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Small Bowel Neuroendocrine Neoplasms: A Single Tertiary Center Real World Experience

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ABSTRACT

Background & Aims: Small bowel neuroendocrine neoplasms (SB-NENs) are a rare type of tumor that is clinically challenging and is often diagnosed in advanced stages. This retrospective study aimed to characterize the clinical presentation, diagnostic workup, and therapeutic strategies, as well as to evaluate the prognosis of patients managed in a tertiary care center in Bucharest, Romania, over five years.
Methods: We conducted an observational, retrospective cohort study on 42 cases of SB-NEN evaluated at our center between January 1, 2020, and March 31, 2025. Data regarding clinicopathological characteristics, treatments, and disease evolution were summarized. Overall survival was estimated at 1, 3, and 5 years.
Results: Computed tomography was the most frequently used imaging method for diagnosis (52.4%). Surgery was the most adopted method for obtaining the pathological specimen, used in 70.7% of cases. The majority of tumors were well-differentiated (85.6%). The overall survival distribution showed a median survival time of 94 months. The cumulative proportion of patients surviving at 1 year was 97.6%, at 3 years was 89.3% and at 5 years was 75.7%. There was a significant difference in overall survival stratified by tumor grading (p=0.006), indicating that this was a significant prognostic factor; the metastatic status and large tumors showed a trend toward statistical significance, but they did not meet the conventional threshold (p=0.068 and 0.103, respectively).
Conclusions: SB-NEN showed favorable outcomes, with surgery improving survival even in some metastatic cases. Lower tumor grade was associated with a better prognosis, while somatostatin analogues (SSA) therapy showed no survival benefit. Patients with large tumors and metastatic disease also showed a trend towards reduced survival.

Key words: small bowel – neuroendocrine neoplasm – surgery – computed tomography – chemotherapy – somatostatin analogue – NET – NEN – NEC.

Abbreviations: AST: aspartate aminotransferase; CS: carcinoid syndrome; CT: computed tomography; LDH: lactate dehydrogenase; ENETS: European Neuroendocrine Tumor Society; MRI: MRI: magnetic resonance imaging; NEC: neuroendocrine carcinoma; NEN: neuroendocrine neoplasm; NET: neuroendocrine tumor; NSE: neuron-specific enolase; NT-proBNP: N-terminal pro-brain natriureticpeptide; OS: overall survival; PRRT: PRRT: peptide receptor radionuclide therapy; SB-NEN: small bowel NEN; SSA: somatostatin analogues; UCCI: Union for International Cancer Control; 5-HIAA/24h: 5-hydroxyindoleacetic acid over 24h urine; ZES: Zollinger–Ellison syndrome.

INTRODUCTION

Neuroendocrine neoplasms (NENs) comprise a heterogeneous group of lesions originating from neuroendocrine cells. This category includes both well-differentiated neuroendocrine tumors (NETs) and poorly differentiated neuroendocrine carcinomas (NECs) [1]. Neuroendocrine tumors are further stratified by proliferative activity into low-grade (G1; Ki-67 < 3%), intermediate-grade (G2; Ki-67 3–20%), and high-grade (G3; Ki-67 > 20%) tumors [2].

The incidence of small bowel NENs (SB-NENs) has steadily increased, making them the most common primary small bowel (SB) malignancy today, surpassing adenocarcinoma and predominantly affecting the ileum [3]. Barsouk et al. [4] report an increase of up to 44% among small bowel neoplasms, while Scott et al. [1] report in 2020 an incidence in the US of 1.2/100,000.

Carcinoid syndrome (CS) is the hallmark of well-differentiated SB-NETs with established liver metastasis; in the presence of CS, the median overall survival (OS) is reduced from 7.1 years to 4.7 years. Caused by excessive secretion of serotonin and other amines, CS can be best assessed (diagnosis and monitoring of disease) by measuring urinary 5-hydroxyindoleacetic acid over 24h urine (u5-HIAA/24h), usually measured twice for accuracy. In general, the majority of patients report flushing and/or diarrhea and/or bronchospasm as main symptoms [5-7].

Other frequent functional syndromes are Zollinger–Ellison Syndrome (ZES) – peptic ulcers from gastrin – and insulinoma-related hypoglycemia. In contrast, non-functioning GI-NENs usually present with mass-related symptoms such as abdominal pain, obstruction, or jaundice [8-10].

Chromogranin A (CgA), once widely used, is no longer recommended for SB-NEN screening due to frequent false-positive results; however, it may support the diagnosis when malignancy is evident, renal or liver function is normal, and in the absence of proton pump inhibitor treatment. In patients with carcinoid syndrome, N-terminal pro-brain natriuretic peptide (NT-proBNP) serves as a marker for cardiac involvement, and it should be used in conjunction with cardiac ultrasound as a screening method for these patients. In aggressive NENs, elevated levels of neuron-specific enolase (NSE), lactate dehydrogenase (LDH), and aspartate aminotransferase (AST) may be helpful, particularly in SB-NEN G3 [11-15].

Morphologic imaging techniques, such as computed tomography (CT) or magnetic resonance imaging (MRI), assess tumor location, while functional imaging with ^{68}Ga–DOTATOC PET/CT scan provides a neuroendocrine-specific whole-body evaluation of disease extent. In unidentified primary tumors, endoscopic approaches (capsule endoscopy or enteroscopy) can aid in diagnosis, particularly for ileal lesions, as ~50% of SB-NENs arise in the ileum [16, 17].

Radical surgical resection remains the only potentially curative approach for SB-NENs and is recommended in both localized and metastatic settings [18]. Adequate lymphadenectomy and manual palpation of the entire small intestine is recommended, ideally performed in a high-volume center [11].

Due to the typically indolent nature of these tumors, recurrence can occur many years postoperatively [19]. Established risk factors for recurrence include advanced stage and a higher tumor proliferation index [20]. Regardless of functionality, in cases of advanced unresectable disease, first-line therapy with somatostatin analogues (SSAs) is indicated for well-differentiated, low-grade tumors for the antiproliferative effect [5, 11].

Additional therapeutic options include peptide receptor radionuclide therapy (PRRT), targeted agents such as Everolimus, and liver-directed treatments (e.g., embolization or image-guided thermal ablation) [21-23]. The prognostic value of palliative surgical interventions, including primary tumor resection in metastatic disease, remains a subject of ongoing debate [24-26].

This retrospective study aimed to characterize the clinical presentation, diagnostic workup, and therapeutic strategies, as well as to evaluate the prognosis of patients with SB-NENs managed at a tertiary care center in Bucharest, Romania, over five years.

METHODS

Study Design and Study Population

We conducted an observational retrospective cohort study on 42 cases of SB-NENs, including duodenal NENs, by searching hospital databases using ICD-10 codes. We examined records of all SB-NENs referred to or diagnosed at the Fundeni Clinical Institute, Bucharest, Romania, between January 1, 2020, and March 31, 2025. The study protocol was first approved by the Local Ethics Committee of the Fundeni Clinical Institute, Bucharest (62893/27.11.2024).

Two independent reviewers reviewed the complete electronic medical records, and only data from patients with histopathologically confirmed SB-NENs were selected. Tissue samples for confirming the neuroendocrine pattern were obtained through surgical resections or biopsies. Key exclusion criteria were benign disease and/or non-SB-NENs. Tumor characteristics, including size, location, lymphatic nodal involvement, distant metastasis at diagnosis, resection margins, and Ki-67 index, were assessed based on imaging procedures, intraoperative observations, and pathological evaluation. Patients presenting with hormone-related symptoms and elevated u5-HIAA levels were classified as having CS, and patients with elevated fasting gastrin levels and clinical symptoms consistent with hypergastrinemia were diagnosed with ZES. Grading was determined by tumor morphology and proliferative activity. Based on the Ki-67 index, tumors were classified as G1 (≤2%), G2 (3–20%), and G3 (>20%). Mitotic rates of <2, 2–20, and >20 per 10 high-power fields (HPF) corresponded to G1, G2, and G3, respectively. When Ki-67 and mitotic rate grades differed, the higher grade was assigned.

The last follow-up date was defined as the most recent patient contact recorded in medical records or the date of death. Follow-up consisted of clinical evaluations and biomarker assessments every three to six months. Imaging evaluations, including CT scans, MRI, and functional imaging, were performed every six to twelve months, tailored individually based on clinical indications.

Statistical Analyses

Data were analyzed using SPSS v20.0 (IBM, Armonk, NY). Normality was assessed with the Kolmogorov-Smirnov test. Parametric data were reported as mean ± SD, while non-parametric data were reported as median (min–max). The independent t-test was used for normally distributed variables, and the Mann-Whitney U test was used for non-normally distributed data. Categorical variables were presented as percentages and compared using Fisher's exact test. Survival curves were generated using the Kaplan-Meier method and were compared with the log-rank test. Two-tailed P-values were reported, and a p-value of less than 0.05 was considered statistically significant.

RESULTS

We identified 42 SB-NEN cases evaluated in our center from 2020 to 2025. More than half of them were males (54.8%), with a median age at diagnosis of 61.5 years. The majority of the population lived in urban areas (81%). The most frequent localization site was jejuno-ileum (83.3%), and in 18 patients, the diagnosis was established by tumor-related symptoms. Half of them had the oncology department as their initial admitting (T0) department, and 28.6% had CS at diagnosis. The presence of comorbidities was noted in 59.5% of subjects. Table I presents the baseline characteristics of the patients.

Table I. Baseline characteristics of SB-NEN subjects (n=42)

Characteristic	N (%)
Male gender	23 (54.8)
Median age [years (range)]	61.5 (39-77)
Urban area [n (%)]	34 (81)
Localization site	
Duodenum	6 (14.3)
Jejuno-ileum	35 (83.3)
Small bowel, Unspecified	1 (2.4)
Diagnosis	
By symptoms related to functional syndrome	7 (16.7)
By tumor-related symptoms	18 (42.9)
By screening programs for other tumors	1 (2.4)
Unknown/Incidental finding	16 (38.1)
T0 department	
Surgery	7 (16.7)
Gastroenterology	12 (28.6)
Internal Medicine	2 (4.8)
Oncology	21 (50)
Functional syndrome	12 (28.6)
Carcinoid syndrome	2 (4.8)
Gastrinoma/ZES	1 (2.4)
Other	
Presence of comorbidities	25 (59.5)

Computed tomography was the primary diagnostic imaging method at baseline, used in 52.4% of cases. Magnetic resonance imaging was used in 11.9% of cases, and endoscopic ultrasound (EUS) was used in only 2.4%. In 7.1% of cases, multiple imaging modalities were needed. Notably, in 26.2% of the cases, the specific imaging method was undocumented, as some patients were addressed to our unit only for a particular treatment.

Surgery was the most used method for obtaining the pathological specimen, adopted in 70.7% of valid cases. Endoscopic ultrasound fine-needle biopsy accounted for 12.2% of cases, while fine-needle aspiration was used in 9.8%. Percutaneous hepatic biopsy was the least common method, applied in 7.3% of cases. The specimen originated from the primary tumor in 51.2% of cases, from both primary tumors and metastases in 31.7% of cases, and from metastases alone in 17.1%.

The pathological features of the 42 patients included in this study are detailed in Table II. The majority of lesions were NETs (85.6%), while poorly differentiated (NECs) accounted for only 4.8% of cases. Tumor grading revealed that 47.6% were classified as G1, 38.1% as G2, and a small proportion (4.8%) as G3. The proliferation index, assessed by Ki-67, was ≤20% in most patients (78.5%), whereas only 4.8% had a Ki-67 index greater than 20%; data were unavailable for 16.7% of patients.

Table II. Neuroendocrine tumors pathology data

Characteristic	N (%)
Differentiation [n (%)]	
Well	36 (85.6)
Poor	2 (4.8)
Not available	4 (9.6)
Grade [n (%)]	
1	20 (47.6)
2	16 (38.1)
3	2 (4.8)
Not available	4 (9.5)
Primary tumor stage (as per ENETS-UICC system) [n (%)]	
pT1	0 (0)
pT2	5 (11.9)
pT3	13 (31)
pT4	7 (16.7)
Not available	17 (40.5)
Regional lymph node metastases [n (%)]	
N0	4 (9.5)
N1	17 (40.5)
N2	4 (9.5)
Not available	17 (40.5)
Sites of metastases [n (%)]	
Liver	17 (40.5)
Liver and Extrahepatic	2 (4.8)
Extrahepatic	2 (4.8)

ENETS: European Neuroendocrine Tumor Society; UICC: Union for International Cancer Control.

Staging of the primary tumor, based on thethe European Neuroendocrine Tumor Society (ENETS) - Union for International Cancer Control (UICC) system, revealed that pT3 was the most common stage (31%), followed by pT4 (16.7%) and pT2 (11.9%). However, tumor stage was not available in 40.5% of cases. Regarding lymph node involvement, 40.5% had N1 disease, 9.5% had N2 disease, and another 9.5% had no lymph node metastasis (N0). Data on nodal status were missing for 40.5% of patients. Metastatic sites were predominantly confined to the liver (40.5%), with 4.8% presenting with both liver and extrahepatic metastases, and another 4.8% with only extrahepatic involvement.

Thirty-five patients (83.3%) underwent surgical resection of their primary tumor, including nine patients (21.4%) with metastatic disease. In only two patients (5.7%), recurrence after surgery with curative intent was noted. The most frequent surgical intervention was small bowel segmental resection in 23 cases (54.8%), followed by right hemicolectomy in 6 cases (14.3%). Regarding the surgical indications based on urgency, 27 surgeries were elective (77.1%), four were urgent (11.4%), and the remaining 4 were emergency surgeries (11.4%).

Nine patients (47.3%) with liver metastases were considered suitable for liver resection, either concomitant with primary tumor resection, in cytoreductive surgery, or as a separate procedure. Four patients (21%) benefited from liver-directed therapies (transarterial chemoembolization) as part of their metastases management.

Lymph node involvement was assessable in 21 of the 42 patients (50%). Among these, 19.0% had less than one metastatic lymph node, 28.6% had between one and three positive nodes, and 52.4% presented with more than three involved lymph nodes. The majority of patients with available data (52.4%) exhibited a higher burden of nodal disease. The median number of lymph nodes retracted was 10, with a median number of involved lymph nodes of 4.5. The lymph node ratio, meaning the ratio between the lymph nodes involved and the lymph nodes retracted (LN ratio), was 0.38.

A total of 30 patients received SSA therapy with Octreotide LAR (70%), Lanreotide Autogel (20%), or they switched from one molecule to the other (10%). The most frequently used chemotherapeutic regimen was capecitabine and temozolomide, administered in 15% of cases. Other regimens included capecitabine and oxaliplatin in 5%, capecitabine alone in 2.5%, and cisplatin combined with etoposide in 2.5% of cases. Regarding the number of chemotherapy lines, 67.5% of patients received no chemotherapy, while 17.5% received one line, 10% received two lines, and 5% underwent three lines of treatment. Everolimus was used in 10% of patients.

The median follow-up time was 40 months. Death was documented in 12 patients (28.6%). The Kaplan–Meier curve for OS is shown in Fig. 1. The OS distribution showed a median survival time of 94 months.

The cumulative proportion of patients surviving at 1 year was 97.6%, at 3 years was 89.3% and at 5 years was 75.7%. These findings suggest relatively favorable survival outcomes over the observed period.

A total of 42 patients were included in the survival analysis stratified by different variables. The results are detailed in Table III.

The OS was also stratified by tumor grading, as shown in Fig. 2. At both 1 and 3 years, the survival rates were high for G1 (95% and 83.3%) and G2 (100% and 81.8%) tumors, suggesting a good short- to mid-term prognosis. However, by 5 years, survival declined in both groups, more markedly in G2 (to approximately 47.7%) compared to G1 (approximately 57.1%). The outcome for G3 was uniformly poor, with no survival beyond 1 year.

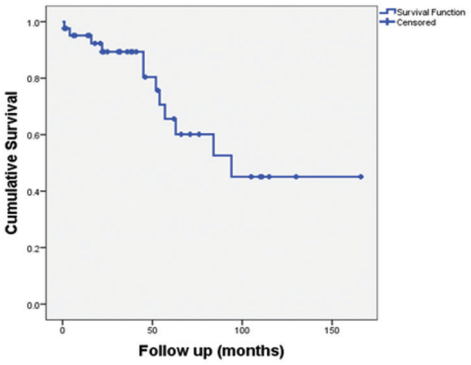

Fig. 1. Kaplan-Meier curve of overall survival.

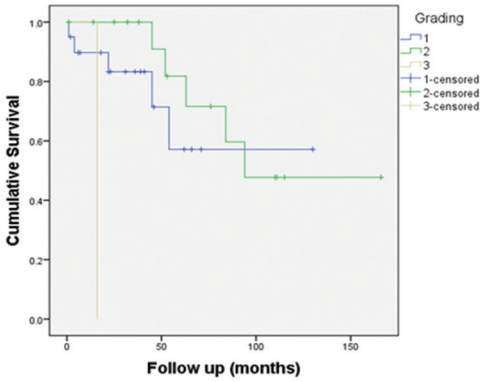

Fig. 2. Kaplan-Meier curves for overall survival stratified by tumor grading.

The log-rank test demonstrated a significant difference in survival across the three grading groups (χ^2=10.286, p=0.006), indicating that tumor grade was a significant prognostic factor.

DISCUSSION

The purpose of this retrospective study, which comprised 42 patients, was to explore the clinicopathological features and outcomes of SB-NEN cases at a tertiary center in an

Table III. Overall survival stratified by different variables

Stratification	Group	1-Year OS, %	3-Year OS, %	5-Year OS, %	Median OS (months) (95%CI)	Mean OS (months) (95%CI)	p
Gender	Female	88	68.4	46.9	57.0 (42.4–71.6)	75.2 (49.6–100.9)	0.101
	Male	90.6	81.6	69.9	Not reached	123.3 (93.1–153.5)	
Tumor size	≤30 mm	96.8	81.7	53.8	Not reached	91.1(69.0–113.2)	0.103
	>30 mm	90	80	40.0	57.0 (50.8–63.2)	52.5(33.6–71.3)	
Metastatic status	Non-metastatic	95.2	83.7	62.7	Not reached	130.2 (95.8–164.6)	0.068
	Metastatic	94.1	59.3	30.5	63.0 (49.3–76.7)	73.0 (50.0–95.9)	
Tumor grading	Grade 1	95	83.3	57.1	Not reached	77.7(47.4–108.0)	**0.006**
	Grade 2	100	81.8	47.7	94.0	89.7 (61.0–118.3)	
	Grade 3	100	0	0	16.0 (only one patient)	16.0 (only one patient)	
SSA treatment	Octreotide LAR	100	87.7	59.8	Not reached	123.5 (93.6–153.5)	0.454
	Lanreotide Autogel	80	53.3	Censored <5y, ↓ to 0% by 115 months	Not reached	80.1 (: 43.7–116.6)	

OS: overall survival; SSA: somatostatin analogues.

Eastern European country over the past 5 years. Demographic characteristics and prognostic factors of survival identified in our study are in accordance with those previously reported.

The most common site of involvement in our study population was the jejuno-ileum (83.3%), which is consistent with rates reported in the existing literature as being the most frequently involved segment of the small bowel [10, 27-29]. Carcinoid syndrome was present in 28.6% of cases at diagnosis, and 45.3% of patients had liver metastases, consistent with the majority of published data describing a frequency of CS in neuroendocrine pathology ranging from 19% to 35% [5, 28-32]. A recent Ottawa cohort study showed that approximately **41%** of patients with SB-NET had stage IV disease at the time of initial diagnosis [28].

Notably, approximately 50% of the patients initially presented to the Oncology Department. This can be attributed to the fact that these individuals were diagnosed in other medical units and subsequently referred to the Oncology Department for treatment and follow-up care.

As a first method of diagnosis, CT scan was used in 52.4% of cases, in accordance with its established role as one of the first-line imaging modalities in SB-NENs due to its high availability and diagnostic accuracy when using optimized, multiphasic protocols [11, 33, 34]. Although MRI was only used in 11.9%, the literature supports its superior sensitivity for detecting small hepatic metastases using hepatocyte-specific contrast agents [34]. A subset of patients lacked specific documented imaging, as they were referred for treatment rather than diagnostic evaluation.

Surgical resection was the predominant method for obtaining the pathological specimen (70.7%), consistent with SB-NEN management guidelines, which advocate surgery as both a diagnostic and therapeutic method in localized disease. Furthermore, most surgical interventions were scheduled as elective procedures, patients being referred to our tertiary high-volume center from other hospitals or different specialties, in accordance with ENETS guidelines, which also recommend, if possible, that surgery be performed in specialized centers [11].

EUS-guided FNB/FNA was used in ~22% of cases, especially when surgical sampling was not indicated or feasible [35].

The predominance of NETs (85.6%) and G1 and G2 lesions mirrors literature findings, which report the majority of SB-NENs as being well-differentiated, similar to a 10-year cohort from Ottawa with 84% well-differentiated lesions [28, 33, 36, 37].

The predominance of pT3 stage (31%) is followed by pT4 (16.7%), primarily due to the late diagnosis of SB-NENs, which often exhibit nonspecific symptoms and are challenging to examine via standard imaging or endoscopy. Lymph node positivity (N1 in 40.5%, N2 in 9.5%) aligns with known high rates (30–40%) of nodal metastases at presentation [38, 39]. Our median number of lymph nodes retracted was 10, which is also in accordance with the data previously published in the literature that suggests a minimum of 8 retrieved lymph nodes to have a lower rate of disease recurrence after R0 resection [40-43].

However, missing complete staging data in 40.5% is a consequence of the retrospective design of the study and variations in work-up. Liver metastases (40.5%) were most common, reflecting metastatic patterns in SB-NENs. A smaller proportion had combined liver and extrahepatic metastases (4.8%) or isolated extrahepatic metastases (4.8%), consistent with aggressive or advanced disease scenarios.

In our cohort, 83.3% of patients underwent surgical removal of the primary tumor, including 21.4% with metastatic disease, and postoperative recurrence was low (5.7%). The current guidelines also recommend primary tumor resection even in metastatic settings, to prevent complications such as bowel obstruction and to potentially improve survival outcomes [44-47]. Regarding the most used surgical technique, segmental small bowel resection predominated (54.8%), followed by right hemicolectomy (14.3%), in accordance with published data [48, 49].

Among patients with liver metastases, 47.3% underwent liver resection and 21% received locoregional therapy (TACE). Evidence supports cytoreductive surgery for metastatic SB-NEN, surgical resection being associated with prolonged survival compared to the standard of care [24, 45, 47]. In our subset of 21 patients with nodal assessment, 80.9% had at least one positive lymph node, with 52.4% exhibiting high nodal burden (>3 nodes). These findings are consistent with published data indicating that mesenteric lymph node metastases are present in over 80% of SB-NEN cases at diagnosis [11].

A total of 71.4% patients were treated with SSA, and 10% received the mTOR inhibitor Everolimus. SSAs are standard first-line therapy due to their antiproliferative and symptom-control effects, with demonstrated positive impact on time to disease progression and progression-free survival as shown by PROMID and CLARINE trials and other studies [11, 44, 50-55]. Treatment with SSAs did not show a significant impact on survival in our cohort, but this result should be interpreted with caution, given the relatively small number of treated patients.

Chemotherapy was less frequently used. The CAPTEM (capecitabine + temozolomide) regimen was used in 15% of cases, with other combinations (capecitabine + oxaliplatin, cisplatin + etoposide) administered to even fewer patients. CAPTEM is increasingly recognized as effective in well-differentiated NETs, particularly in pancreatic NENs, though data are more limited in midgut SB-NENs [11, 56, 57].

Our cohort had a median follow-up of 40 months, with 12 deaths (28.6%) and a median OS of 94 months. The OS rates were 97.6% at 1 year, 89.3% at 3 years, and 75.7% at 5 years, indicating relatively favorable outcomes. These survival rates are consistent with prior reports [29, 33]. For example, a large Canadian series showed a 5-year OS of 100%, 91%, 97%, and 73% for stages I–IV, respectively [28].

Stratified survival analysis exhibited key prognostic factors. Tumor grade was a statistically significant factor (p=0.006), with G1 tumors showing sustained survival (~57% at 5 years), G2 tumors exhibiting lower survival (~47.7%), and G3 tumors showing uniformly poor outcomes. This pattern is also described in the specific literature as G1 NETs often exhibit minimal mortality, G2 intermediate, and G3 poor prognosis [11, 58]. Daskalakis et al. [59] proposed recently a reclassification of grading based on 5% and 10% cut-offs that proved more indicative of survival outcomes.

Although metastatic status suggested clinically meaningful differences, the log-rank test showed a borderline result (p=0.068), indicating a trend toward statistical significance that did not meet the conventional threshold. The difference might have been limited by sample size. These findings are comparable to existing data, which show that localized SB-NENs have a 5-year OS of 70–100%, versus 35–60% when metastases are present [28], even higher than the rate reported by Modlin et al. [60] that showed five-year survival rates at all disease stages of 62.6 +/- 1%

Therefore, our data support the recognized survival benefit of adequate primary and metastatic resection followed by SSA or systemic therapies.

Other factors (sex, tumor size, and SSA type) did not reach statistical significance, although a trend consistent with existing reports was observed: smaller tumors (<30 mm) and males tended to have more prolonged survival.

To our knowledge, this is the first study in a Romanian population to assess the treatment options and outcomes of SB-NENs in a well-defined cohort in a tertiary center. The inclusion of diverse clinical and pathological parameters, along with standardized data abstraction methods, strengthens the analysis and highlights key factors that influence outcomes. Despite its single-center design, the extended data collection period and manual validation of electronic records by multiple independent reviewers provide a solid foundation for evaluating therapeutic strategies and advancing the understanding of SB-NEN characteristics and management, offering valuable insights from an Eastern European cohort.

The main limitations of this study include its retrospective, single-center design and relatively small cohort size, which may reduce statistical power and the reliability and confidence in the study's conclusions. The lack of a control group further constrains the evaluation of treatment efficacy. Additionally, diagnostic delays during the COVID-19 pandemic (2020–2022) may have led to more advanced disease at presentation, which could potentially affect outcomes. These factors should be considered when interpreting the findings and their relevance to broader clinical settings.

Despite limitations such as sample size and retrospective design, our data provide meaningful real-world insights from a Romanian population, which is underrepresented in the literature. Future prospective studies with longer follow-up period would help refine survival analysis and stratify subgroups more precisely.

CONCLUSIONS

The study highlights favorable survival outcomes in patients with SB-NENs, with a median OS of 94 months and a 5-year survival rate of 75.7%. Surgical resection, even in selected liver-metastatic cases, was associated with prolonged survival, highlighting its central role in the management of the disease. Tumor grading significantly influenced prognosis, with G1 and G2 tumors showing considerably better outcomes compared to G3 tumors. Trends also suggested worse survival in patients with larger tumors and metastatic disease, though not statistically significant.

Conflicts of interest: None to declare.

Authors' contribution: R.I.D, T.S., and D.I. conceived and designed the study; A.G.P, V.B., T.D., G.B., V.H., I.G.L., M.C.G., and G.C. collected data. D.I. performed the statistical analyses. R.I.D. drafted the manuscript. A.E.C., V.M.C. and T.S. revised and edited the manuscript. M.M., C.G., L.G. and P.C. were responsible for the project administration. All authors critically revised the manuscript, approved the final version to be published, and agree to be accountable for all aspects of the work.

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