or MRI in 90.8% and 84.6% of patients respectively, and EUS-FNA/B in 112 patients (86.2%); cytological examination was negative for 12 patients (10.7%). Tumour was located in the pancreatic body without involving the tail in 59 patients (45.4%) and invaded the pancreatic tail in 71 patients, with or without involving the pancreatic body (54.6%). Resection of adjacent organ(s) was required in 18 patients (13.8%) because of multiple tumour involvement, including colon (n = 7; amongst whom, other organs were involved in 5), stomach (n = 12; other organs involved in 4), left kidney (n = 4; other organs involved in 3), liver (n = 1), and the fourth duodenum (n = 1).

Pathological analysis

At pathological examination, the median tumour size was 31.5 ± 22.5 mm, with a median length of the resected pancreas of 90.0 ± 35.0 mm. The pathological tumour characteristics are

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Table 1 Patient characteristics

	Total (n = 130)	Body Group (n = 59)	Tail Group (n = 71)	p value
Centre, n (%)				
- Saint-Luc	69 (53)	31 (53)	38 (54)	0.911
- Erasme	61 (47)	28 (47)	33 (46)	
Sex ratio (M/F)	0.94 (63/67)	0.90 (28/31)	0.97 (35/36)	0.835
Age, y (median ± IQR)	64 ± 18	68 ± 18	61 ± 18	0.006
BMI, kg/m^2 (median ± IQR)	25.4 ± 4.7	25.2 ± 4.3	25.5 ± 6.0	0.630
Comorbidities, n (%)				
- Coronary disease	14 (11)	10 (17)	4 (6)	0.038
- COPD	3 (2)	1 (2)	2 (3)	0.671
- Diabetes	29 (22)	13 (22)	16 (23)	0.946
- Smoking	29 (22)	12 (20)	17 (24)	0.623
Symptoms, n (%)	92 (71)	41 (69)	51 (72)	0.770
Weight loss > 3 kg, n (%)	34 (26)	21 (36)	13 (18)	0.026
Indication, n (%)				
- Ductal adenocarcinoma	85 (65)	45 (76)	40 (56)	0.009
- Neuroendocrine neoplasm	37 (28)	9 (15)	28 (39)	
- Other carcinoma	8 (6)	5 (8)	3 (4)	
Adjacent organ resection, n (%)	18 (14)	4 (7)	14 (20)	0.033
Surgical approach, n (%)				
- Laparotomy	111 (85)	51 (86)	60 (85)	0.756
- Laparoscopy	19 (15)	8 (14)	11 (15)	

BMI, body mass index; COPD, chronic obstructive pulmonary disease.

Table 2 Pathological findings

	Total (n = 130)	Body Group (n = 59)	Tail Group (n = 71)	p value
Pancreas length, mm (median)	90 ± 35	100 ± 40	80 ± 21	0.001
Lesion size, mm (median)	32 ± 21	30 ± 17	35 ± 22	0.024
Margin resection status, n (%)				
- R0	106 (82)	43 (73)	63 (89)	0.020
- R1	24 (19)	16 (27)	8 (11)	
- R2	0	0	0	
Perineural invasion, n (%)	75 (58)	39 (66)	36 (51)	0.077
Microvascular invasion, n (%)	57 (45)	27 (47)	30 (43)	0.675
Lymphatic invasion, n (%)	52 (40)	23 (39)	29 (41)	0.829
Periadipose tissue invasion, n (%)	86 (67)	39 (67)	47 (66)	0.900
T stage, n (%)				
- 1	18 (14)	7 (12)	11 (16)	0.148
- 2	21 (16)	13 (22)	8 (11)	
- 3	84 (65)	38 (64)	46 (65)	
- 4	7 (5)	1 (2)	6 (9)	
N stage, n (%)				
- 0	68 (52)	33 (56)	35 (49)	0.337
- 1	55 (42)	22 (37)	33 (47)	
- 2	2 (2)	2 (3)	0	
- x	5 (4)	2 (3)	3 (4)	
Total LN analysed, n (median, Q1 - Q3)	16 (8–24)	17 (11–23)	13 (7–24)	0.547

LN, lymph nodes.

listed in Table 2. Complete R0 resection with tumour-free margins was obtained in 81.5% of cases, more frequently in the Tail group compared to the Body group (88.7% vs. 72.9%, p = 0.020). The majority of lesions were classified T3 (64.6%) according to TNM classification, and positive LN status was present in 43.8% of patients. The median number of total LN in the DPS specimens was 16 (8–24). Splenic LN, when reported, were observed to be few in numbers in the splenic hilum, even frequently absent. However, they were only specifically reported at pathological analysis for 49 patients (37.7%, 49/130, 36 with adenocarcinoma, 13 with neuroendocrine neoplasms).

Splenic involvement

Concerning adenocarcinoma patients, 8 patients from the Tail group (8/40, 20.0%) were observed at pathological examination to have a direct splenic hilar invasion with or without splenic parenchymal invasion, whereas this was not the case for any adenocarcinoma patient from the Body group (Table 3). One of these 8 adenocarcinoma patients with splenic hilar invasion from group T was also found to have both a positive splenic LN and splenic parenchymal involvement.

In patients with neuroendocrine neoplasms, direct splenic hilar (+/− parenchymal) invasion was observed in 5 T patients (5/28, 17.9%), but again in none belonging to the Body group. No positive LN was found in the splenic hilum. At univariate analysis, adjacent organ resection, tumour tail involvement and LN positive status were associated with direct splenic involvement (Table 4).

Discussion

While DPS is the gold standard for curative treatment of neoplasia of body and tail pancreatic neoplasia, the oncological benefits of

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Table 3 Spleen pathology

	Total	Body Group	Tail Group	p value
Ductal adenocarcinoma	85	45	40	
Direct splenic area invasion, n (%)	8 (9)	0	8 (20)	0.002
- Splenic hilum invasion only	4	0	4	
- Splenic hilum + spleen invasion	4	0	4	
Splenic LN				
- Patients with splenic LN found, n	36	19	17	
- Number of splenic LN analysed, n (median, Q1 - Q3)	0 (0–1)	0 (0–1)	0 (0–1)	
- Splenic LN positivity, n	1	0	1	
Neuroendocrine neoplasm	37	9	28	
Direct invasion, n (%)	5 (14)	0	5 (18)	0.173
- Splenic hilum invasion only	4	0	4	
- Splenic hilum + spleen invasion	1	0	1	
Splenic LN				
- Patients with splenic LN found, n	13	10	3	
- Number of splenic LN analysed, n (median, Q1 - Q3)	0 (0–1)	0 (0–1)	0 (0–1)	
- Splenic LN positivity, n	0	0	0	
Other carcinoma	8	5	3	
Direct splenic area invasion, n	0	0	0	
Splenic LN				
- Patients with splenic LN found, n	0	0	0	

LN, lymph nodes.

the splenectomy have never been demonstrated. In the present study, we observed the absence of direct splenic involvement and splenic LN invasion in all tumours that did not involve the pancreatic tail, including (adeno)carcinomas and neuroendocrine neoplasia. For lesions invading the pancreatic tail, around 20% involved the splenic hilum by contiguity, and splenic LN were occasionally invaded (1.5%). The benefit of splenectomy in case of pancreatic body neoplasia should therefore be questioned, whereas splenic vessels lymphadenectomy continues to be required. For patients with a pancreatic tumour involving the pancreatic tail, a splenectomy remains entirely justified.

The oncological reasons for performing a splenectomy in the case of distal pancreatic malignancies are classically described as a lymphadenectomy enlarged to splenic vessels and splenic hilum and a wider surgical posterior margin, including the prerenal fascia.[1] Some studies have reported the exceptional invasion of splenic hilum LN, and questioned the use of splenectomy in case of distal pancreatic malignancy.[1,9–11] In a Japanese series of 85 patients, Kim *et al.* reported that only 4 patients had splenic hilar LN metastases, remarking on the fact that these 4 patients (4.7%) had a large tail tumour.[1] In the present study, findings of LN in the splenic hilum were very rare, and when observed, they were free from malignant cells, except in one patient with a pancreatic tail adenocarcinoma. In theory, the first lymphatic relays of the left pancreas are located within the peripancreatic tissue and splenic hilum, before draining either via the splenic artery route towards the coeliac and superior mesenteric LN, or via a direct posterior pathway to the para-aortic LN.[11–13] O'Morchoe reported that LN from the tail and left side of the body empty into the splenic hilum LN, whereas those from the right side of the body and pancreatic neck travel towards the right, but he could not draw any separation line between the right and left areas of drainage.[12] Our hypothesis is that tumours involving the pancreatic body only, without pancreatic tail involvement, will not develop positive LN in the splenic hilum because the direction of the lymphatic stream goes posteriorly and/or towards the coeliac and superior mesenteric LN (Fig. 1).

Direct involvement of the spleen is evidently an indication for splenectomy, and is logically observed only in tumours with tail invasion. In the present study, direct splenic involvement by contiguity was observed in 18.3% of all T patients, involving usually either the perinervous tissue within the splenic hilum, or both the hilum and the spleen itself. No tissue within the splenic hilum was invaded in patients with pancreatic body tumours. The same observations were reported by Collard *et al.*, highlighting the important role of preoperative CT for evaluation of the splenic involvement.[5] However, the sensitivity and specificity of CT scan evaluations were not 100%, as observed in the

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Table 4 Risk factors for having direct splenic involvement

	Spleen involvement (n = 13)	No spleen involvement (n = 117)	p value
Age (≥70 vs. < 70 y)	3/10	41/76	0.387
Sex (M vs. F)	6/7	60/57	0.861
BMI (≥30 vs. <30)	1/12	17/100	0.498
Diabetes (yes vs. no)	3/10	26/91	0.944
Smoking (yes vs. no)	2/11	27/90	0.527
Pain (yes vs. no)	5/8	63/54	0.292
Weight loss (yes vs. no)	1/12	33/84	0.110
Adjacent organ resection (yes vs. no)	5/8	13/104	0.007
Lesion size ≥30 mm (≥30 vs. <30 mm)	12/1	87/30	0.150
Tumoral tail involvement (yes vs. no)	13/0	58/59	0.001
Perineural invasion (yes vs. no)	10/3	65/52	0.139
Microvascular invasion (yes vs. no)	9/4	48/67	0.059
Lymphatic invasion (yes vs. no)	7/6	45/72	0.283
Periadipose tissue invasion (yes vs. no)	9/4	77/39	0.836
T stage (1/2 vs. 3/4)	12/1	79/38	0.064
LN positivity (yes vs. no)	11/2	46/71	0.002

BMI, body mass index; LN, lymph nodes.

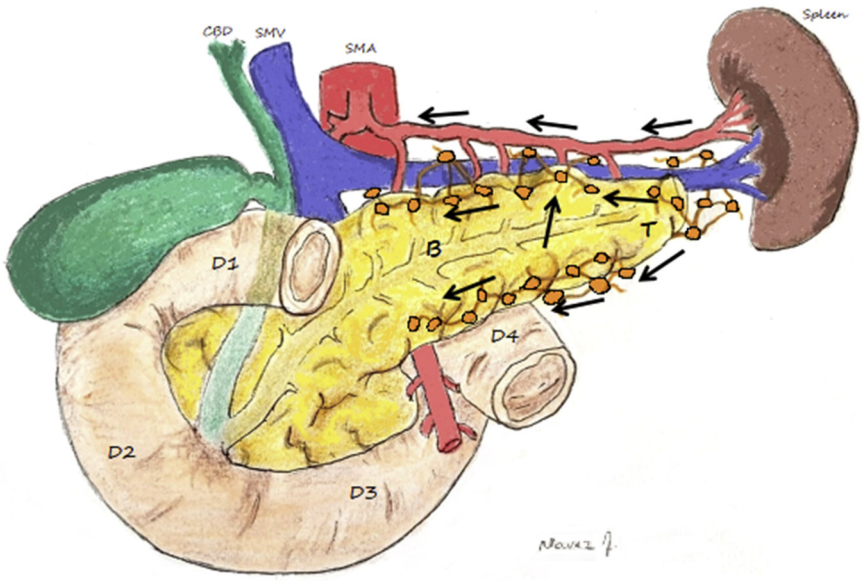

Figure 1 Lymphatic drainage (arrows) of the distal pancreas, including splenic, superior body and inferior body lymph nodes (colour-coded orange). B, pancreatic body; T, pancreatic tail; SMA, superior mesenteric artery; SMV, superior mesenteric vein; CBD, common bile duct; D, duodenum

abovementioned study, and a few patients with a tail tumour could thus present unsuspected splenic hilum invasion.[5] A splenectomy remains therefore justified in patients with a lesion invading the pancreatic tail.

The spleen is a lymphoid organ that plays an important role in the immune system, particularly regarding blood cells storage and encapsulated bacteria infections. During postoperative course and long-term follow-up, the risks of infectious complications and overwhelming infections are increased, as well as those of portal vein thrombosis, thrombocytosis and hypercoagulable conditions.[4,14–16] In addition to more short and long-term complications, the overall survival rate of asplenic

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patients with cancer could be also decreased.[17] Moreover, the topic has been much debated ever since a 1995 Danish study suggested an increased cancer risk in splenectomised patients.[18] In a more recent 27-year follow-up of a large cohort of splenectomised American veterans, 13% of patients were diagnosed with cancer and a higher mortality risk due to any type of cancer, including solid tumours and haematological disorders.[19] The cancer risk could also be applicable for cancer recurrence after oncological surgery, as suggested after gastrectomy or pancreatectomy for cancer.[20,21] We could thus hypothesize that spleen preservation in patients with pancreatic cancer could be potentially beneficial, particularly in cases of no splenic involvement.

Over the last decades, pancreatic surgery has seen vast improvements and spleen-preserving DP has proven to be safe with good outcomes.[2] In 1988, Warshaw described the feasibility of spleen-preserving DP with splenic vessels resection, and blood supply of the spleen is then ensured by the short gastric vessels and the left gastro-epiploic artery.[22] This procedure is safely and routinely performed for benign and premalignant lesions, albeit associated with a slightly higher morbidity than splenic vessels preservation, due to the risk of splenic infarction requiring splenectomy in 2–5% of cases.[3] Splenomegaly, and paucity/absence of short gastric vessels (e.g. history of bariatric surgery) constitute contraindications to this technique.[2,3] Splenic vessels removal is essential for regional lymphadenectomy in case of malignant indications, in addition to a larger posterior margin to decrease the risk of incomplete resection. Consequently spleen-preserving DP with splenic vessels removal could be a good alternative in selective patients with pancreatic body neoplasia. In this setting, the oncological value of minimally invasive surgery in distal pancreatectomies for invasive cancer could be further studied, especially regarding the surgical margins and the quality of lymphadenectomy.

The main limitation of our study is its retrospective design, which limits the pathological analysis to a revision of specimen slides and pathological reports, and does not enable a station 10 LN analysis if this was not specifically found at the time of surgery. The authors therefore strongly encourage the specific description of splenic hilar LN on pathological reports.

In conclusion, the present study questioned the benefits of splenectomy during DP in cases of malignant tumours located only within the pancreatic body, in view of the absence of direct splenic invasion or splenic hilar LN involvement. Resection of splenic vessels remains nevertheless essential for regional lymphadenectomy, rendering spleen-preserving DP with splenic vessels removal (Warshaw technique) the favoured procedure for pancreatic body tumours. Splenectomy remains fully justified when the pancreatic tail is involved by the malignancy. Further studies are needed to confirm these results, although one immediately applied important outcome of our study was already to encourage the specific description of splenic hilar LN in all our pathological DPS reports.

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Conflict of Interest

None to declare.

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