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ORIGINAL ARTICLE – ENDOCRINE TUMORS

Surgical Management of Small Bowel Neuroendocrine Tumors: Specific Requirements and Their Impact on Staging and Prognosis

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ABSTRACT

Background. Small bowel neuroendocrine tumors (SB-NETs) are characterized by two main features: they usually are metastatic at diagnosis and multiple in 30 % of cases. As such, SB-NETs require specific surgical management. This retrospective study examined local recurrence, survival, and prognosis of SB-NETs after adapted surgery.

Methods. All consecutive patients with SB-NETs who underwent resection of at least one primary tumor between 1 January 2000 and 1 January 2013 were analyzed. The preoperative morphologic workup, histologic classification, and metastatic lymph node (LN) ratio (LNs involved/removed) were recorded.

Results. The study enrolled 107 patients, 35 (33 %) of whom had multiple SB-NETs (range 1–44; mean 3.1). Preoperative imaging and perioperative surgical examination missed 61 and 33 % of SB-NETs, respectively, in contrast to pathologic examination. Of the 107 patients, 43 % had carcinoid syndrome, 70 % had metastatic disease, and 90 % had LN involvement. The median number of LNs retrieved was 12 (range 1–69). The LN ratio (LNs involved/removed) was 0.25. The highest tumoral grades were G1 (in 61 % of patients) and G2 (in 37 % of patients). Of the 107 patients, 13 (12 %) had local LN recurrence. The rate of LN recurrence-free survival at 5 years was 88 %. The median overall survival (OS) time was 128 months (range 91–165 months). In the multivariate analysis, high chromogranin A (CgA) levels and peritoneal carcinomatosis were significantly associated with shorter OS.

Conclusions. Systematic palpation of the entire small bowel detects more multiple NETs than preoperative imaging. Systematic surgery with extensive LN resection is associated with low local recurrence. High CgA levels and carcinomatosis are linked with shorter survival.

Small bowel (jejunal and ileal) neuroendocrine tumors (SB-NETs) account for 25 % of gastroenteropancreatic NETs. Their incidence rate has risen, from 1.09 per 100,000 in 1973 to 5.25 per 100,000 in 2004 in the US population.[1] Small bowel NETs raise two main challenges (1) about 30 % of cases are multiple, and (2) more than 50 % of cases (up to 80 % in some series) are metastatic at diagnosis.[2] This requires an adapted surgical strategy.

In contrast to pancreatic NETs,[3] expert groups recommend the removal of the primary SB-NE6T, even in metastatic (stage 4) disease, to prevent local complications such as bowel ischemia, perforation, and obstruction.[4–6] This expert recommendation is supported by retrospective studies.[7–10] However, several steps of the surgical approach remain to be definitively standardized. One step is the detection of multiple tumors. Two main issues are raised. First, how comfortable are we in detecting them preoperatively? One study reported a diagnostic yield of only 45 % for identification of primary SB-NETs with video capsule endoscopy (VCE),[11] and our group reported the value of computed tomography (CT) enteroclysis in for identifying suspected SB-NETs,[12] but in both studies, the sensitivity for detecting multiple NETs with these imaging methods remains low.

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Second, what is the best surgical option when multiple SB-NETs are discovered perioperatively? The second step of the surgical approach, currently debated, is the extent and impact of lymph node (LN) resection. Landry et al.[13] reported that regional mesenteric lymphadenectomy, with resection of at least seven LNs, is associated with improved survival. In addition, Wang et al.[14] reported that lymphatic mapping helps to define resection margins for multiple SB-NETs. Hence, it is important to standardize this strategy. Therefore, we designed a retrospective study based on 107 cases treated in the same referral center aimed at evaluating the preoperative workup, its value in detecting multiple SB-NETs, and the impact of an adapted surgical strategy on both the postoperative course and prognostic factors, either validated [World Health Organization (WHO) classification and tumor-node-metastasis (TNM) staging][15] or suspected (age, 5-HIAA > 2ULN, carcinoid heart disease, tumor size, grade, tumor burden, tumor progression slope, and surgery of primary tumor).[15,16]

PATIENTS AND METHODS

Population

All consecutive patients with SB-NET who underwent resection of at least one primary tumor between 1 January 2000 and 1 January 2013 in Lyon ENETS Center of Excellence were included in the study. Patients with duodenal SB-NETs and unresected primary tumors were excluded.

Preoperative Data

The following clinical parameters were recorded from a specific database maintained at our institution for all patients referred for NETs: sex, age, clinical presentation (carcinoid syndrome, bowel obstruction, subocclusion, abdominal pain), and evidence of regional and distant metastases. Carcinoid syndrome was defined in patients presenting with flushing, diarrhea, or both and high urine 5-HIAA levels (>47 μmol/24 h). Biologic markers [urine 5-HIAA and serum chromogranin A (CgA)] were recorded when available. Morphologic data with the type of imaging performed [CT, magnetic resonance imaging (MRI), enteroclysis CT, somatostatin receptor scintigraphy, VCE, cardiac ultrasound] and their results, especially the number of SB-NETs found by each imaging procedure; location of metastatic spreading; and presence of carcinoid heart disease were collected. Carcinoid heart disease was defined as tricuspid or pulmonic valve abnormalities (regurgitation or stenosis) found by cardiac ultrasound. In France, DOTA-TOC and F-DOPA PET were not available outside clinical trials during the study period.

Surgical Procedure

Patients with carcinoid syndrome received a continuous infusion of octreotide (2000 μg/day) before, during, and at least 24 h after surgery. The abdomen was opened via a median laparotomy, considered to be safer than laparoscopy for two reasons: optimal exploration of the entire abdominal cavity and vascular control at the origin of superior mesenteric vessels.

As a first step, the abdominal cavity was explored, and the full length of small bowel was analyzed visually and through bidigital palpation and compression (Fig. 1a–c). Indeed, submucosally extending carcinoid tumors of a small size were mainly found by compression in our experience. Any suspected tumor was tagged with a polypropylene suture. The distance from the most proximally suspected tumor to the ileocecal valve was noted. Then, visual searches for miliary liver metastases were performed as well as perioperative ultrasound and liver biopsies when further liver surgery was scheduled (Fig. 1d).

The second step was the resection, starting with dissection of the mesenteric vessels to ascertain whether the mesenteric LN block was resectable. The retroperitoneum was opened along the white line of Toldt, followed by the Kocher maneuver to explore the proximal portion of the superior mesenteric artery from the right (Fig. 1e, f). This strategy allowed ligation of vascular branches without any threat to the jejunal blood supply. Lymphadenectomy at that level was performed above the right colic vessels, which led to a right hemicolectomy.

Next, the dissection was pursued on the left border of the superior mesenteric vessels. A minimum of three jejunal branches had to be free to avoid the risk of short bowel length. The resection procedure then was based on the length of the devascularized small bowel. Due to the collateral circulation, the ischemic small bowel was always shorter than expected. Care was taken to remove all suspected, tagged tumors within the length of resected small bowel. Extensive lymphadenectomy then was performed from the small bowel section to the superior mesenteric dissection, with special attention paid to any jejunal pedicle that could be preserved. The length of the remaining small bowel was measured and recorded. The ileocolic anastomosis was performed manually. Cholecystectomy was undertaken last.

Pathologic Data

For macroscopic examination, surgical specimens were received fresh. The intestinal segment was open along its antimesenteric border. The whole specimen was carefully examined visually and by manual palpation. All detected tumors were marked. After fixation, detected tumors were

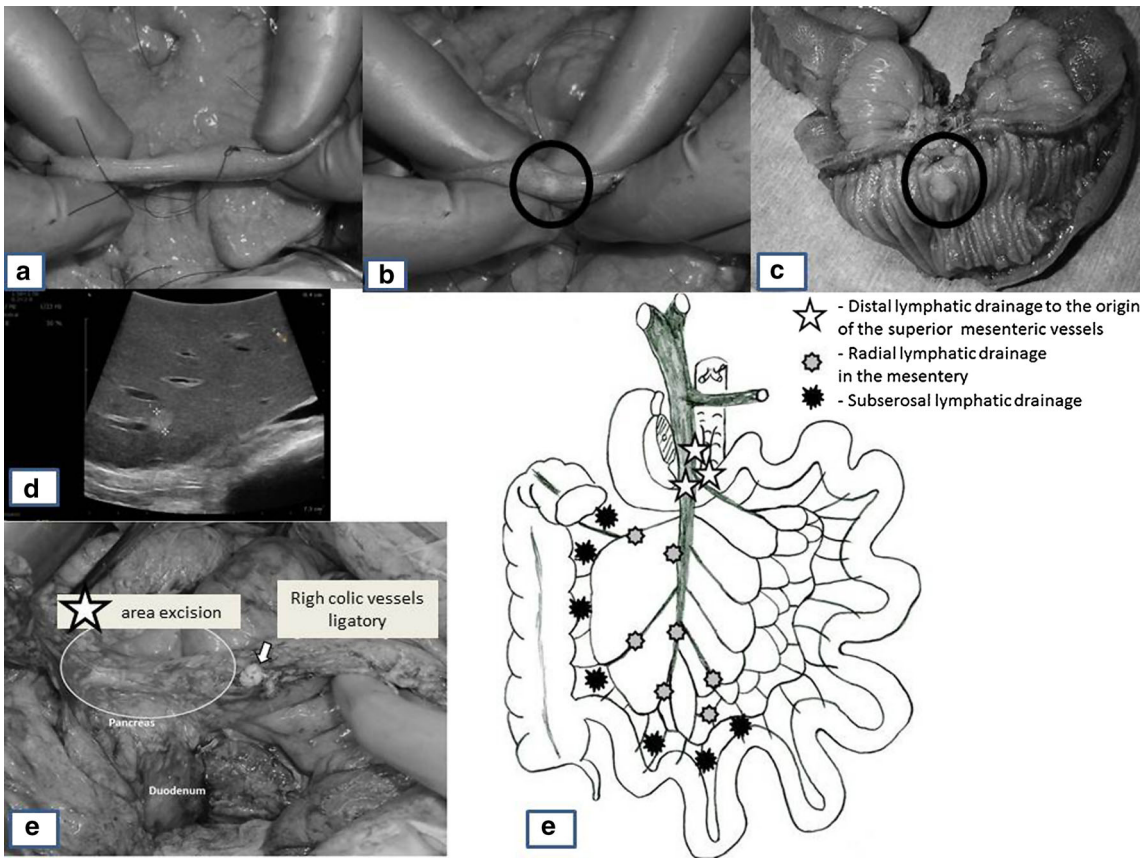

FIG. 1 Exploration of the small bowel is performed **a** before and **b** after digital compression showing the tumor not visible by simple inspection, **c** subsequently confirmed on the surgical specimen. **d** Intraoperative ultrasound detects millimetric liver metastases not seen at magnetic resonance imaging (MRI). **e** Different areas of lymphadenectomy with subserosal lymphatic drainage (*black circle*), radial lymphatic drainage in the mesentery (*gray circle*), and distal lymphatic drainage to the origin of the superior mesenteric vessel (*black and white star*). **f** The photography performed during surgery shows the cleaning area of the distal lymphatic drainage at the start of the superior mesenteric artery

sampled, and careful search was made for LNs. Finally, the intestinal segment was cut in 5-mm-thick parallel sections to identify additional tiny tumor lesions.

Histologic examination was performed by two expert pathologists, members of the French national referent network (TENpath). The following features were noted: number of tumors, maximum diameter, extent of local invasion, evidence of angioinvasion, and/or perineural invasion. The number of LNs retrieved, the number of LNs involved, and the LN ratio (LNs involved/LNs removed) were collected. The following information also was provided: morphologic differentiation, histologic grade,[17] Ki67 index, histologic classification according to WHO 2010 guidelines,[18] and pTNM stage according to ENETS proposals [17] and the seventh edition of the American Joint Committee on Cancer (AJCC) cancer staging.[19] In the event of multiple tumors, the largest or most invasive tumor was described.

The SB-NET count in the pathologic specimen was considered the final reference. The accuracy ratio was defined as the percentage between the number of SB-NETs found by radiologic examination or counted intraoperatively and the final reference number identified by pathologic examination of the operative specimen.

Postoperative Data

All medical and surgical complications were gathered as preoperative, early postoperative (<30 days), and late postoperative. Postoperative characteristics were collected including occurrence of locoregional recurrence, time of its occurrence, duration of follow-up evaluation, status at the end of the follow-up period, and cause of death. Thoraco-abdomino-pelvic CT scans were performed every 6 months for 5 years and then yearly.

Statistical Analysis

Overall survival (OS) was calculated from the date of SB-NET surgery to the date of death or last follow-up visit. Local recurrence-free survival (LRFS) was calculated from

the date of SB-NET surgery to the date of first occurrence of locoregional LNs on abdominal CT scans, death, or last follow-up visit. Both OS and LRFS were assessed using Kaplan–Meier analysis, and comparisons were performed using the log-rank test. A p value lower than 0.05 was considered statistically significant. Cox proportional hazard models were developed using relevant clinicopathologic variables to determine the association of each parameter with OS. For continuous variables, the cutoff level chosen was their median value. Only variables with a p value lower than 0.10 at univariate analysis were introduced into the Cox model. Relative risks were expressed as hazard ratios (HRs) with 95 % confidence intervals (CIs). The cutoff date for the final analysis was 1 January 2014. All statistical analyses were performed using the Statistical Package for Social Sciences version 17.0 (SPSS, Chicago, IL, USA).

RESULTS

Preoperative Data

The study enrolled 107 patients (62 males, 58 %) with resection of SB-NETs from 2000 to 2012 (Table 1). The median age was 62 years. No patient had hereditary tumor syndromes. One man had a familial history of SB-NETs. Of the 107 patients, 46 (43 %) had clinical evidence of carcinoid syndrome. Among the 84 patients who underwent cardiac ultrasonography, 11 (13 %) had carcinoid heart disease. All the patients had a thoraco-abdomino-pelvic CT scan, which showed that 70 % had metastatic disease, mainly in the liver (65 %) or in distant LNs (17 %); 75 % had a mensenteric mass; and 15 % had ischemic bowel segments (defined during surgical examination as localized or diffuse purple discolorations of ischemic bowel). Somatostatin receptor scintigraphy showed high uptake in 78 (87 %) of 90 patients on primary and/or metastatic lesions. A histologic preoperative diagnosis was obtained for 77 patients (72 %): 50 (46.7 %) diagnoses from biopsy of liver metastases and/or 27 (25.2) on primary tumor from ileocolonoscopy. Before surgery, 29 patients (27 %) had already been treated with long-acting somatostatin.

TABLE 1 Preoperative characteristics of patients with small bowel neuroendocrine tumors

	All patients ($n = 107$) n (%)
Clinical data	
Male	62 (58)
Median age, years (range)	62 (36–88)
Carcinoid syndrome	46 (43)
Subocclusion	13 (12)
Occlusion	7 (6)
Biologic data n (range)	
Median chromogranin A in 91 patients	130 (10–39,130)
Median 5-HIAA in 72 patients	99 (5–3250)
Morphologic data	
Preoperative MRI	29 (25)
Preoperative thoraco-abdomino-pelvic CT scan	107 (100)
Mesenteric tumor	82 (77)
Retractile mesenteritis	53 (50)
Ischemic segments	16 (15)
Mesenteric vein thrombosis	1 (1)
No. of metastatic sites	
0	31 (29)
1	54 (50)
>1	22 (21)
Location of metastases	
Liver metastases	70 (65)
Carcinomatosis	7 (6)
Bone metastases	5 (5)
Lung metastases	5 (5)
Brain metastases	0 (0)
Mesenteric nodes	72 (69)
Distant nodes	18 (17)
Cardiac US performed	84 (79)
Carcinoid heart disease/US performed	11 (13)
Uptake of FDG PET	6/12 (13)
Uptake of SRS	79/90 (87)
Preoperative histologic diagnosis	77 (72)

5-HIAA 5-hydroxyindoleacetic acid, *MRI* magnetic resonance imaging, *CT* computed tomography, *US* ultrasound, *FDG* fluorodeoxyglucose, *PET* positron emission tomography, *SRS* somatostatin receptor scintigraphy

Surgical Data

The median operative time was 251 min (range 60–435 min), longer for multiple than for unifocal tumors (240 vs. 325 min; $p = 0.001$). Abdominal exploration enabled the diagnosis of more peritoneal carcinomatosis (14 %) than had been diagnosed at preoperative staging (6 %). Miliary liver metastases were found in 15 patients (14 %). A total of 23 patients (22 %) also underwent hepatectomy, and 66 % underwent cholecystectomy, especially when postoperative liver embolization was scheduled. This was consistently performed during the last 4 years of the study.

Early and late postoperative morbidities were recorded. The only morbidity that occurred during surgical procedure was carcinoid crisis (15 %), treated with high-dose somatostatin analogs. One patient died of acute tricuspid insufficiency 3 days after surgery. In this patient, grade 1 tricuspid cardiopathy was identified preoperatively.

Despite high doses of preoperative somatostatin analogs, as described in the Methods section, he presented with a severe carcinoid syndrome during the procedure. Due to the occurrence of small bowel subocclusions, the decision was made to perform a small bowel resection before chemo-embolization of its liver metastases and before valvular replacement was made. The early postoperative morbidity rate was 25 %, and the late postoperative morbidity rate was 11 % (Appendix Table 5). Overall, the 90-day mortality rate was 1 %.

Pathologic Data

The median length of small bowel resection was 50 cm (range 5–450 cm). The median tumor size was 1.7 cm (range 0.1–4.3 cm). All tumors displayed a well-differentiated morphologic appearance. According to the 2010 WHO classification, the unique or largest tumor was classified as NET G1 in 61 % of the patients and as NET G2 in 37 %. The median Ki67 index in the unique and largest tumor was 1.1 % (range, 0–22 %). Necrosis was rare (5 %). In 76 patients, the unique and largest tumor was staged pT3 (75 %) according to either ENETS or UICC TNM classification (Table 2).

Most of the patients (90 %) presented with regional LN involvement. The median number of LNs involved per patient was 3 (range 0–27). The median number of LNs removed was 12 (range 0–69), and the median LN ratio (LNs involved/LNs removed) was 0.25 (range 0–1).

Detection of Multiple Small Bowel NETs

For 35 patients (33 %), multiple tumors were diagnosed from pathologic specimens. This number was underestimated by all preoperative procedures, which missed 61 % of SB-NETs (Appendix Table 4). Despite palpation of the entire small bowel, surgeons missed 33 % of SB-NETs. They found a mean number of 2.3 tumors (range 0–31 tumors) when preoperative staging found a mean number of 1.3 tumors (range 0–8 tumors). When methods were classified from least to best contributive, their abilities to find SB-NETs (with pathology as the reference) were as follows: barium small bowel follow-through procedure (15 %), CT scan (21 %), enteroclysis CT scan (35 %), VCE (52 %), and surgeon (67 %). Of 20 VCEs, 4 (20 %) induced obstruction.

Local Recurrence, Overall Survival, and Prognostic Factors

The median follow-up period was 54 months (range 1–160 months). Local LN recurrence was experienced by 13 patients (12 %). The median time of LRFS was not

TABLE 2 Surgical and histologic characteristics of patients with small bowel neuroendocrine tumors

	All patients ($n = 107$) *n* (%)
Results of surgical inspection	
Retractile mesenteritis	63 (59)
Small bowel ischemia	15 (14)
Miliary liver metastases	15 (14)
Carcinomatosis	15 (14)
Type of surgery	
Median surgery time, min (range)	295 (60–435)
Carcinoid syndrome during surgery despite high dose of somatostatin analogs	16 (15)
Type of resection	
Right hemicolectomy ± small bowel	40 (38)
Ileocecal resection ± small bowel	9 (8)
Small bowel resection	58 (54)
Median length of small bowel removed, cm (range)	50 (5–450)
Cholecystectomy	71 (66)
Hepatectomy	23 (22)
Histologic features of primary tumors	
Multiple tumors	35 (33)
Median no. of tumors, *n* (range)	1 (1–44)
Median distance of tumors from ileocecal valve, cm (range)	68 (2–275)
Median tumor size, cm (range)	1.7 (0.1–43)
pT (ENETS-UICC)	
pT1	5 (5)
pT2	14 (14)
pT3	76 (75)
pT4	6 (6)
n/a	6
Perineural invasion	58/88 (66)
Angioinvasion	55/95 (58)
WHO 2010 classification	
NET G1	61 (61)
NET G2	36 (37)
NET G3	1 (1)
NA	9
Median Ki 67 (range) (82 patients)	1.1 (0–22)
Necrosis	4/80 (5)
Lymph nodes (LN)	
Median no. of LNs removed, *n* (range)	12.0 (0–69)
Patients with involved LN metastasis	78 (90)
Median no. of LNs involved, *n* (range)	3.0 (0–27)
Median LN ratio (no. of LN metastases/LN removed) (range)	0.25 (0–1)
Histologic carcinomatosis	15 (14)

ENETS European Neuroendocrine Tumor Society, *UICC* Unio Internationalis Contra Cancrum, *WHO* World Health Organization, *NET* neuroendocrine tumor, *G* grade, *NA* not assessable

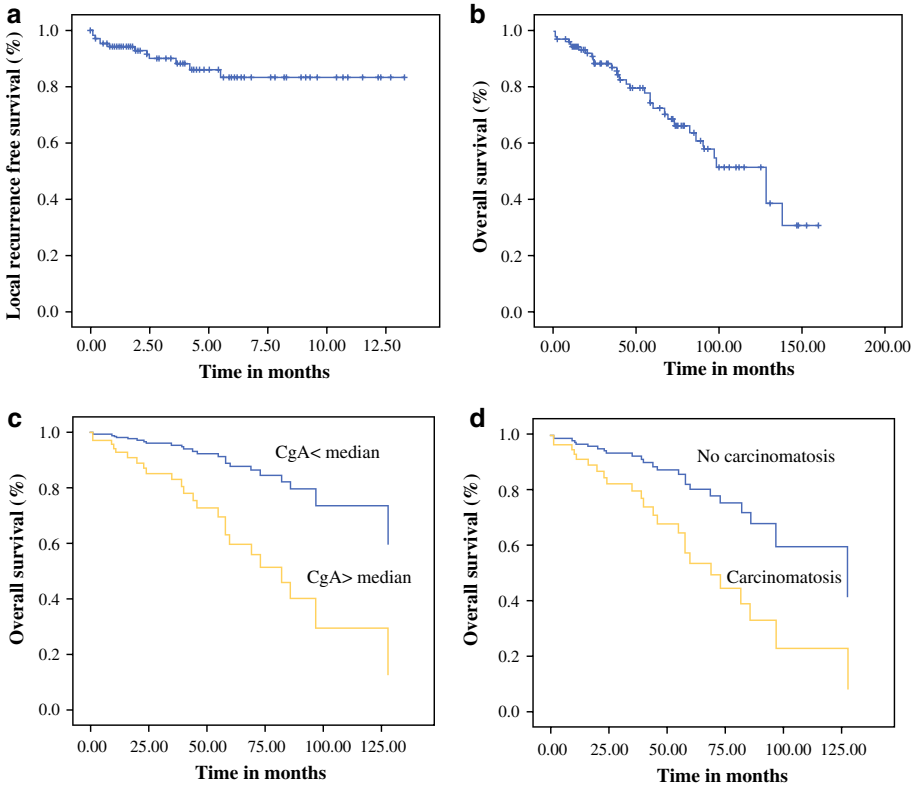

FIG. 2 **a** Local recurrence-free survival and **b** overall survival curves (Kaplan–Meier) of patients with small bowel neuroendocrine tumors (SB-NETs). Overall survival according to presence of **c** high serum chromogranin A (CgA) levels and **d** histological carcinomatosis after multivariate analysis

reached (Fig. 2a). The LRFS at 5 years was 88 %. At the end of the follow-up period, 75 patients (70 %) were alive. The causes of death were disease ($n = 13$), carcinoid heart disease ($n = 2$), cardiac infarcts or pulmonary embolisms ($n = 5$), perforation after colonoscopy ($n = 1$), and unknown cause ($n = 11$). No patient died of complications due to local LN recurrence.

The median OS from surgery was 128 months (range 91–165 months) (Fig. 2b). The OS at 5 years was 79 %. The results of the uni- and multivariate analyses are presented in Table 3. According to the multivariate analysis, the patients with high serum CgA and those with histologic carcinomatosis experienced worse OS (Fig. 2c, d).

DISCUSSION

We report a substantial cohort of patients who underwent resection of primary SB-NETs by a single surgical team. The study was based on the removal of primary tumors despite metastatic disease according to the current recommendations [4–6] emerging from retrospective analysis [7–9] and one systematic review.[10] Currently, no randomized controlled trial is available to answer this question. The literature is unable to provide the gold standard for lymphadenectomy needed in SB-NETs.

Our team usually performs an extensive LN resection (median of 12 LNs removed vs. 8 in the study reported by Landry et al.[13]). Norlén et al.[20] reported that mesenteric and distant abdominal LN metastases are independent prognostic factors and should therefore be resected.[21] In our study, removing LNs up to the origin of the superior mesenteric artery in its retropancreatic portion (Fig. 1e) did not increase morbidity or mortality and led to a low local recurrence rate (12 %) without local complications. However, due to the study size, the low rate of local recurrence, and the high rate of patients with stage 4 disease (70 %), we were unable to demonstrate survival benefit from an extensive LN resection, as shown with Surveillance, Epidemiology, and End Results (SEER) data (1364 patients) by Landry et al.,[13] who reported a better survival with removal of more than seven LNs. We were unable to find any predictive factor for local recurrence due to the low number of events. With the "reverse" surgery described in the Methods section (lymphadenectomy followed by small bowel resection), the length of the resection was reduced. Among our 70 patients (65 %) with synchronous liver metastases, 23 underwent hepatectomy. Currently, however, our team usually does not perform liver resection during the same surgical procedure.

Second, we explored prognostic factors of OS in a series of SB-NETs with homogeneous preoperative workup and surgical management. The 5-year OS rate (79 %) was similar to that reported by Strosberg et al.[9] (72 %) for stage 4 disease. Our aim was not to study the value of primary tumor resection or TNM staging [15] because all our patients had their primary tumor removed, and most of them had metastatic disease. The median Ki67 index was low

TABLE 3 Prognostic factors of overall survival after uni- and multivariate analyses

	Univariate p value	Multivariate p value; HR (CI 95 %)
Sex (female vs. male)	0.43	–
Median age (> vs. <)	0.047	0.27; 0.61 (0.25–1.47)
Carcinoid syndrome (yes vs. no)	0.58	–
Subocclusion (yes vs. no)	0.48	–
Occlusion (yes vs. no)	0.38	–
Cardiac heart disease (yes vs. no)	0.16	–
Median chromogranin A (> vs.<)	0.001	0.03; 0.31 (0.11–0.90)
Multiple tumors (yes vs. no)	0.17	–
Positive SRS (yes vs. no)	0.92	–
Positive PET FGD (yes vs. no)	0.94	–
Mesenteric nodes (yes vs. no)	0.095	0.69; 0.73 (0.16–3.42)
Ischemic segments (yes vs. no)	0.03	0.20; 0.51 (0.18–1.43)
No. of metastatic sites	0.28	
Perineural invasion (yes vs. no)	0.39	–
Angioinvasion (yes vs. no)	0.67	–
pT (yes vs. no)	0.74	–
Ki67 index (> vs. < 2)	0.27	
WHO 2010 classification	0.23	–
pN (yes vs. no)	0.71	–
Median LN involved (> vs.<)	0.68	
Median LN removed (> vs.<)	0.22	
Median LN ratio (> vs. <)	0.68	–
Histologic carcinomatosis (yes vs. no)	0.026	0.09; 0.41 (0.15–1.16)
Liver metastases by surgeon inspection (yes vs. no)	0.36	–

HR hazard ratio, *CI* confidence interval, *SRS* somatostatin receptor scintigraphy, *PET* positron emission tomography, *FDG* fluorodeoxyglucose, *WHO* World Health Organization, *LN* lymph node

(1.1 %), lower than 5 % in 89 % of the patients. This narrow range precluded any prognostic value of the Ki67 index, at variance with pancreatic NETs. In our study, the patients with high serum CgA levels had a worse prognosis after the multivariate analysis (Table 3).

Third, the current study focused on detection of multiple SB-NETs. We showed that even with advances in imaging, 61 % of tumors were missed at preoperative procedures. Therefore, the surgeon is advised to explore and perform palpation of the entire small bowel to detect all possible SB-NETs. Due to the small size of such tumors, palpation, even performed carefully, still can miss tumors, as we showed in our results. Van Tuyl et al.[11] reported a high identification rate for primary SB-NETs with VCE, but in fact VCE missed 55 % of tumors. The number of VCE procedures was quite low in our study ($n = 20$). Indeed, we decided to stop its use due to the high rate of VCE blockages (20 %) in the small bowel and its inability to provide additional useful information to surgeons.

In conclusion, systematic palpation of the entire small bowel detects more multiple NETs than preoperative imaging. Systematic surgery with extensive LN resection results in low local recurrence. High CgA levels and carcinomatosis are linked with shorter survival.

CONFLICT OF INTEREST There are no conflicts of interest.

APPENDIX

See Appendix Tables 4 and 5.

TABLE 4 Mean number (range) of small bowel neuroendocrine tumors regarding the type of examination

	All patients ($n = 107$) Mean (range)	% Tumors found (pathologist as ref)
All modalities	1.3 (0–8)	39
CT scan ($n = 107$)	0.7 (0–8)	21
Enteroclysis CT scan ($n = 63$)	1.2 (0–8)	35
Enteroclysis MRI ($n = 3$)	0.03 (0–2)	25
Barium small bowel follow-through ($n = 12$)	0.2 (0–1)	15
Video capsule endoscopy ($n = 20$)	2.3 (0–8)	52
Surgeon ($n = 107$)	2.3 (0–31)	67
Pathologist ($n = 107$)	3.4 (1–44)	100

CT computed tomography, *MRI* magnetic resonance imaging

TABLE 5 Early and late postoperative morbidities

	Early postoperative morbidity *n* (%)	Late postoperative morbidity *n* (%)
All morbidity	27 (25)	12 (11)
Anastomotic leak	0	1 (6)
Cholecystis	0	1 (6)
Cystitis	6 (20)	0
Pneumonia	1 (3)	0
Abdominal abscess	1 (3)	0
Wound abscess	3 (10)	0
Sepsis of unknown origin	4 (13)	0
Abdominal parietal bleeding	4 (13)	0
Gastric ulcer	1 (3)	0
Small bowel occlusion	4 (13)	3 (18)
Inferior mesenteric vein thrombosis	0	1 (6)
Mesenteric angor	0	1 (6)
Acute pancreatitis	1 (3)	0
Scar defects	2 (7)	0
Tricuspid insufficiency	0	3 (18)
Subdural hematoma	0	1 (6)
Uretero hydronephrosis	0	1 (6)

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