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Current Approaches to Surgical Treatment and Perioperative Management of Small Intestinal Neuroendocrine Tumors

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Abstract

Small intestinal neuroendocrine tumors (SI-NETs) represent the most common neoplasms of the small bowel, with their incidence steadily rising. Surgery remains a cornerstone in the multidisciplinary management of SI-NETs, serving either a curative purpose—though complete (R0) resection is achievable in only about 20% of cases due to advanced disease at diagnosis—or a palliative role. Surgeons must consider the tumor's hormonal activity, typical patterns of metastasis at presentation, and strategies for bowel-sparing procedures to prevent short bowel syndrome. This review summarizes current surgical indications and techniques, as well as perioperative and postoperative management strategies for SI-NETs.

Keywords: Surgery, Carcinoid syndrome, Small bowel neuroendocrine tumor, Carcinoid crisis

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Introduction

Small intestinal neuroendocrine tumors (SI-NETs) represent the most frequent tumors of the small bowel [1]. Although they typically progress slowly, these tumors have a pronounced tendency to spread to regional lymph nodes and distant organs, resulting in five-year overall survival rates of 70%–100% for localized disease and 35%–60% when metastases are present [2–4]. As shown in **Figure 1**, SI-NETs are usually small (<20 mm), most often located in the distal ileum, and multifocal in 30%–50% of cases [4–6]. At the time of diagnosis, over 80% of patients have mesenteric lymph node metastases (MLNM), which are frequently larger than the primary tumor and associated with dense desmoplastic reactions causing retractile mesenteritis [7–11]. Extension of MLNM into the small bowel or mesenteric vessels may result in acute complications such as abdominal pain, bowel obstruction, mesenteric ischemia, or gastrointestinal bleeding, with up to a quarter of patients requiring emergency surgery [5,12]. The liver is the most common site of distant spread, affecting roughly half of patients, followed by the peritoneum, where carcinomatosis occurs in about 20% [10,11].

SI-NETs are also hormonally active, producing substances like serotonin, tachykinins, and prostaglandins. These secretions contribute to mesenteric fibrosis, carcinoid syndrome, carcinoid crisis, and carcinoid heart disease, usually in the context of extensive liver involvement that allows hormones to bypass first-pass metabolism [13].

Surgical intervention remains a central component of SI-NET treatment. Curative resections are possible but limited to approximately 20% of patients due to advanced disease at diagnosis; in other cases, surgery is performed with palliative intent [14, 15]. This review focuses on the indications, operative strategies, and perioperative and postoperative considerations for managing SI-NETs.

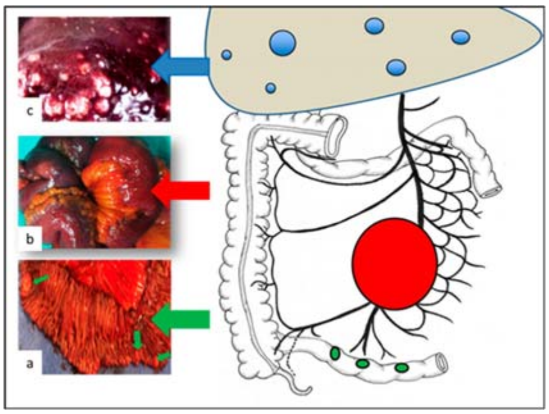


Figure 1. Classical presentation of small-intestinal neuroendocrine tumors (SI-NETs). (a) Primary tumors are usually small (<20 mm), located in the distal ileum, and multifocal in 30%–50% of cases; (b) Mesenteric lymph node metastases (MLNM) are present in over 80% of patients at diagnosis and are often larger than the primary tumor; (c) Liver metastases occur in approximately 50% of cases at diagnosis, typically multiple and affecting both lobes.

Preoperative imaging

Preoperative imaging for SI-NETs is both time- and resource-intensive, requiring a combination of anatomical and functional modalities. The primary goal is to accurately map and stage disease to guide treatment planning, though tumor burden is often underestimated across all imaging techniques [16,17].

Morphological imaging

Morphological imaging provides detailed anatomical information, such as lesion size and precise location. Contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI) are routinely employed for diagnosis, staging, and follow-up [14].

Functional imaging

Functional imaging offers whole-body assessment, allowing detection of both abdominal and extra-abdominal lesions, as well as evaluation of tumor behavior relevant to therapies like peptide receptor radionuclide therapy (PRRT). Three main functional imaging modalities are used in SI-NETs:

1. Somatostatin Receptor Imaging (SSTRI): Provides diagnostic, prognostic, and theranostic information. High uptake correlates with better survival and predicts PRRT efficacy [18, 19]. SSTRI includes somatostatin receptor scintigraphy and PET/CT with 68Gallium-labeled analogues (68Ga-DOTATOC, 68Ga-DOTATATE, 68Ga-DOTA-NOC), with 68Ga-PET preferred due to its superior sensitivity for well-differentiated NETs [20].

2. 18F-Fluorodihydroxyphenylalanine PET (FDOPA-PET): Offers excellent diagnostic accuracy relative to morphological imaging and SSTR scintigraphy, though comparisons with 68Ga-PET are limited [21–23]. FDOPA-PET lacks a theranostic role, and its prognostic utility remains under investigation. It can serve as an alternative when 68Ga-PET is unavailable.

3. 18F-Fluorodeoxyglucose PET (FDG-PET): Primarily provides prognostic information, as high FDG uptake is associated with poorer outcomes, even in well-differentiated SI-NETs [24–26]. Combining FDG-PET with SSTRI enables **metabolic grading**, which can outperform Ki67 in predicting tumor aggressiveness by offering whole-body assessment and reducing sampling bias.

Imaging of primary tumor(s)

Primary SI-NETs are not always detectable with imaging and may only be suspected in cases of typical MLNM with retractile mesenteritis or neuroendocrine liver metastases accompanied by elevated urinary 5-hydroxyindoleacetic acid (5-HIAA), in the absence of pancreatic or pulmonary tumors on CT. Additional non-invasive modalities, such as CT or MR enteroclysis and capsule endoscopy, can improve detection rates but do not replace intraoperative manual palpation, which remains essential for identifying small or multifocal lesions [16, 27, 28].

Imaging of mesenteric lymph node metastases (MLNM)

The challenge with MLNM lies not in detecting the nodes but in determining their resectability. Surgeons must carefully assess the lesion, avoiding assumptions that the MLNM complex is either inextricable or requires unnecessary laparotomy [29]. Preoperative evaluation should focus on the first jejunal arteries along the right side of the superior mesenteric artery using arterial-phase contrast-enhanced CT or MRI. Preservation of at least three jejunal arteries is typically considered necessary to maintain adequate vascularized small bowel length [29].

Our team has previously proposed a classification system based on the spatial relationship between MLNM and superior mesenteric vessels to guide surgical planning and predict resection feasibility **(Figure 2)** [29].

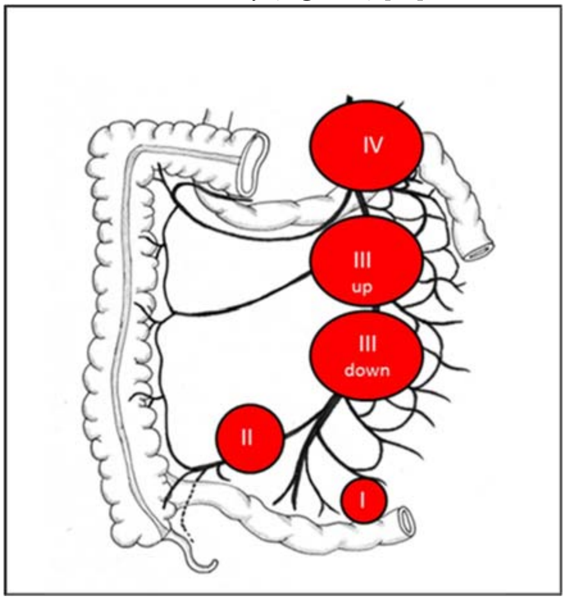


Figure 2. Classification of mesenteric lymph node metastases (MLNM) relative to the superior mesenteric vessels

Stage 0: No suspicious MLNM detected.
Stage I: MLNM located near the small intestine without involvement of the superior mesenteric artery (SMA) lymph nodes.
Stage II: MLNM involving distal SMA branches near their origin.
Stage III: MLNM involving the SMA trunk but sparing the first jejunal arteries; subdivided into III 'up' (<3–4 free jejunal branches) and III 'down' (>3–4 free jejunal branches).
Stage IV: MLNM involving the SMA trunk and the first jejunal arteries.

Imaging of liver metastases

Metabolic imaging alone is insufficient for preoperative assessment of liver metastases. Liver MRI, which demonstrates higher sensitivity than CT for detecting metastases [30, 31], is recommended to determine resectability. MRI protocols should include T2-weighted and diffusion-weighted sequences, which enhance lesion detection. Despite comprehensive imaging, additional metastases are often identified intraoperatively and on pathological examination, as fewer than 50% of liver metastases are detected preoperatively; micro-metastases (<1 mm) frequently occur outside the visible macro-metastases [32–34].
Liver metastases can be classified based on preoperative imaging:
Type I: Single metastasis of any size.
Type II: Single dominant metastasis with smaller lesions in both lobes.
Type III: Diffuse, bilobar metastatic involvement [35].

Peritoneal carcinomatosis imaging

Peritoneal carcinomatosis and ovarian metastases occur in approximately 20% and 4% of SI-NET patients, respectively [3]. CT and MRI have limited sensitivity for detecting peritoneal disease [36]. Similarly, metabolic imaging with FDOPA-PET or 68Ga-PET lacks full accuracy, as evidenced in small case series [16, 36]. Currently, no imaging modality reliably evaluates peritoneal involvement preoperatively.

Pre- and Perioperative Management of Hormonal Syndromes

The perioperative period is crucial for preparing patients for surgery, encompassing both general oncological optimization and SI-NET–specific interventions. General preparation includes nutritional support, optimization of comorbidities, and behavioral modification (e.g., smoking cessation), whereas SI-NET–specific preparation addresses carcinoid syndrome, carcinoid heart disease, and the prevention of carcinoid crisis. This review focuses on the SI-NET–specific aspects.

Diagnosis and management of carcinoid syndrome

Carcinoid syndrome presents with episodic facial flushing (60–85%), diarrhea (60–80%), abdominal cramps, hypotension, and intermittent bronchospasm [13]. Although preoperative prevalence is relatively low (~32.4%) [37], acute and chronic complications significantly affect survival and quality of life [38].
Diagnosis is confirmed via 24-hour urinary 5-hydroxyindoleacetic acid (5-HIAA), a serotonin metabolite, which demonstrates up to 100% sensitivity and 85–90% specificity [39]. Urinary 5-HIAA also quantifies syndrome severity and helps predict carcinoid heart disease risk. Plasma 5-HIAA is under investigation as a simpler alternative for screening and disease monitoring [40]. Chromogranin A is not recommended for preoperative evaluation but is commonly measured for follow-up.
Upon confirmation or suspicion of carcinoid syndrome, patients should begin antisecretory therapy with somatostatin analogues prior to any invasive procedures [41]. Current protocols do not specify fixed dosing, but commonly used regimens include:
Octreotide long-acting release (LAR): 20–30 mg intramuscularly every 4 weeks [42].
Lanreotide: 120 mg subcutaneously every 4 weeks [43].

Cardiac Evaluation

Carcinoid heart disease represents the most serious complication of carcinoid syndrome and primarily affects the right heart valves, particularly the tricuspid valve, causing regurgitation in up to 90% of cases and progressive right ventricular dysfunction [38, 44, 45]. It occurs in approximately 40% of patients with carcinoid syndrome [44].

Diagnosis relies on transthoracic echocardiography performed by a clinician experienced in carcinoid heart disease in SI-NET patients. Given that many patients are initially asymptomatic, the European Neuroendocrine Tumor Society (ENETS) recommends echocardiography for any patient with elevated urinary 5-HIAA, independent of symptomatic carcinoid syndrome [14]. Urinary 5-HIAA levels ≥300 µmol/24 h are an independent predictor of onset or progression of carcinoid heart disease [46].

Cardiac biomarkers such as N-terminal pro-brain natriuretic peptide (NT-pro-BNP) are both diagnostically and prognostically valuable. NT-pro-BNP demonstrates a sensitivity of 92% and specificity of 91% at a threshold of 260 pg/mL (31 pmol/L) [47, 48]. Significantly elevated NT-pro-BNP levels should prompt preoperative echocardiographic evaluation.

Once diagnosed, carcinoid heart disease requires cardiologic optimization prior to any oncologic surgery [44]. Management includes pharmacologic treatment of heart failure (e.g., diuretics) and administration of somatostatin analogues to control carcinoid syndrome and prevent disease progression. In cases of severe valvular regurgitation, cardiac valve surgery must precede abdominal surgery.

Prevention and Management of Carcinoid Crisis

Carcinoid crisis is an acute, potentially life-threatening extension of carcinoid syndrome, though its pathophysiology remains incompletely understood [49]. It can occur during any invasive procedure in SI-NET patients, manifesting as severe hemodynamic instability, arrhythmias, cardiac failure, and refractory bronchospasm, which may increase postoperative morbidity if prolonged [50, 51]. Major risk factors include the presence of liver metastases and a prior history of carcinoid syndrome, though crises may also occur in patients without these factors [50, 52].

Octreotide remains the primary pharmacologic agent for both prevention and management of carcinoid crisis, although evidence supporting its perioperative efficacy is limited and inconsistent [50–56]. Retrospective studies report varying rates of crisis despite octreotide prophylaxis, and only one controlled study demonstrated complete prevention of complications during surgery in treated patients [53]. Nevertheless, octreotide does not appear harmful, as it has not been associated with increased rates of anastomotic leakage.

Perioperative prophylaxis generally involves continuous octreotide infusion (100–500 mcg/h), particularly in high-risk patients [15, 25]. Anesthesiologists should remain prepared to manage crises using bolus octreotide and vasopressors (e.g., vasopressin, phenylephrine) to minimize hypotension and reduce postoperative complications.

Surgery

Surgical intervention is a cornerstone of SI-NET management and can be curative if complete R0 resection is achieved. However, R0 resection is attainable in only ~20% of patients due to advanced disease at diagnosis [57].

Surgery of primary tumor and mesenteric lymph node metastases with curative intent

Surgery remains the gold standard for curative treatment of SI-NETs. Key principles include resection of all primary tumors combined with systematic mesenteric lymphadenectomy, while preserving as much small bowel as possible to avoid short bowel syndrome [14, 15, 29, 57]. The extent of small bowel resection does not correlate with the number of lymph nodes removed.

A "pizza pie" approach, involving extensive resection of both small bowel and mesentery, is discouraged. Instead, a targeted resection of the tumor and associated mesenteric lymph nodes with bowel preservation is recommended **(Figure 3)** [25]. Such complex procedures are best performed in specialized centers with expertise in SI-NET surgery.

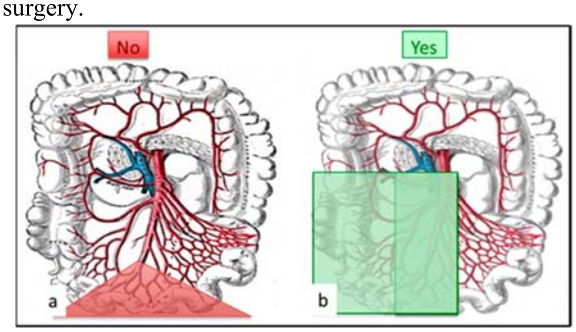


Figure 3. Surgical Approach: (a) Avoid the "pizza pie" approach: extensive intestinal resection with inadequate lymphadenectomy. (b) Appropriate lymphadenectomy entails removal of at least 8 (ideally 12) lymph nodes along with small bowel resection. Resection of the ileocecal valve and right colon may be necessary, particularly in LN-stage III patients

Exploration of the abdomen

Abdominal exploration is the initial step in SI-NET surgery, as preoperative imaging may miss up to 60–70% of lesions [17, 57, 58]. The surgeon must manually palpate the entire small bowel and inspect for peritoneal carcinomatosis, ovarian involvement, and liver metastases.

Manual palpation is essential to identify multiple synchronous tumors, which are undetected on imaging in over 60% of patients [6, 59, 60]. Nonetheless, palpation is not infallible, as additional lesions may be identified during pathological examination, highlighting the possibility of residual small primary tumors [17]. Following palpation, the surgeon marks the most proximal and distal tumors to define the bowel segment for resection.

The liver surface should also be carefully examined, as preoperative imaging fails to detect nearly half of liver metastases [34]. Intraoperative ultrasound can supplement palpation and visual inspection, although pathology often identifies even more metastases, particularly micro-metastases [32–34].

Surgery of mesenteric lymph node metastases (MLNM)

Lymphadenectomy constitutes the second step and should precede bowel resection. The extent of resection is guided by the remaining vascularized intestine after mesenteric dissection **(Figure 4)**. Lymphadenectomy can be technically demanding, especially with extensive mesenteric fibrosis or large MLNM encasing the superior mesenteric vessels (LN stage III).

Lymphadenectomy is indicated even for small primary tumors (<1 cm), as MLNM are present in approximately 80% of cases **(Table 1)** and their removal improves survival while preventing acute local complications [3, 7, 9, 17, 25, 61]. Despite broad consensus on its necessity, up to 20% of patients in large series do not undergo lymph node resection during SI-NET surgery [7, 8]. Surgeons should therefore recognize that lymphadenectomy is an essential component of curative SI-NET surgery.

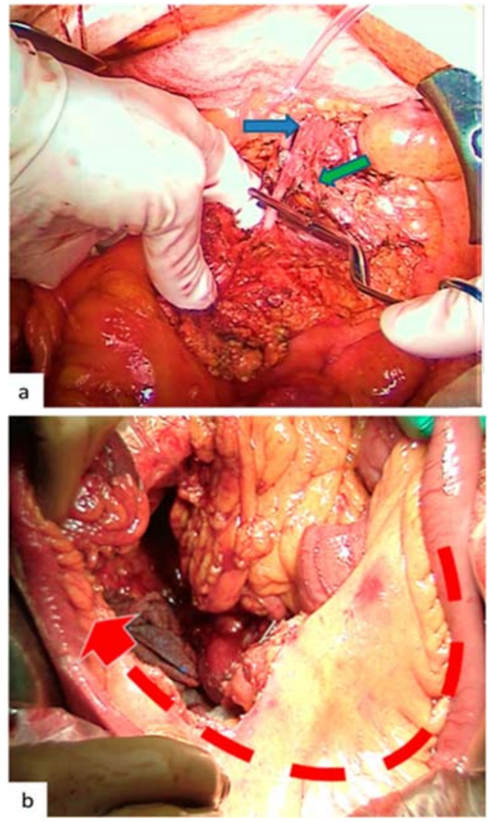


Figure 4. Operative view during the lymphadenectomy. (a) Clamping test after the dissection of the mesenteric superior artery and before the resection of the small bowel to visualize the remnant vascularized bowel. The blue arrow shows the mesenteric superior artery, and the green arrow shows the firsts jejunal arteries. (b) Small bowel vascularized by the remnant jejunal arteries

Table 1. Rate of MLNM in SI-NET

Author	Study Period	Patients(n)	Disease Stage	Presence of MLNM *(%)	Presence of MLNM When Primary Tumor <1 cm *(%)	Patients Without Any Lymph Nodes Resection(%)
Chen[9]	2004–2014	1925	Stage I-III	80.3	-	-
Landry[7]	1997–2004	1364	Stage I-IV	82	-	16.2
Motz[8]	1998–2013	11,852	Stage I-III	79.3	46.7	19.2
Norlén[3]	1985–2010	517	Stage I-IV	93	-	-

* when at least one lymph node was removed.

Lymphadenectomy

Retrospective registry analyses suggest that removing at least 8, and potentially up to 12, lymph nodes is associated with improved overall survival [7–9]. French guidelines recommend considering a “re-intervention” using FDOPA-PET or 68Ga-PET evaluation if fewer than 8 nodes were resected postoperatively, a scenario most often encountered following emergency surgery [25].

The upper limit of lymphadenectomy remains debated. In the absence of a retro-pancreatic target on preoperative imaging, dissection is typically limited to the trunk of the superior mesenteric vessels below the pancreas. However, Pasquer *et al.* reported skip metastases in 14 of 21 patients (mainly those with metastatic disease) and suggested extending dissection to the retro-pancreatic area [59]. The risk–benefit balance of such extensive surgery in patients without liver metastases is unclear due to potential morbidity. Lymphatic mapping using isosulfan or methylene blue, infrared fluorescent navigation, or radio-guided techniques may help define optimal lymph node harvest boundaries, though these methods are not yet standard practice [62–64].

Bowel Resection

The extent of bowel resection depends on: (i) the number of palpated primary tumors, (ii) their location (typically in the distal ileum), and (iii) the remnant vascularized intestine after mesenteric dissection. Proximal tumors may be treated with limited small bowel enterectomy to preserve the ileocecal valve and reduce postoperative intestinal symptoms. However, right hemicolectomy is often required due to tumor location in the terminal ileum or involvement of the right colic artery. Preservation of maximal small bowel length is crucial to prevent malabsorption and bile-salt-induced diarrhea [65]. Postoperative diarrhea, when present, may necessitate medical treatment (e.g., cholestyramine) or nutritional support [14].

Emergency surgery

Approximately 80% of SI-NET patients present with nonspecific symptoms predominantly related to MLNM rather than the primary tumor [4, 5, 66]. Between 12.5% and 33% require emergency surgery [5, 12, 67], most commonly for small bowel obstruction (80%), abdominal pain (10%), or less frequently, mesenteric ischemia, intussusception, or gastrointestinal bleeding [5, 12].

Emergency interventions carry challenges, including: (i) increased postoperative complications, (ii) suboptimal oncologic resection (incomplete lymphadenectomy, residual tumors, or excessive bowel resection), and (iii) higher risk of earlier recurrence [5, 12]. Referral to specialized centers is recommended [68], although full oncologic resection may not be possible emergently. In such cases, surgery should prioritize life-threatening conditions with limited bowel resection to facilitate later reoperation if needed. A subsequent re-intervention may be indicated when the initial procedure was non-optimal (R2 resection), fewer than eight lymph nodes were removed, bowel palpation was incomplete, or postoperative imaging shows residual disease [25].

Surgery of liver metastases in curative intent

About 50% of SI-NET patients have liver metastases at diagnosis [10]. Radical treatment of these lesions is the only potentially curative option and remains the standard of care, although it has not been rigorously compared with alternative therapies [35, 69]. Radical strategies include resection (metastasectomy, partial hepatectomy, or liver transplantation) alone or combined with percutaneous or intraoperative thermal ablation (radiofrequency or microwave). Liver-directed procedures can safely be combined with primary tumor resection and mesenteric lymphadenectomy [70].

Candidates for radical liver treatment should be evaluated in multidisciplinary meetings. ENETS guidelines recommend proceeding only if predicted morbidity is <30% and mortality <5% [71]. Ideal candidates include patients with: (i) type I or II liver metastases, (ii) stable disease, (iii) no extra-abdominal metastases on functional imaging, (iv) good performance status, and (v) absence of carcinoid heart disease [25, 68, 69]. For type II liver metastases, a two-stage approach may be performed: resection of left-lobe lesions with right portal vein ligation, followed by right hepatectomy [69, 72].

Despite achieving radical treatment, recurrence is common due to the presence of micro-metastases even after resection of macroscopic lesions [32–34, 73, 74]. Liver transplantation may be considered in selected patients with unresectable hepatic disease and no extrahepatic involvement, provided all extrahepatic lesions are resected pre-transplant. However, patient selection criteria remain imprecise [75]. Reported five-year overall and disease-free survival after liver transplantation ranges from 47–71% and 31–57%, respectively, suggesting that liver transplantation may be more palliative than curative [75].

Table 2. Recurrence after radical liver surgery for neuroendocrine tumor (NET) liver metastases

Author	Year	Patients (*n*)	Length of Follow-Up (Years)	Relapse (%)
Chen [76]	1998	3	5	67
Chamberlain [77]	2000	28	5	89
Jaeck [78]	2001	4	3	31
Sarmiento [73]	2003	90	10	94
Elias [79]	2003	14	10	89
Kianmanesh [72]	2008	23	4	48
Scigliano [80]	2009	41	5	78
Bertani [81]	2015	78	8	81

Peritoneal carcinomatosis

Peritoneal carcinomatosis occurs in roughly 20% of SI-NET patients [11] and is considered an independent factor for poor prognosis. Although not immediately fatal, it negatively impacts quality of life in about one-fifth of affected patients [3, 82]. When possible, complete surgical resection is considered the only potentially curative treatment. Surgery for peritoneal carcinomatosis may also improve prognosis and prevent local complications such as chronic obstruction and pain [15, 68, 83–85].

Peptide receptor radionuclide therapy (PRRT) appears to have limited efficacy in this setting. Merola *et al.* reported disease progression in nearly 40% of patients and complications such as bowel obstruction or ascites in approximately 30%, possibly due to radiation-induced peritonitis or paralytic ileus [82].

Perioperative scoring systems are used to assess the extent and resectability of peritoneal disease. The Peritoneal Carcinomatosis Index (PCI) is the most commonly applied, although it has not been validated specifically for SI-NETs. A PCI >20 may predict incomplete resection [86, 87]. To evaluate disease comprehensively, ENETS proposed the Gravity Peritoneal Carcinomatosis Score (GPS), which considers both peritoneal and extra-peritoneal disease locations. GPS has not been prospectively validated, but surgery is generally avoided in GPS-C patients (peritoneal disease with extensive liver involvement or extra-abdominal lymph node metastases) [83].

The role of hyperthermic intraperitoneal chemotherapy (HIPEC) remains uncertain. The largest series by Elias *et al.* reported high morbidity and no survival benefit in 28 SI-NET patients, leading to the abandonment of HIPEC as an adjunct [85]. Current NANETS and French guidelines do not recommend HIPEC in SI-NETs [15, 25]. It may be considered only in highly selected, fit patients with predominantly peritoneal disease, pending further studies.

Palliative Surgery

Palliative interventions aim to alleviate symptoms and delay fatal outcomes, primarily caused by liver failure from metastases or bowel complications. Cytoreductive surgery forms part of a multimodal palliative approach, though evidence from randomized trials remains limited.

Resection of local disease in the setting of unresectable liver metastases

Symptomatic local disease, which occurs in nearly 80% of patients, should be resected to relieve symptoms [15, 68, 88]. The management of asymptomatic primary tumors in the presence of unresectable liver metastases remains controversial, with only retrospective data available [89, 90].

Arguments for resection include: (i) prevention of local complications, (ii) control of locoregional disease to facilitate hepatic therapy, and (iii) potential improvement in overall survival. A recent meta-analysis suggested better five-year survival with resection (73.1% vs. 36.6%) and low 30-day mortality (<2%) [88]. However, Daskalakis *et al.* reported no survival advantage after propensity matching, though surgical interventions in the non-resected group may have influenced outcomes [90].

Guidelines vary: ENETS, UKINETS, NANETS, and TNCD recommend resection of asymptomatic local disease with unresectable liver metastases, whereas the NCCN does not [25, 69, 91, 92]. Ultimately, decisions should be made in a multidisciplinary setting, prioritizing resection for life-threatening mesenteric lymph node metastases (MLNM).

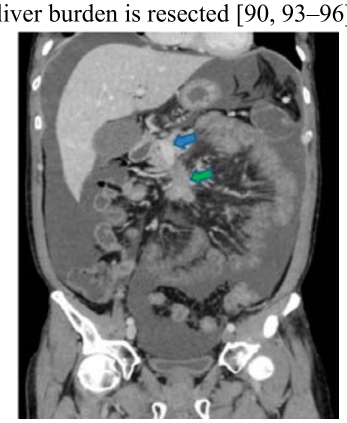
Palliative surgery for inextirpable bulky MLNM

Extensive MLNM with fibrosis may be unresectable when surrounding the mesenteric vessel origins (LN stage IV). Symptoms range from none to chronic mesenteric ischemia or bowel obstruction. Asymptomatic patients with collateral circulation may be managed medically. Symptomatic patients benefit from aggressive surgical intervention, including radical or partial debulking while preserving the first jejunal arteries to maintain small bowel vascularization **(Figure 5)** [15, 68, 88, 90, 93, 94]. Surgery should be performed at specialized centers [68].

If debulking is impossible or fails to relieve symptoms, placement of a self-expanding stent in the superior mesenteric vein via the portal vein has been attempted in a few cases, though results are inconclusive [90, 95].

Palliative debulking of liver metastases

In patients with unresectable liver metastases, palliative surgery and/or thermal ablation is part of a broader multimodal strategy that includes arterial embolization, chemoembolization, PRRT, and potentially liver transplantation. Although randomized trial evidence is lacking, palliative liver surgery may reduce local or hormonal symptoms and potentially improve survival. Clinical benefit is generally observed when 70–90% of the metastatic liver burden is resected [90, 93–96].



(a)

(b)

Figure 5. Mesenteric Ischemia from Extensive MLNM. (a) CT scan showing stenosis of the superior mesenteric vein (blue arrow) alongside mesenteric lymph node metastases (green arrow). (b) Surgical debulking performed to relieve mesenteric ischemia caused by lymph nodes encasing the mesenteric vessels

Surgical Approach: Open vs. Laparoscopic

Open laparotomy remains the preferred approach for curative SI-NET surgery because it allows complete inspection of the abdominal cavity, palpation of the small intestine, and precise control of the superior mesenteric vessels [68]. Purely laparoscopic procedures for curative intent are still debated [15, 57, 58].

Current recommendations from NANETS and ENETS favor a hybrid approach: laparoscopic assistance combined with manual palpation after externalizing the bowel through a hand port, as described by Wang *et al.* [15, 68, 97] **(Figure 6)**. This method is unsuitable when comprehensive lymph node removal is unlikely—for instance, in cases of large mesenteric metastases or nodes closely associated with the superior mesenteric artery [57]. Patients with retro-pancreatic lymph nodes, peritoneal carcinomatosis, or significant abdominal obesity that prevents bowel exteriorization are generally not candidates for this technique.

In palliative settings, laparoscopic resection may be preferable for removing primary lesions in patients with unresectable liver metastases, offering a less invasive alternative with potential recovery benefits.

Figure 6. Hybrid Surgical Procedure for SI-NETs (a) Laparoscopic preparation phase. (b) Externalization of the entire small intestine, right colon, and mesentery to allow thorough palpation. (c) Postoperative view showing limited surgical trauma

Prophylactic Cholecystectomy

Gallstone formation is common in SI-NET patients, with prevalence ranging from 36% to 63%, and a five-year cumulative risk of requiring cholecystectomy or biliary drainage near 20%, substantially higher than in the general population [98–101]. Major risk factors include long-term somatostatin analogue therapy and prior ileal resection [98, 102]. Additionally, ischemic cholecystitis may occur after trans-arterial embolization for liver metastases [103]. Current ENETS and NANETS guidelines recommend considering cholecystectomy during SI-NET surgery if long-term somatostatin analogue treatment is anticipated [14, 15]. This procedure generally does not increase surgical morbidity or mortality [104]. The decision should take into account technical aspects (emergency versus elective surgery, operative risk) and clinical factors (existing gallstones, history of biliary complications, planned somatostatin analogue therapy, or embolization) [14, 101].

Neoadjuvant Therapy

Preoperative tumor downsizing remains an appealing concept to convert non-resectable or borderline lesions (LN stage III–IV, liver metastases type II–III) into resectable ones. However, SI-NETs are typically resistant to cytotoxic and targeted chemotherapy, and somatostatin analogues, while prolonging survival, do not reduce tumor size. Peptide receptor radionuclide therapy (PRRT) has shown partial responses in about 18% of patients in the NETTER-1 trial [105], but evidence for its neoadjuvant use is limited to a few case reports with inconsistent outcomes [106]. Further studies are needed to clarify its role.

Postoperative Management

Follow-up Evaluation

Recurrence after curative R0 resection occurs in roughly 50% of SI-NET patients without distant metastases [5]. Due to the indolent nature of these tumors, metastatic recurrence may appear years later, necessitating surveillance for at least 20 years, or even lifelong in younger patients or those at high risk [15].

Follow-up typically combines anatomical imaging (CT or MRI with diffusion-weighted sequences), functional imaging (based on preoperative positive modalities), and biochemical markers (chromogranin A, 5-HIAA) at intervals of 3–6 months initially, then 6–12 months for five years, and annually or every five years thereafter [25, 107]. MRI is preferred for liver lesions due to lack of ionizing radiation, while CT can monitor extrahepatic sites. Biochemical markers may detect recurrence months before imaging, although evidence is mixed. NT-pro-BNP can be monitored to detect early cardiac involvement.

For unresected liver metastases, imaging and biochemical follow-up is recommended every 3–6 months initially, then spaced to 6–12 months for stable disease [25, 107].

Adjuvant therapy

There is no established systemic adjuvant therapy post-curative SI-NET resection [14]. Somatostatin analogues are reserved for antiproliferative or antisecretory purposes in metastatic or symptomatic disease [41, 42]. PRRT has shown improved progression-free survival in advanced SI-NETs progressing on somatostatin analogues [105], but its use as adjuvant therapy after curative resection is investigational (TERAVECT trial). Chemotherapy is not indicated in this setting.

Conclusions

Surgical management of SI-NETs presents unique challenges but can significantly improve both survival and quality of life. **Figure 7** presents an algorithm for surgical decision-making regarding local disease. Given the rising incidence of SI-NETs, surgeons should be aware of tumor-specific management considerations, including hormonal activity, common patterns of dissemination, and the importance of bowel-sparing techniques to prevent short bowel syndrome.

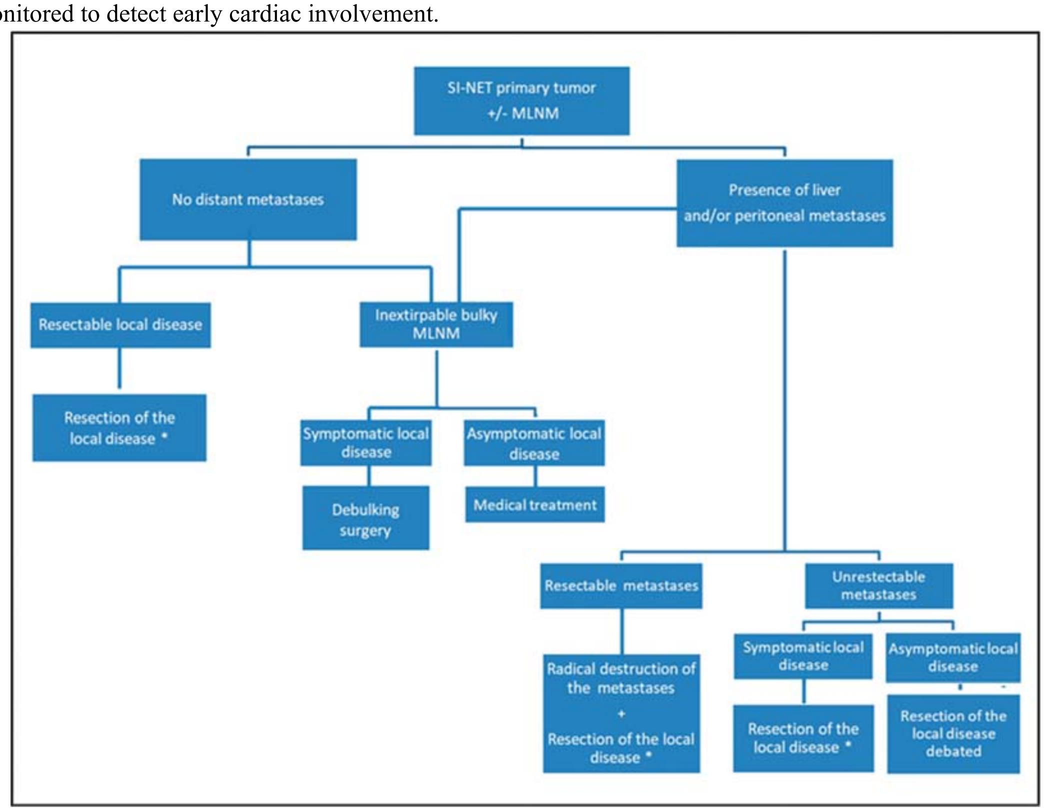


Figure 7. Proposed algorithm diagram for surgical indications of resection for SI-NET local disease

* Resection of all the primary tumors (after manual palpation of the entire small bowel) + systematic mesenteric lymphadenectomy (with at least 8 or 12 removed LN).

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