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Original Article

Locally advanced gastrointestinal stromal tumors: Surgical strategies and outcomes in a referral hospital in Sub-Saharan Africa

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ABSTRACT

Introduction: Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the gastrointestinal tract but remain rare overall. Locally advanced forms present therapeutic challenges, particularly in low-resource settings.

Methods: We conducted a descriptive cross-sectional study with retrospective data collection at the Hubert Koutoukou Maga National University Hospital Center (CNHU-HKM) in Benin. All patients with locally advanced GIST managed between January 2010 and January 2025 were included. Clinical features, management strategies and surgical outcomes were analyzed.

Results: Nine patients with locally advanced GIST were identified (male-to-female ratio 3.5:1). The stomach was the most frequent primary site (n = 5). Adjacent organ invasion involved the pancreas (n = 5), the spleen (n = 5), and the colon (n = 2). Seven patients received neoadjuvant imatinib. Seven patients underwent open surgical resection, which included en bloc removal of the primary tumor along with the involved adjacent organs or structures, in order to achieve complete (R0) resection whenever technically feasible. At last follow-up, five patients were alive (including one awaiting reoperation for local recurrence), three were lost to follow-up, and one had died.

Conclusion: This small series demonstrates the feasibility of integrating neoadjuvant therapy with surgery for locally advanced GIST in a low-resource African setting. The high rate of R0 resections achieved underscores the value of multimodal management, even in contexts where diagnosis is often delayed and therapeutic resources are limited.

1. Introduction

Gastrointestinal stromal tumors (GISTs) are mesenchymal neoplasms arising most frequently from the interstitial cells of Cajal or their multipotent precursors (Corless et al., 2004). Although they represent the most common mesenchymal tumors of the gastrointestinal tract, they account for only 0.2% of all digestive malignancies, with an estimated incidence of 12–15 cases per million inhabitants per year in countries such as France (Corless et al., 2004; Kindblom et al., 1998). Their histological and molecular features are now well established (Hirota et al., 1998).

Historically, surgical resection was the only therapeutic option for GISTs, yielding poor outcomes in advanced stages. The introduction of tyrosine kinase inhibitors (TKIs), particularly imatinib, has revolutionized management (Demetri et al., 2002; Verweij et al., 2004). Targeted therapy has substantially improved survival in patients with

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unresectable tumors and has enabled new multimodal strategies, involving neoadjuvant therapy followed by surgery (Rutkowski et al., 2013).

Locally advanced GISTs represent a major therapeutic challenge. They are typically characterized by large tumor size, infiltration of adjacent organs, or anatomical locations that render upfront surgery technically difficult, highly morbid, or at high risk for incomplete resection (R1/R2) (Casali et al., 2022). In such cases, neoadjuvant treatment aims to downsize tumors, facilitate R0 resection, reduce surgical morbidity, and potentially lower recurrence risk (Iwatsuki et al., 2018). Although international guidelines endorse this approach (Iwatsuki et al., 2018), its implementation and outcomes vary widely between settings, according to resource availability, access to TKIs, and surgical expertise.

In Sub-Saharan Africa, and specifically in the Republic of Benin, cancer management faces unique challenges: delayed diagnosis, limited access to immunohistochemistry and molecular testing, inconsistent availability of systemic therapies, restricted surgical resources, and low universal health coverage (Sharma et al., 2023). For GISTs, the lack of routine molecular profiling, inconsistent drug supply, and the need for specialized surgical expertise may compromise optimal care. In a previous retrospective study conducted by our team at the same institution over a 10-year period (2010–2020), we reported 15 cases of GIST of all stages, with locally advanced forms accounting for the majority (8/15) (Gbessi et al., 2022). This earlier work highlighted the predominance of advanced presentations but did not specifically examine clinicopathological characteristics or the surgical management of locally advanced GISTs, which are the focus of the present study.

This study reports the experience of our team at a referral hospital in Benin over a longer period (2010–2025) in managing locally advanced GISTs. We describe the neoadjuvant and surgical strategies implemented, as well as postoperative outcomes, while highlighting the contextual challenges of delivering comprehensive care in a resource-limited setting.

2. Patients and methods

We conducted a descriptive cross-sectional study with retrospective data collection at the Hubert Koutoukou Maga National University Hospital Center (CNHU-HKM), the national referral center for cancer care in Benin. Cases were identified through the archives of the departments of visceral surgery and gastroenterology at CNHU-HKM. All patients with locally advanced GIST managed between January 2010 and January 2025 were reviewed. Inclusion criteria were histologically and immunohistochemically confirmed GISTs fulfilling the definition of locally advanced disease, defined as tumor infiltration of at least one adjacent organ based on clinical, radiologic, or intraoperative findings (Pracht et al., 2024). Metastatic GISTs and cases showing discordance between histopathological and immunohistochemical findings were excluded. The modified Joensuu National Institutes of Health (NIH) risk classification was applied for recurrence risk assessment when available in the pathology report. Vital status was ascertained using active follow-up methods: phone contact where available and home visits when necessary. According to the institutional protocol, neoadjuvant imatinib was administered at a standard dose of 400 mg/day. The intended duration of treatment was nine months, provided that no radiologic progression was observed. Tumor response was assessed every three months using contrast-enhanced CT scans. Because RECIST (Response Evaluation Criteria in Solid Tumors) criteria could not be systematically applied in our setting, radiologic response was assessed based on changes in maximal tumor diameter and clinical improvement. Dose escalation to 800 mg/day was recommended only in cases of documented progression under standard-dose therapy. Data were entered into Epidata 4.6 and analyzed with Epidata Analysis version 3.0.0.1. Given the small sample size, analyses were descriptive only.

3. Results

Nine cases of locally advanced gastrointestinal stromal tumors (GISTs) were identified during the study period. All patients included in this study fulfilled the operational definition of locally advanced disease, with unequivocal invasion of at least one adjacent organ. We did not encounter borderline presentations during the review period.

Patients' ages ranged from 40 to 68 years, with a clear male predominance (male-to-female ratio = 3.5:1; 7 men and 2 women). The stomach was the most common primary site (n = 5), followed by the colon (n = 1), jejunum (n = 1), rectum (n = 1), and greater omentum (n = 1), corresponding to an extragastrointestinal stromal tumor (EGIST). Tumor invasion involved adjacent structures depending on the primary location, including the pancreas (n = 5), spleen (n = 5), colon (n = 2), jejunum (n = 1), abdominal wall (n = 1), diaphragm (n = 1), and perirectal tissues (n = 1) (see Fig. 1).

In one case, the histopathological diagnosis was established through laparoscopic biopsy; in six cases, biopsy was performed endoscopically, and in the two remaining cases, the diagnosis was made on the surgical specimen after resection. Histological examination revealed spindle-cell morphology in eight cases and epithelioid morphology in one case (Fig. 2). Seven of the nine patients received neoadjuvant imatinib at the standard dose of 400 mg/day, according to the institutional protocol. The intended duration of treatment was nine months, with contrast-enhanced CT scans performed every three months. Because RECIST criteria could not be systematically applied in our setting, radiologic response was assessed based on variations in maximal tumor diameter and clinical improvement. No patient showed radiologic progression during neoadjuvant therapy. Among the nine patients, seven underwent open surgical resection (Fig. 3), while the remaining two were lost to follow-up before surgery. None of the 7 operated patients experienced any major postoperative complication, and there were no cases of perioperative mortality. Resection margins were assessable in all resected patients and were complete (R0) in every case (7/7). Adjuvant imatinib therapy was subsequently indicated in seven cases. Adherence to adjuvant imatinib therapy varied among patients, primarily due to treatment-related adverse effects—most notably skin lightning, which had sociocultural implications in the local context—and irregular follow-up. Some patients who became asymptomatic after surgery chose to discontinue treatment before completing the recommended 6-year course of adjuvant imatinib for high-risk GIST, as defined in the

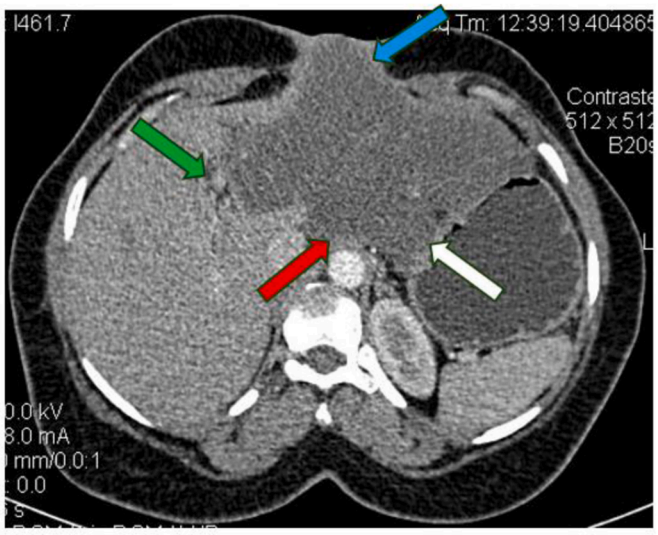

Fig. 1. Locally advanced gastric GIST (white arrow) invading the anterior abdominal wall (blue arrow), liver (green arrow), and major abdominal vessels (red arrow).

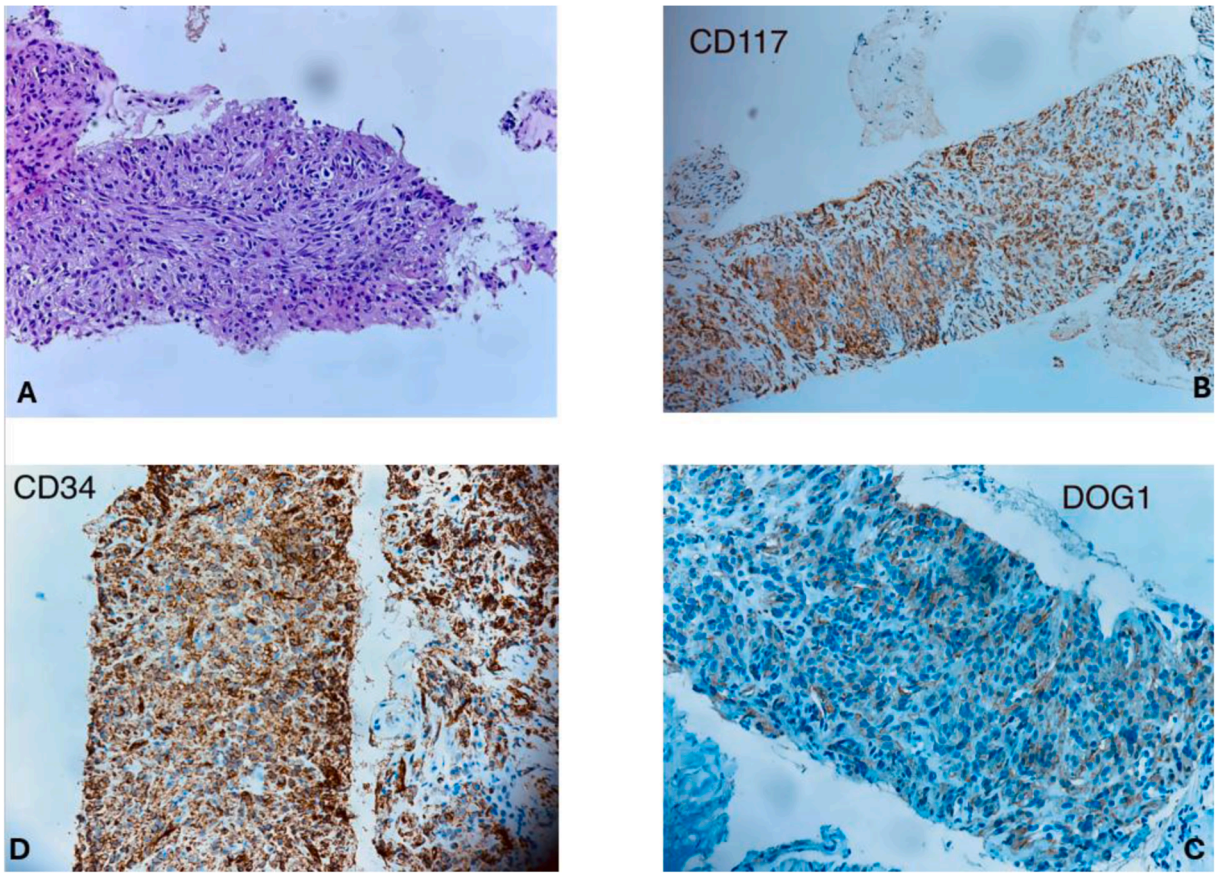

Fig. 2. Spindle-cell GIST (**A**) with immunohistochemical expression of CD117 (**B**), DOG1 (**C**), and CD34 (**D**). Courtesy of Dr. Takin Romulus.

Thésaurus National de Cancérologie Digestive—the national French guideline adopted in our institution (Pracht et al., 2024). The duration of follow-up ranged from 1 to 6 years. One patient died 4 years after surgery, outside the hospital, in a context of disease recurrence following poor adherence to adjuvant imatinib therapy. Another patient experienced a local recurrence at 5 years and is currently awaiting reoperation, also with a history of suboptimal adherence to adjuvant therapy.

Detailed patient characteristics are summarized in Table 1.

4. Discussion

4.1. Epidemiological and clinical considerations

Gastrointestinal stromal tumors (GISTs) are rare digestive neoplasms. Only nine cases of locally advanced forms were identified over a 15-year study period in our institution, a national referral hospital serving a population of approximately 14 million inhabitants. This finding highlights both the rarity of these tumors and the diagnostic challenges encountered in African settings.

Our findings are consistent with previous regional reports, including those of Gbessi et al. from the same hospital, who reported 15 cases of GIST of all stages over a 10-year period, with locally advanced forms being predominant (8 out of 15 cases) (Gbessi et al., 2022).The male predominance observed in our series contrasts with most Western cohorts, which generally report either a balanced sex distribution or a slight female predominance (Søreide et al., 2016). Gastric localization accounted for two-thirds of cases, consistent with international data (60–70% in large series) (Casali et al., 2022).

Preoperative endoscopic biopsy was performed in six patients, in line with current recommendations advocating histologic confirmation and c-KIT expression assessment before initiating neoadjuvant therapy. The high proportion of positive preoperative biopsies in our series contrasts with previous reports indicating that superficial endoscopic biopsies performed with standard forceps are usually negative, as the tumor originates and develops within the muscularis propria of the gastrointestinal wall. Our findings may suggest, although not definitively, that endoscopic biopsies are more likely to be diagnostic in locally advanced GISTs, possibly due to mucosal ulceration or deeper tumor extension at presentation (Casali et al., 2022; Pracht et al., 2024). The indication for a biopsy—whether performed via endoscopic ultrasound guidance, percutaneous route, or surgical approach—should be considered on a case-by-case basis. When conducted percutaneously or laparoscopically, such procedures carry a risk of bleeding and potential peritoneal dissemination (Casali et al., 2022; Joensuu et al., 2012).

4.2. Role and perspectives of neoadjuvant imatinib in the management of locally advanced GISTs

In this study, the predominant management strategy was neoadjuvant targeted therapy. Only two patients underwent upfront resection, both due to the absence of preoperative histological confirmation and intraoperative discovery of the tumor mass. Wide and potentially mutilating excision is justified only when it allows complete removal of the tumor with a clear margin of healthy tissue around its circumference, thereby minimizing the risk of tumor rupture. Such an aggressive approach should, however, be adapted according to the organs involved and the patient's overall condition (Pracht et al., 2024).

The predominant use of neoadjuvant imatinib in our series aligns with European Society for Medical Oncology (ESMO) guidelines. Prospective studies (Demetri et al., 2007) have reported response rates of 60–80%, allowing conversion of initially unresectable tumors to resectable disease.

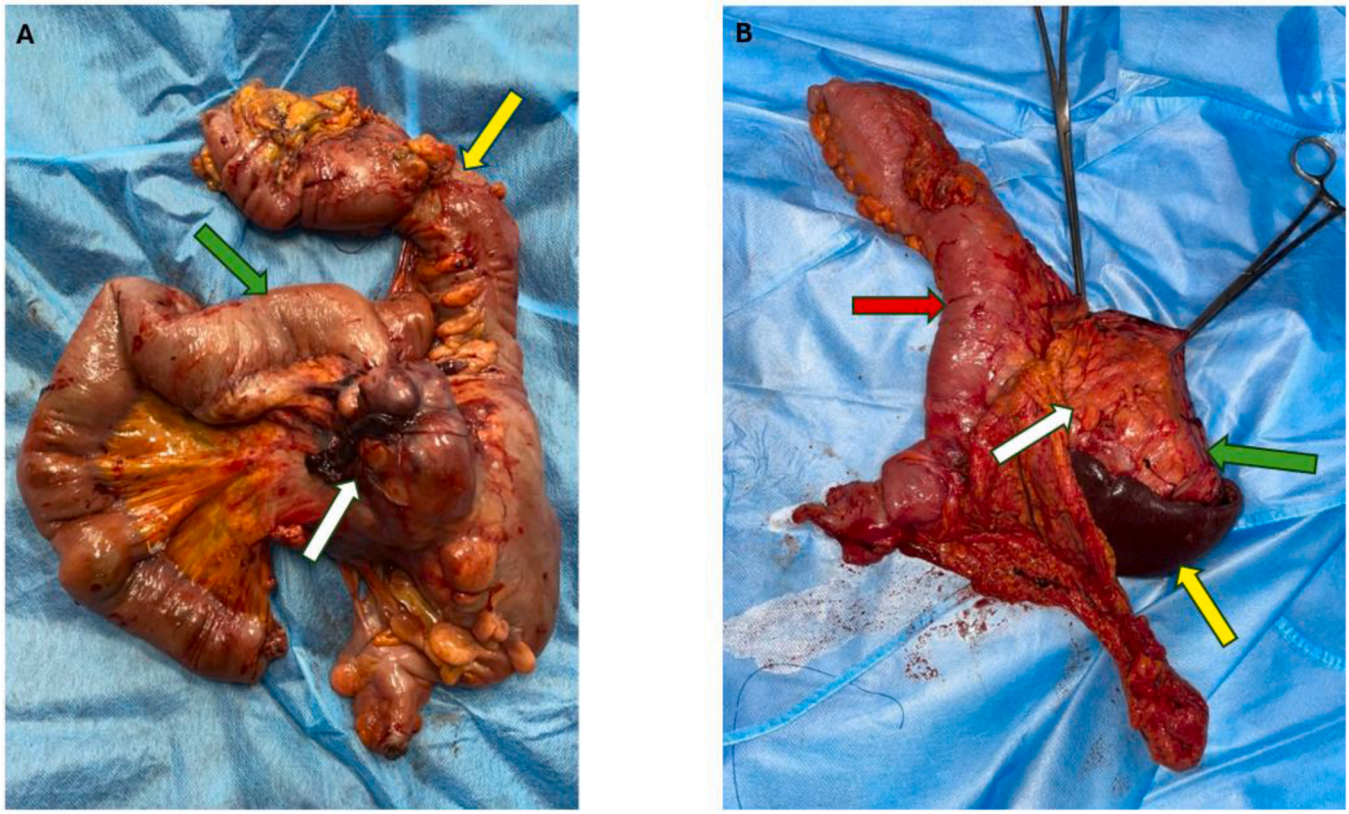

Fig. 3. Surgical specimens obtained after nine months of neoadjuvant imatinib, showing a favorable treatment response. **(A)** Surgical specimen of a left colectomy (yellow arrow) extended to the first jejunal loop (green arrow) for a locally advanced GIST (white arrow). **(B)** Surgical specimen of an atypical gastrectomy (clamp) extended to the pancreatic tail (green arrow), spleen (yellow arrow), and left colic flexure (red arrow) for a locally advanced GIST (white arrow**).**

The complete (R0) resection rates achieved in our center compare favorably with international reports, which describe R0 rates of 85–95% following neoadjuvant imatinib (Demetri et al., 2007). This study demonstrates that integrating neoadjuvant imatinib with surgery is both feasible and effective in managing locally advanced GISTs in resource-limited African settings.

Although our sample is small, the high R0 resection rate observed in our cohort is consistent with reports from high-volume centers and underscores the critical role of tumor response in facilitating optimal surgical outcomes. Cai et al. have recently proposed a refined prognostic model to better assess therapeutic benefit and optimize surgical and adjuvant decision-making (Li et al., 2024). Although such tools are not yet routinely available in our context, our findings reinforce the importance of a multimodal approach and underscore the need to adapt emerging prognostic strategies to low-resource environments.

4.3. Surgical implications of locally advanced GISTs in sub-saharan Africa

Adjacent organ invasion was frequent in our series, underscoring the technical complexity of surgical management in these cases. Extended en bloc resections were consistently required, with the primary goal of achieving complete (R0) tumor removal.

The surgical management of locally advanced GISTs in sub-Saharan Africa presents deep and multidimensional challenges, largely driven by socioeconomic disparities and systemic healthcare limitations.

Delayed diagnosis remains the foremost obstacle, with most patients presenting at an advanced stage with large, symptomatic, and locally invasive tumors that complicate primary surgical resection (Afuwape et al., 2011).

Limited access to neoadjuvant tyrosine kinase inhibitors (TKIs) such as imatinib—due to prohibitive costs and inconsistent availability—deprives surgeons of a crucial tool for tumor downsizing and safer R0 resections (Henke et al., 2020).

Intraoperatively, surgeons often face the absence of advanced dissection instruments, limited transfusion capacity, and a lack of intraoperative monitoring systems, making these procedures technically demanding and increasing postoperative morbidity (Achanga et al., 2025).

Additionally, the scarcity of pathology laboratories capable of performing immunohistochemistry (CD117, DOG1) and molecular testing results in diagnostic delays and hampers accurate risk stratification, which is critical for guiding adjuvant therapy (Kim and Lee, 2024).

Consequently, surgical strategies must be adapted to resource-limited environments, aiming for macroscopically complete resections while minimizing morbidity in systems where postoperative management and sustained access to TKIs remain uncertain (Afuwape et al., 2011).

4.4. Impact of limited access to targeted therapy and molecular biology

In Benin, imatinib is provided free of charge through an initiative supported by the Max Foundation (The Max Foundation).

Molecular analysis plays a pivotal role in surgical decision-making, particularly in cases of locally advanced GIST where resection would be extensive or potentially mutilating and the likelihood of achieving complete excision is uncertain. In such circumstances, initiating neoadjuvant imatinib therapy represents a rational alternative, provided that mutational testing identifies a genotype predictive of therapeutic response.

Table 1
Clinical, pathological, therapeutic, and outcome characteristics of patients with locally advanced GIST.

Patient	Age at diagnosis (years)	Sex	Tumor site	Invaded organs	Pre-op biopsy[a]	Histology	Immunohistochemistry	Neoadjuvant therapy	Surgery/ Resectability	Resection status	Recurrence risk	Adjuvant therapy[b]	Survival	Comments
01	68	Male	Stomach	Spleen, pancreas	Yes (laparoscopy)	Spindle cell	KIT+, DOG1+	Imatinib-9 Months	Atypical gastrectomy with en bloc resection of the pancreatic tail and spleen	R0	High	Imatinib	Alive (6 years)	Imatinib interrupted; local recurrence; awaiting reoperation
02	62	Female	Jejunum	Transverse colon	No	Spindle cell	KIT+, $CD34^{+}$	No	En bloc resection involving segmental resection of the jejunum and transverse colon.	R0	High	Imatinib	Deceased (5 years)	A tumor was discovered during a laparotomy performed for bowel obstruction and was resected. Postoperative treatment with imatinib was initiated but adherence irregular
03	43	Male	Greater omentum	Abdominal wall	No	Spindle cell	KIT+	No	Omentectomy with en bloc resection of the involved abdominal wall	R0	High	Imatinib	Alive (4 years)	A laparotomy was performed for an abdominal mass associated with hemoperitoneum following a road traffic accident
04	66	Male	Stomach	Pancreas and Spleen	Yes (Endoscopy)	Epithelioid	KIT+, DOG1+, $CD34^{+}$	Imatinib-9 Months	Atypical gastrectomy with en bloc resection of the pancreatic tail and spleen	R0	High	Imatinib	Lost to follow-up (after surgery)	Patient lost to follow-up after surgery and initiation of Imatinib
05	40	Male	Stomach	Spleen, distal pancreas, diaphragm	Yes (Endoscopy)	Spindle cell	KIT+	Imatinib-9 Months	Total gastrectomy with en bloc splenectomy, distal pancreatectomy, and diaphragmatic resection	R0	High	Imatinib	Alive (4 years)	N/A
06	41	Male	Stomach	Pancreas and Spleen	Yes	Spindle cell	KIT+	Imatinib-9 Months	Lost to follow-up	N/A	N/A	N/A	Lost to follow-up (before surgery)	N/A
07	63	Female	Stomach	Spleen, pancreas, left colon	Yes (Endoscopy)	Spindle cell	KIT+, DOG1+	Imatinib-9 Months	Atypical gastrectomy with en bloc resection of the pancreatic tail, spleen, and left colic flexure	R0	High	Imatinib	Alive (1 year)	N/A
08	65	Male	Descending colon	First jejunal loop	Yes (Endoscopy)	Spindle cell	N/A	Imatinib-9 Months	Left colectomy with en bloc resection of the first jejunal loop	R0	High	Imatinib	Alive (1 year)	N/A
09	46	Male	Rectum	Perirectal tissues	Yes (Endoscopy)	Spindle cell	KIT+, DOG1+	Imatinib-9 Months	Lost to follow-up	N/A	N/A	N/A	Lost to follow-up (before surgery)	Favorable response on imatinib; refused surgery; lost to follow-up.

[a] Pre-op biopsy: histological confirmation obtained before surgery.
[b] *For GISTs at high risk of recurrence, adjuvant imatinib is recommended for a planned duration of 6 years* (Pracht et al., 2024).

Moreover, GISTs harboring certain mutations—particularly those involving exon 9 of the *KIT* gene—require a double standard dose of imatinib (800 mg/day instead of 400 mg) to achieve optimal therapeutic response (Gronchi et al., 2010). Although some studies have demonstrated only a progression-free survival (PFS) advantage without a significant overall survival (OS) benefit, this difference may still hold clinical relevance by improving resectability or quality of life (Gastrointestinal Stromal Tumor et al., 2010).

In our setting, molecular genotyping is entirely unavailable, and treatment decisions regarding tyrosine kinase inhibitor (TKI) dosing cannot be guided by mutational status. Consequently, all patients in this series received the locally available standard dose of imatinib at 400 mg/day, according to the hospital protocol used in our institution. In the absence of mutational testing—particularly for KIT exon 9 variants, which may require an 800 mg/day regimen—our local protocol recommends an empirical escalation to a double dose (800 mg/day) only in cases of documented radiologic progression under standard-dose therapy.

Finally, imatinib remains the only targeted agent freely available for GIST treatment in the country. In cases of resistance, no alternative TKIs are accessible for resource-limited patients. Consequently, the absence of molecular biology capabilities and the unavailability of second-line TKIs significantly limit our ability to tailor therapy according to mutational status or to offer appropriate alternatives in the event of resistance.

4.5. Study limitations

The main limitations of our study include the small sample size, missing data (particularly regarding survival outcomes and recurrence risk), heterogeneous follow-up, and loss to follow-up in approximately one-third of patients. These factors limit the generalizability of our findings and preclude inferential statistical analysis.

Furthermore, owing to the retrospective nature of the study and incomplete documentation in several medical records, certain operative parameters—such as estimated intraoperative blood loss and standardized reporting of postoperative complications (e.g., Clavien–Dindo classification)—were not consistently available. As a result, these variables could not be incorporated into the analysis. Nevertheless, it is important to note that no major postoperative complications or perioperative mortality were recorded among the operated patients.

5. Conclusion

This study suggests that, even in resource-limited settings, a multimodal approach combining neoadjuvant imatinib with surgery can facilitate complete resection of locally advanced GIST and may improve operative feasibility. Although based on a small retrospective cohort, the consistently favorable responses to neoadjuvant therapy and the high rate of R0 resections observed here support the integration of this strategy in similar contexts where delayed diagnosis and limited access to molecular testing remain major challenges. Strengthening molecular diagnostic capacity, ensuring continuous availability of tyrosine kinase inhibitors, and implementing structured long-term follow-up programs could further enhance outcomes for patients with locally advanced GIST in Sub-Saharan Africa.

CRediT authorship contribution statement

Freddy Houéhanou Rodrigue Gnangnon: Writing – review & editing, Writing – original draft, Validation, Methodology, Data curation, Conceptualization. **Ismaïl Lawani:** Writing – review & editing, Validation, Conceptualization. **Sonia Fernande Djedeme:** Writing – review & editing, Writing – original draft, Validation, Formal analysis, Data curation. **Adémola Lionel Destiny Padonou:** Writing – original draft, Investigation, Data curation. **Roland Goudou:** Writing – original draft, Validation. **Dansou Gaspard Gbessi:** Writing – review & editing, Writing – original draft, Validation. **Aboudou Raïmi Kpossou:** Writing – review & editing, Writing – original draft, Validation. **Jean Sehonou:** Writing – review & editing, Writing – original draft, Validation.

Ethics approval

This study represents a partial analysis of the research protocol on the Epidemiology and Prognostic Factors of Digestive Cancers in Southern Benin. The protocol was reviewed and approved by the Health Sciences Research Ethics Committee (Comité Local d'Éthique pour la Recherche Biomédicale) of the University of Parakou, Benin (Ref: 1093/2025/CLERB-UP/P/SP/SA). Written informed consent was obtained from patients whose images appear in this article. For the retrospective review of medical records, the ethics committee granted a waiver of additional consent.

Reporting guideline

This study adheres to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement for cross-sectional studies; a completed checklist is available upon request.

Availability of data and materials

The anonymized dataset supporting the findings of this study is available from the corresponding author upon reasonable request and with the required authorization from CNHU-HKM, in accordance with institutional and national data protection policies.

Note on the use of artificial intelligence

In the preparation of this article, the authors occasionally used a generative AI tool (ChatGPT, OpenAI) to assist with linguistic refinement and translation. All content was reviewed, validated, and finalized by the authors.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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