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REVIEW ARTICLE

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Strategies for care of patients with gastrointestinal stromal tumor or soft tissue sarcoma during COVID-19 pandemic: A guide for surgical oncologists

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Abstract

The coronavirus disease-2019 (COVID-19) pandemic is deeply impacting the accessibility of cancer patients to surgery. In resource-limited conditions, the standard of care might not be deliverable, but evidence to support alternative management strategies often exists. By revisiting available treatment options, this review provides surgical oncologists with an evidence-based framework for treating patients with gastrointestinal stromal tumor, extremity/truncal soft tissue sarcoma, and retroperitoneal sarcoma to rapidly adapt their decision-making to the constant evolution of the COVID-19 pandemic.

KEYWORDS

COVID-19, gastrointestinal stromal tumor, retroperitoneal sarcoma, sarcoma, soft tissue sarcoma

1 | INTRODUCTION

The coronavirus disease-2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is redefining medical care and priorities globally. Elective surgery has been drastically reduced and surgical wait lists are subject to rolling reprioritization. Navigating cancer care within this larger framework presents the clinician with multiple logistical and ethical challenges. Surgical oncologists are faced with deviating from standard practice in an attempt to balance the needs of and risks to individuals with cancer with the demands of healthcare systems that are in crisis.[1] Even under normal operating conditions, the appropriate management of patients with soft tissue sarcoma (STS) requires complex decision making by experts. STS tumor biology is highly variable as there are more than 100 histological subtypes.[2] Many of the surgical procedures for STS are also complex, requiring careful preoperative planning with multiple surgical teams, and can be resource intensive (blood products, intensive care, ventilators, etc). Outcomes of patients with STS are improved when care is provided at

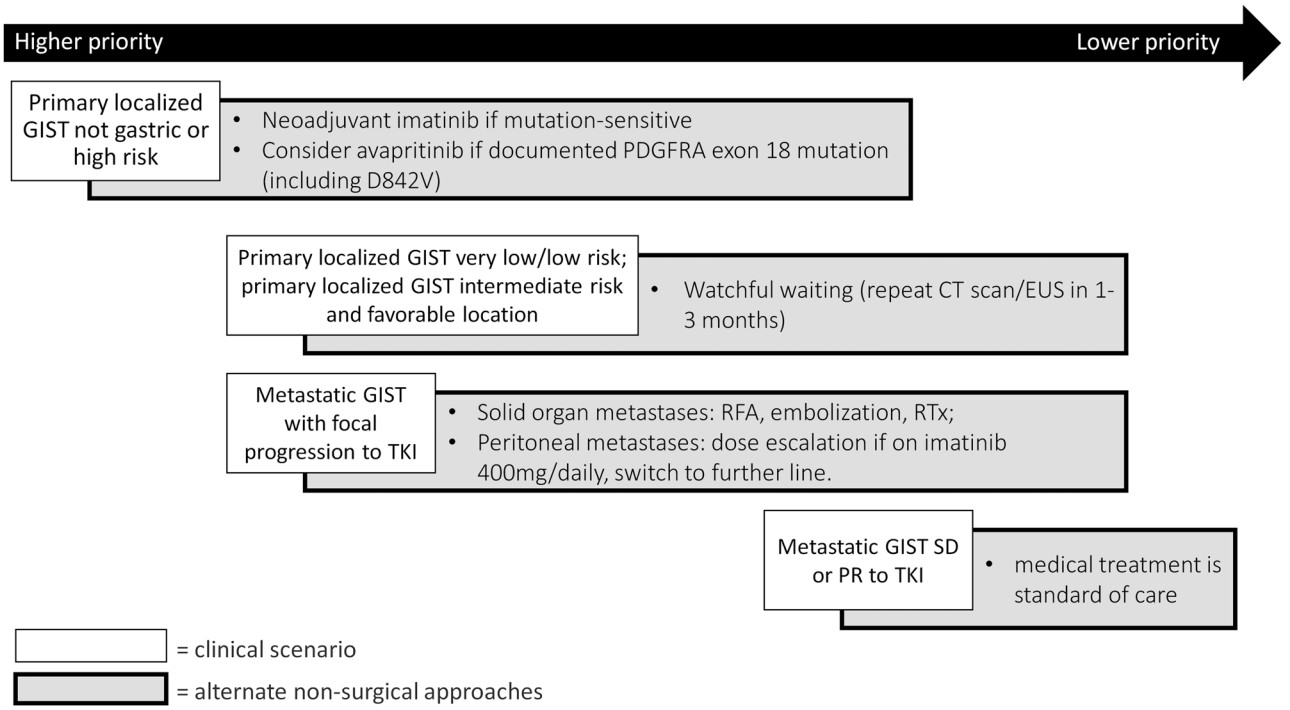

FIGURE 1 Prioritization of surgical intervention in elective patients with gastrointestinal stromal tumor (GIST). This framework is intended to guide prioritization for elective surgery in GIST patients. Surgical emergencies/urgencies (i.e., tumor bleeding, progressive unrelenting symptoms) are not covered. Patient categories represent the most common clinical scenarios. Patient priority and alternate treatments should be personalized and discussed in the context of multidisciplinary tumor boards. The different spacing between boxes on the priority line reflect a conceptual difference in patient prioritization as suggested by Hanna et al.[15] EUS, endoscopic ultrasound; GIST, gastrointestinal stromal tumor; PDGFRA, platelet-derived growth factor receptor alpha; PR, partial response; RFA, radiofrequency ablation; RT, radiotherapy; SD, stable disease; TKI, tyrosine kinase inhibitor

high-volume expert centers; however, this poses an additional challenge in the pandemic landscape.[3–6]

Documents briefly discussing prioritizing principles and alternative options for patients with STS have been released by the Society of Surgical Oncology, by the European Society of Medical Oncology, and by the French Sarcoma Group.[7–9] However, decision making under crisis/resource-limited conditions requires analysis of multiple variables that are interrelated and vary by jurisdiction. These variables include the local pandemic phase, availability of the full spectrum of medical resources; institutional policies, and prevailing cultural values related, as an example, to the perception of risk. Evidence-based guidelines for a rare tumor type are challenging to generate and follow at the best of times. In the face of an evolving pandemic or similar catastrophe, this challenge is compounded. Clinicians will benefit from guidance that is based on what applicable evidence exists, specialized expert opinion, and common sense.

In this article, we aim to provide data that illuminate the appropriate prioritization of STS surgery in times of crisis, and that support the selection of alternative multimodality management options, to assist surgeons in optimizing the care of patients with gastrointestinal stromal tumor (GIST) and STS in the context of the present COVID-19 pandemic, and beyond.

2 | APPROACH

In the majority of primary GIST and STS, surgery is the curative modality. As the benefit of surgery is limited in locally recurrent and metastatic patients, we focus on primary GIST and STS, highlighting risk stratification, the perceived impact of delayed surgery, the projected burden of resource utilization along with surgical morbidity, and restricted indications for urgent surgery. We review the evidence for alternative nonsurgical approaches that may be employed until definitive surgical management can be performed and highlight their known relevant limitations. Finally, a framework to prioritize patients for surgery in resource-limited conditions is provided for each disease site.

3 | GASTROINTESTINAL STROMAL TUMOR

The curative treatment for localized GIST is surgery. Indications for surgery for patients with GIST include curable primary tumor, limited focal progression of recurrent/metastatic disease on tyrosine kinase inhibitors (TKI), and treatment of complications.

The chance of tumor recurrence, and thus the chance of cure, after complete surgery depends upon tumor site, size, mitotic rate,

and intraoperative tumor rupture. These factors are combined in risk-stratification tools such as the modified NIH criteria, the Miettinen and Lasota classification, the GIST nomogram, or the prognostic contour maps.[10–13] Some of these tools are categorical and distinguish low-risk versus intermediate-risk versus high-risk patients, who have a 10-year progression-free survival when treated with surgery alone of about 90% or higher versus 80%–90% versus 30%–60%, respectively.[12]

These risk-stratification tools were developed based on series of patients treated with surgery to predict the *chance of tumor recurrence* after resection. Nevertheless, there is evidence suggesting that the *progression rate* of GIST left untreated might correlate with these same risk categories, with high-risk GIST progressing more rapidly.[14] Hence, risk stratification tools might be useful to inform the choice of alternative treatments to surgery.

Criteria for assigning priority for surgery in patients with GIST and alternative multimodality management options in the face of the COVID-19 pandemic are discussed in the following paragraphs and summarized in Figure 1 and Table 1.

3.1 | Surgical resources and anticipated morbidity

Resource utilization and postoperative morbidity associated with resection of GIST vary with tumor site and type of operation. Less complex procedures with lower morbidity include endoscopic resections of gastric or rectal GIST, partial gastrectomy (postoperative complications after wedge resection 4%–12%), local resection of the duodenum (90-day morbidity 24%, ≥grade 3 complications 5%), segmental small bowel resection, and local excision of rectal GIST (perioperative ≥3 complications related to the rectal repair 17%).[16–20] More resource-intensive procedures include multivisceral resections, total gastrectomy, pancreaticoduodenectomy (90-day morbidity 70%, ≥grade 3 complications 43%), and abdominal-perineal resection.[19]

In terms of surgical technique, outside the current pandemic laparoscopy was shown to be less resource intensive (shorter OR time, shorter hospital stay, limited blood loss) and safe (less overall complications) in patients with small bowel and gastric GIST, though there is likely an inherent selection bias.[21–23] In the specific scenario of the COVID-19 pandemic, concerns regarding the theoretical risk of viral transmission to healthcare workers via aerosolization during laparoscopy have been raised, especially at the pandemic outbreak. Surgical societies have recommended modifications of the surgical practice to minimize this potential risk. Recommendations included the use of adequate personal protective equipment, enhancement of OR ventilation, use of lower CO_2 pressure, use of smoke extractors and CO_2 filters, minimization of the use of energy devices. In the lack of evidence about the laparoscopy-associated risk of SARS-CoV-2 transmission, the decision to pursue laparoscopy should be personalized weighting individual patient risk, safety of the operating room environment, and expected benefit from the minimally invasive approach.[24,25] Use of neoadjuvant imatinib does not appear to significantly increase perioperative morbidity, while surgery in patients on Sunitinib is associated with a complication rate as high as 54%.[26,27] Thus, the extent of intervention and anticipated use of resources is variable across GIST patients, and assessment of other key tumor features including risk category and local resource allocation will aid in determining if upfront surgery can be performed or if alternate strategies are necessary.

3.2 | Alternate nonsurgical approaches

3.2.1 | Watchful waiting

Watchful waiting is a management option already routinely considered in patients with gastric GIST less than 2 cm, which are very low or low risk.[28,29] This approach may be considered for gastric GIST more than 2 cm or for smaller GIST in other locations, while being mindful of increasing risk of tumor progression associated with increasing risk category. If watchful waiting is pursued in patients who would otherwise have undergone upfront surgical resection in the pre-COVID era, a CT scan should be repeated early (i.e., in 1–3 months) to monitor for disease progression.

3.2.2 | Neoadjuvant tyrosine kinase inhibitors

Neoadjuvant imatinib is commonly used to downsize GISTs that are locally advanced, unresectable, or borderline resectable when upfront surgery would be associated with high morbidity or risk of positive margins. During a phase of restricted access to surgical care, imatinib may be a valuable option to avoid interval tumor progression in intermediate- or high-risk tumors carrying imatinib-sensitive mutations that would otherwise be resected.

The decision to pursue watchful waiting versus neoadjuvant imatinib as a delay strategy for patients with GIST that would normally be resected upfront should be based on several considerations. First, tumors close to EGJ, duodenal papilla, or anal sphincter, whose progression might upscale the surgical procedure from a local resection to a radical procedure, would benefit more from neoadjuvant imatinib as a temporizing strategy. Second, even if imatinib is overall well tolerated, patients are exposed to side effects such as myelosuppression (grade ≥ 3 experienced by up to a fifth of the patients) that might be worrisome if the patient acquires a SARS-CoV-2 infection.[30] Finally, initial watchful waiting would not preclude the chance of initiating imatinib upon tumor progression.

Neoadjuvant imatinib is usually continued until the desired response or maximal response (according to Choi criteria) has been achieved or if the patient becomes intolerant. During this pandemic, surgery might not be feasible at the desired time, and patients who have already achieved the desired response might need to stay on imatinib longer than anticipated. Knowing that 40% of secondary resistance will appear before 2 years from imatinib initiation in advanced disease, caution should be taken when neoadjuvant imatinib

TABLE 1 Risk stratification, resources required, and impact of delay in surgical intervention in gastrointestinal stromal tumor (GIST) and soft tissue sarcoma (STS) patients

		Benefit of timely surgical intervention	Resource Utilization With Surgery	Risk to patient without surgery	Alternate nonsurgical treatment	Caveats
GIST	High-risk	High	Variable	Variable	Neoadj imatinib	Emergency surgery for bleeding, GI perforation, development of resistance to TKI
	Low-risk	Low	Variable	Limited	Observation	
Extremity/truncal STS	High-risk	High	Variable	High	Neoadj CT, RT	Emergency surgery for limb salvage
	Low-risk	Low	Variable	Low	Observation, RT	
RPS	High-grade	High	High	High	Neoadj CT, RT	Consider surgery if patient has progressive unrelenting symptoms
	Low-grade	Low	Variable	Low	Observation, RT	
Desmoid		Low	Variable	Limited	Observation, medical therapy, and/or RT	Emergency surgery for GI perforation in mesenteric desmoids
Small round cell sarcoma (Ewing's, alveolar/embryonal RMS, DSRCT)		High	Variable	High	Standard of care is neoadjuvant CT+/− RT	Emergency surgery for progression/complications
Schwannoma		Low	Variable	Low	Observation	

Abbreviations: CT, chemotherapy; DSRCT, desmoplastic small round cell tumor; GIST, gastrointestinal stromal tumor; neoadj, neoadjuvant; RMS, rhabdomyosarcoma; RT, radiotherapy; STS, soft tissue sarcoma; TKI, tyrosine kinase inhibitor.

is prolonged up to 15 or 18 months. In patients with exon 11 mutation not involving 557–558 codons, the extension of treatment with neoadjuvant imatinib could be safer since patients harboring 557 and/or 558 mutated codons exhibited a shorter event-free survival.[31]

For patients with unresectable or metastatic GIST with mutations in PDGFRA exon 18 (including D842V), avapritinib has been approved by the FDA on the basis of the results of the NAVIGATOR Phase I trial. In case of inability to operate on patients with exon-18 mutant GIST, this therapeutic option might be explored.[32]

3.3 | Metastatic GIST

In patients with metastatic GIST, imatinib is the standard treatment and this should not be discontinued until progression, even in case of initial radiological complete response. Surgery may also be considered in patients experiencing unifocal progression to delay the switch to a second-line TKI or to treat complications. In the face of pandemic-related scarcity of surgical resources, alternate localized treatments might be considered such as ablative therapies for solid organ metastases and radiotherapy or embolization for tumor-associated bleeding.[33–35]

4 | STS OF THE EXTREMITY AND TRUNK

The mainstay of treatment for localized STS of the extremity and trunk (originating from the soft tissues of the back or of the abdominal or chest wall) is surgery with adequate margins. Extremity and truncal STS encompass a wide range of histologies with each subtype characterized by unique local and distant recurrence risks and sensitivities to radiotherapy and chemotherapy. In both extremity and truncal STS, the occurrence of distant metastases is the main cause of tumor-related death. On the contrary, the potential implication of local recurrence (LR) on survival varies with site. In the extremity—except for the very proximal sites where a recurrent tumor might directly invade the pelvis, the neck, or the chest—LR is salvageable with conservative surgery or amputation. In the trunk, LR might not be salvageable and could directly lead to patient death due to invasion of vital structure. In general, high-risk STSs are characterized by high-grade and large tumor size (>5 cm), with more aggressive histology including angiosarcoma, synovial sarcoma, leiomyosarcoma, and malignant peripheral nerve sheath tumor (MPNST).[36] Low-risk STS include tumors that are low-grade and smaller (<5 cm). Atypical lipomatous tumors (ALT) and dermatofibrosarcoma protuberans (DFSP) typically present a particularly indolent course.

Overall, 5-year overall survival (OS), LR, and distant metastases (DM) for patients with primary STS of the extremity treated in reference centers is 76%, 7%, and 25%, respectively.[36] Survival after wide excision is mainly related to tumor size, grade, and histology. Quality of surgical margins and radiotherapy administration concur in defining the risk of local recurrence.[36–39] These factors have been combined in prognostic tools and two free-to-download apps—Sarculator and Persarc—include models to predict postresection OS, LR, and DM in patients with extremity STS.[40,41] Even though these tools were created for post-op use, they may have some utility to risk stratify patients by inputting data from imaging and biopsy. In particular, the key prognostic factors to predict survival (tumor size, histology, grade, and patient's age) are available preoperatively, with the caveat of a possible change in tumor grade at final pathology.

Criteria for prioritizing surgery and options available in extremity and truncal STS are summarized in Figure 2 and Table 1.

4.1 | Surgical resources and morbidity

Surgical complexity across STS of the extremity and trunk varies from superficial wide excisions to multicompartmental resections with vascular, orthopedic, or plastic reconstructions. Thus, utilization of hospital resources and risk of postoperative morbidity, such as major wound complications, vary accordingly and accurate preoperative planning in the context of surgical resources limitations is essential.

A recent meta-analysis of 21 studies and more than 5,000 patients operated for extremity STS, identified an overall wound complication rate of 30% and a reoperation rate of 13%.[42–44] The type of surgical procedure strongly influences postoperative complications rate and resource burden. For example, in a study of 78 patients who underwent hindquarter amputation wound complication rate was 49%, in-hospital mortality was 6%, and median hospital stay was 24 days.[45]

4.2 | Alternate nonsurgical approaches

4.2.1 | Watchful waiting

When surgery must be postponed due to resource limitations, watchful waiting can be considered in patients with ALT and DFSP. They are typically slow growing and, in most locations, modest tumor growth would not alter the surgical plan. The outcome after surgery is excellent with disease-specific survival rates more than 95% at 5 years.[46,47]

The probability of an ALT developing a dedifferentiated component is very low, close to 1%, and this is usually observed only after tumor recurrence.[48] About 5% of DFSP harbor a fibrosarcomatous component that is more aggressive and is associated with a faster growth rate and a metastatic risk that is in the 15% range.[46,49,50] When a fibrosarcomatous component is present or if the tumor develops more rapid growth, imatinib is an option to control tumor growth when immediate surgical resection is not feasible. If the patient could not receive or tolerate imatinib, earlier surgical prioritization is recommended.[51]

Other low-grade extremity/truncal STSs such as low-grade myxoid liposarcoma or low-grade myxofibrosarcoma usually have

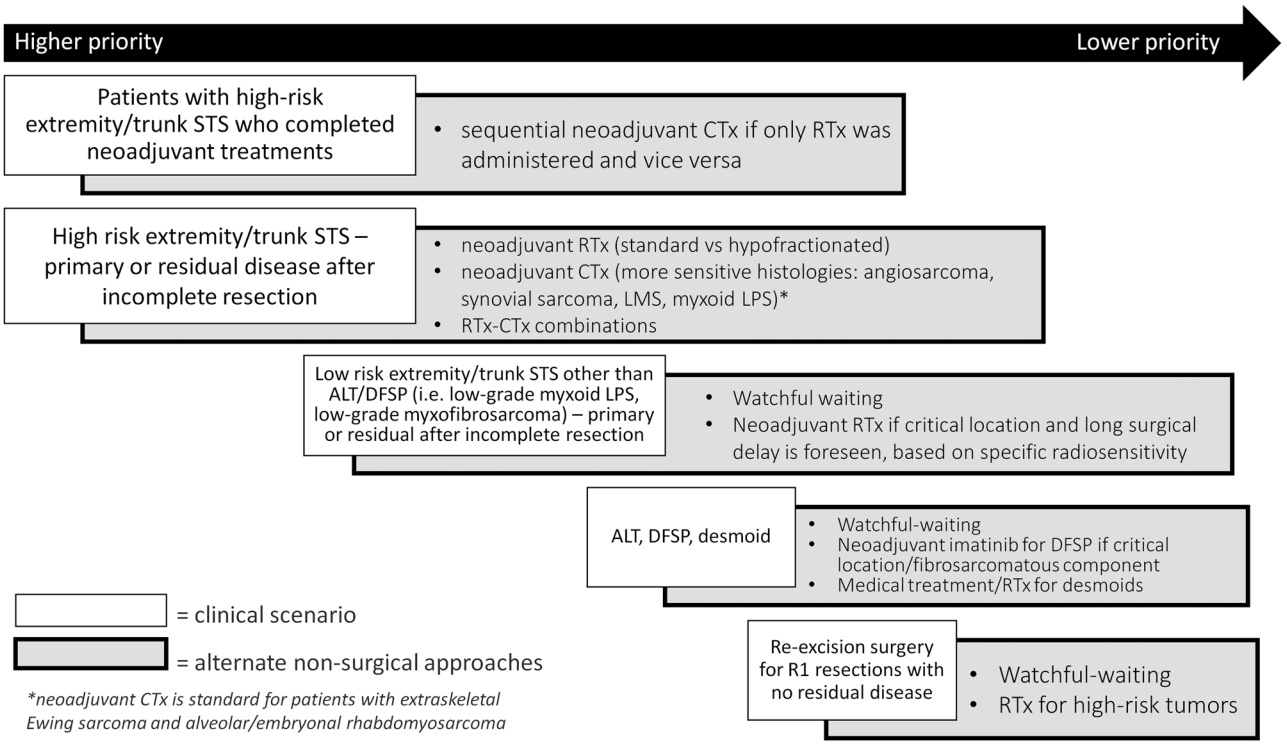

FIGURE 2 Prioritization of surgical intervention in elective patients with extremity and truncal soft tissue sarcoma (STS). This framework is intended to guide prioritization for elective surgery in extremity and truncal STS patients. Surgical emergencies/urgencies (i.e., tumor bleeding, progressive unrelenting symptoms) are not covered. Patient categories define the most common clinical scenarios. Patient priority and alternate treatments should be personalized and discussed in the context of multidisciplinary tumor boards. The different spacing between boxes on the priority line reflects a conceptual difference in patient prioritization as suggested by Hanna et al.[15] ALT, atypical lipomatous tumor; CT, chemotherapy; DFSP, dermatofibrosarcoma protuberans; LMS, leiomyosarcoma; LPS, liposarcoma; RT, radiotherapy; R1, microscopically positive margins; STS, soft tissue sarcoma

low metastatic potential and relatively slow growth rates. Active clinical and radiological surveillance might be considered if surgery needs to be delayed. On the other hand, neoadjuvant radiotherapy can be considered as a deferral strategy on a case-by-case basis, particularly in the setting of tumor abutment of critical structures, tumor growth, or developing of worrisome features at imaging.

4.2.2 | Neoadjuvant radiotherapy

Radiotherapy is usually considered in the multidisciplinary care of patients at high-risk of LR, bearing in mind that some particularly radiosensitive histological subtypes such as myxoid liposarcoma, angiosarcoma, myxofibrosarcoma, and synovial sarcoma have been described.[36] Preoperative and postoperative radiotherapy are equally effective in improving local control. Preoperative radiotherapy is associated with lower rates of late, irreversible toxicities but it portends a higher risk of acute wound healing complications.[43,52] In the neoadjuvant setting, RT is usually administered for a total of 50 Gy in 25–28 fractions over 5 weeks and surgery is planned about 4–6 weeks after. This should be the modality of choice in the context of limited surgical resources.

Hypofractionated radiotherapy has been evaluated in extremity/truncal STS in several studies but there is no randomized evidence.[53,54] Hypofractionated RT could be considered in rather small STS (less than 10 cm), if patients can be operated on quite rapidly since it reduces considerably the duration of treatment, also considering anticipated hospital/OR resources in the postradiation window.[55]

4.2.3 | Neoadjuvant chemotherapy

For adult-type STS, administration of chemotherapy varies across expert sarcoma centers. Histological subtypes that are more commonly treated with chemotherapy include synovial sarcoma, angiosarcoma, high-grade myxoid liposarcoma, undifferentiated pleomorphic sarcoma, and leiomyosarcoma.[36] The relative benefit associated with chemotherapy administration in patients with localized STS is unclear; however, higher risk tumors seem to benefit the most.[56]

When cytoreduction is the main objective, combination chemotherapy of doxorubicin and ifosfamide is usually administered, for a total of 3–5 cycles.

4.3 | Re-excision surgery

Twenty to fifty percent of patients with extremity STS are referred to a sarcoma center only after inadequate or incomplete excision performed elsewhere. For patients with high-risk ESTS, a policy of routine re-resection is standard of care in most sarcoma centers, regardless of the presence of macroscopic residual disease. This strategy is associated with residual tumor found in the specimen in up to 83% of patients in series including high-risk patients only.[57] Compared to patients who underwent upfront definitive surgery, patients who required re-excision surgery were more likely to need plastic reconstruction or amputation.[57] Thus, re-excisions are often more resource-consuming than primary surgeries. From an oncological perspective, when a policy of accurate preoperative planning, aggressive re-excision, and multimodality management is in place, outcomes are not significantly different between patients with high-risk STS treated with wide excision upfront versus unplanned surgery and re-excision.[57–59] However, a selective watchful waiting approach may be reasonable, especially in a resource-limited setting, in patients who underwent unplanned but complete gross tumor excision in the absence of tumor fracture/piecemeal resection. In a French study comparing selective watchful waiting approach to systematic re-excision, patients managed by the former approach had shorter LR-free survival but no difference in OS, distant metastasis-free survival, and amputation rate.[60]

Under resource-scarce circumstances, patients with macroscopic residual disease after incomplete excision of a high-risk STS should be prioritized. For those patients, delay strategies discussed for patients with high-risk STS should be considered (radiotherapy and chemotherapy). A policy of initial watchful waiting, with or without radiotherapy, is a valuable option for patients without residual gross disease. Re-excision of low-grade, superficial STS should be assigned a lower priority. However, these patients should undergo active surveillance.

4.4 | Recurrent STS of the extremity and trunk

Isolated LR from STS still has surgery as a potentially curative option. Criteria for prioritization should be based on disease biology, tumor site (vicinity to critical structure) and chance of long-term disease control. In this sense, there are tools available to predict the personalized impact of LR on extremity STS survivor's prognosis.[61,62] Radiotherapy and chemotherapy should be considered as mitigating strategies when surgery needs to be delayed with the same principles discussed for primary STS of the extremity and trunk and taking into consideration treatments previously administered at primary surgery, disease-free interval, and expected functional outcome.

5 | RETROPERITONEAL SARCOMA

Surgery is the only potentially curative treatment for patients with primary retroperitoneal sarcoma (RPS).[63] The 5-year overall survival in primary localized RPS treated in expert centers is 67%.[64]

From a biological perspective, RPSs are heterogeneous. In particular, their growth rate, metastatic potential, and prognosis differ widely (Table 2).[64] In the setting of primary localized disease, prognosis is mainly related to patient's age, histological subtype, tumor grade, size, multifocality, and completeness of surgical resection. These factors have been combined in a prognostic nomogram that predicts 7-year OS and DFS after surgery, a nomogram that is cited in the 8th American Joint Committee on Cancer staging system.[65] This prognostic tool was designed to be used in the postoperative setting. In the current scenario, it might be useful to provide a personalized rough estimation of the chance of long-term cure to assist surgical oncologists in patient prioritization and choice of alternative strategies, with the caveat that some of the variables (such as completeness of resection) will have to be inferred.

Criteria for case prioritization and mitigating strategies are summarized in Figure 3 and Table 1.

TABLE 2 Expected growth rate and oncological outcomes in different retroperitoneal sarcoma histological subtypes

	Growth rate	5-yr CCI of LR	5-yr CCI of DM	5-yr OS
WDLPS	Slow, can develop dedifferentiated components with rapid change in growth rate	23%	0%	90%
G1-2 DDLPS	Variable, usually low	43%	9%	67%
G3 DDLPS	Can be fast growing	36%	31%	37%
LMS	Can be fast growing	10%	50%	60%
SFT	Slow growing (classic low-grade variant)	10%	13%	81%
MPNST	Can be fast growing	20%	17%	67%
UPS	Can be fast growing	42%	41%	38%

Abbreviations: CCI, crude cumulative incidence; DDLPS, dedifferentiated liposarcoma; DM, distant metastases; G1, low-grade; G2, intermediate-grade; G3, high-grade; LMS, leiomyosarcoma; LR, local recurrence; MPNST, malignant peripheral nerve sheath tumor; OS, overall survival; SFT, solitary fibrous tumor; UPS, undifferentiated pleomorphic sarcoma; WDLPS, well-differentiated liposarcoma.

5.1 | Surgical resources and morbidity

Surgical resection of primary RPS is often more complex and resource intensive compared to resection of GIST or extremity/truncal STS. Preoperatively, patients might need nutritional and physical prehabilitation.[66] Multivisceral resection is required in about 70% of cases,[64] and thus considerable preoperative planning and coordination of multidisciplinary care involving other specialists such as urologists, vascular surgeons, orthopedic surgeons, is essential. Retroperitoneal sarcoma surgery, when performed in specialized sarcoma centers, is associated with a 16% Clavien-Dindo ≥3 morbidity and a 30-day mortality of about 2%. Generally, the median operating time is 4 h (interquartile range [IQR] 2.7–5.5) and the median number of units of packed red blood cells administered is 1 (IQR 0–3).[67] Postoperatively, patients may be admitted to subintensive or intensive care unit. The median length of stay is 10 days.[68] Often, patients need nutritional support and physiotherapy in the postoperative setting.

5.2 | Alternate nonsurgical approaches

5.2.1 | Watchful waiting

Watchful waiting can be considered in patients with indolent histological subtypes, such as well-differentiated liposarcoma and typical, low-mitotic, solitary fibrous tumor (SFT). Both are characterized by slow growth rate and minimal metastatic potential. During watchful waiting, radiological surveillance should be performed with evaluation by expert clinicians, as the appearance of a dedifferentiated component or a significant tumor growth would result in prioritizing the patient for intervention. In the absence of worrisome symptoms or worrisome imaging/histologic features, it is reasonable to plan the first CT scan in 3 months' time.

5.2.2 | Neoadjuvant radiotherapy

Routine use of neoadjuvant radiotherapy is controversial and highly center dependent. A recent phase III randomized control trial (RCT) of preoperative radiotherapy and surgery versus surgery alone in primary RPS patients (EORTC 62092-22092, STRASS trial) showed no difference in abdominal recurrence-free survival (ARFS, primary endpoint) between the two arms. Nevertheless, in a post hoc sensitivity analysis, 3-year ARFS was higher in patients with liposarcoma treated in the radiotherapy arm (71.6% versus 60.4%, n.b.: progression during radiotherapy was not considered an event in this analysis).[69]

In the context of the current pandemic, neoadjuvant radiotherapy can be considered as a temporizing strategy, especially in patients with tumors that are at high-risk of LR (i.e., dedifferentiated

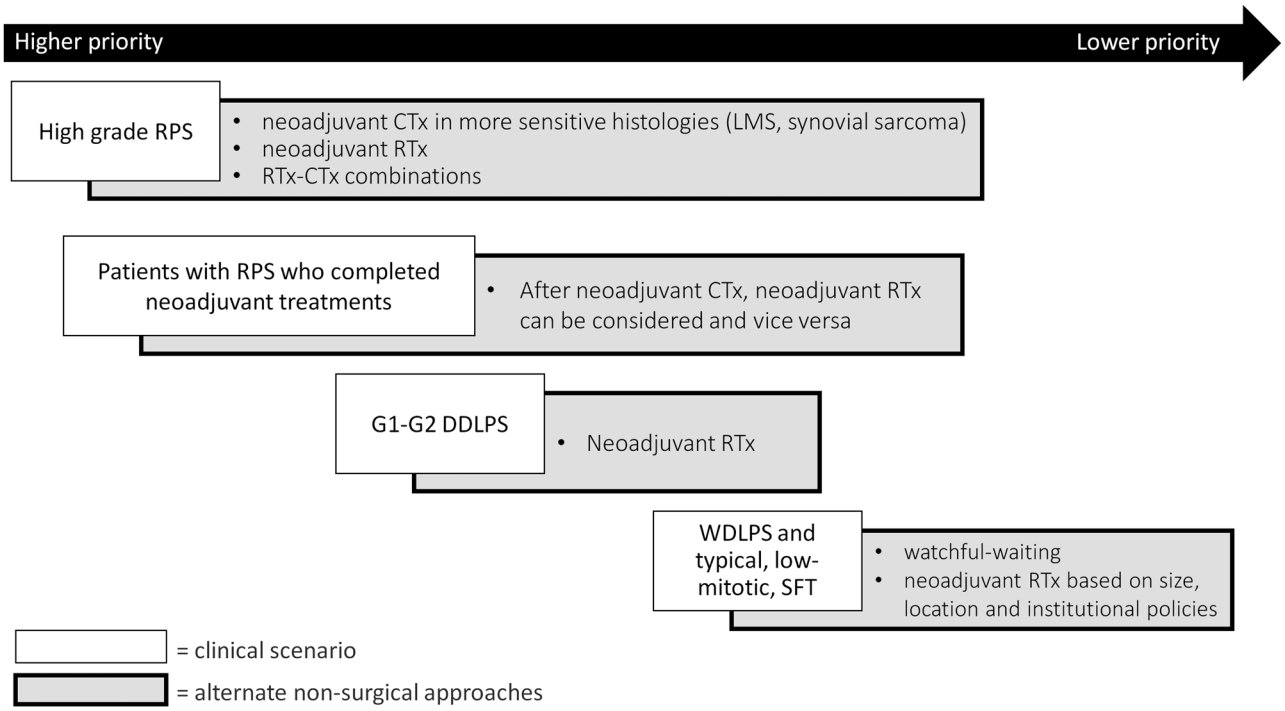

FIGURE 3 Prioritization of surgical intervention in elective patients with retroperitoneal sarcoma (RPS). This framework is intended to guide prioritization for elective surgery in RPS patients. Surgical emergencies/urgencies (i.e., bowel obstruction, progressive unrelenting symptoms) are not covered and patient priority and alternate treatments should be personalized and discussed in the context of multidisciplinary tumor boards. The different spacing between boxes on the priority line reflect a conceptual difference in patient prioritization as suggested by Hanna et al.[15] CT, chemotherapy; DDLPS, dedifferentiated liposarcoma; G1, low-grade; G2, intermediate-grade; LMS, leiomyosarcoma; RPS, retroperitoneal sarcoma; RT, radiotherapy; SFT, solitary fibrous tumor; WDLPS, well-differentiated liposarcoma

liposarcoma, MPNST, and undifferentiated pleomorphic sarcoma) and for those that are highly radiosensitive, such as SFTs. Since the prognosis of typical, low-mitotic, SFT is excellent with surgery alone, selective radiotherapy can be considered in SFT in difficult locations where progression during observation would compromise future resection.[70] Finally, up to 14% of patients progress during radiotherapy and an alternative treatment modality (i.e., chemotherapy) should be considered if the surgical intervention cannot be delivered.

Radiotherapy for RPS is usually administered over 5 weeks in 25–28 daily fractions for a total of 50 Gy and surgery is planned after 4–8 weeks depending on patient status, tumor response, and availability of surgical resources. High priority for surgery should be given to those patients who have already completed/are completing neoadjuvant radiotherapy, to avoid excess delay beyond 8-week postradiotherapy. As opposed to other solid tumors, hypofractionated radiotherapy cannot be considered in RPS. Its use is limited by tolerance of adjacent normal tissues, especially bowel and duodenum. In particular, there is no prospective study having evaluated neoadjuvant hypofractionated radiotherapy in RPS.

5.2.3 | Neoadjuvant chemotherapy

Neoadjuvant chemotherapy is not routinely recommended in patients with primary RPS. Data about the efficacy of chemotherapy for RPS are mainly extrapolated from RCTs and meta-analyses in patients with high-risk STS of the extremity, although definitive evidence of chemotherapy-derived survival benefit remains lacking.[56,71–74] The use of neoadjuvant chemotherapy as a delay strategy should be considered, especially in histological subtypes that are more chemosensitive such as leiomyosarcoma and synovial sarcoma, and in patients with high-grade tumors, especially if borderline resectable and in consideration of their high-risk of distant failure. When chemotherapy is administered in the neoadjuvant setting, combinations of doxorubicin and ifosfamide, or doxorubicin and dacarbazine in leiomyosarcoma, are commonly used in patients with good performance status to maximize the chance of obtaining tumor shrinkage.

6 | DESMOID AND SCHWANNOMA

Desmoid or aggressive fibromatosis is a benign solid tumor that is commonly managed by sarcoma experts. In the past decade, surgery has been increasingly restricted as the initial intervention in this patient population. A recent global desmoid consensus document advocates for upfront active surveillance for the first 1–2 years after diagnosis.[75] Indications for surgery during a pandemic would include emergencies such as bowel perforation, otherwise, medical therapies and radiation could be implemented in patients experiencing increasing symptoms and/or progression.

Extremity, pelvic or retroperitoneal schwannomas can be safely managed with ongoing imaging surveillance and pain management where needed.[76]

7 | SMALL ROUND CELL SARCOMA

Neoadjuvant chemotherapy with dedicated regimens is standard for patients with extraskeletal Ewing sarcoma, Ewing-like sarcoma, and alveolar/embryonal rhabdomyosarcoma and it should be expedited given the rapid growth of these histological subtypes, their very high rate of chemosensitivity, and the lack of equally effective treatments.[77] Desmoplastic small round cell tumor typically presents with extensive serosal implants in the abdominal cavity and has a dismal prognosis. Surgery is not curative but can be part of multimodality therapy including chemotherapy, radiotherapy. Medical therapy should be prioritized in a context of resource limitation.[78]

8 | DISCUSSION

This review synthesizes data that may aid in decision making and patient prioritization based on a comprehensive review of sarcoma care for GIST and STS and is presented by experts in countries that have been moderately to profoundly impacted by the current COVID 19 pandemic.

The international sarcoma collaborative community remains steadfast in its commitment to providing guidance in deferral of care and is resolved to synergize our collective experience so that the data and wisdom gained from the “new normal” imposed by a pandemic can be developed and refined with the goal of continuing to optimize care for cancer patients.

Collection of data regarding the impact of the pandemic on patient outcomes will be beneficial for advancing knowledge for future pandemic planning and will facilitate decision making when resources are no longer restricted, as we continue to strive for the best outcomes for patients with cancer within our global community.

CONFLICT OF INTERESTS

Cecile Le Péchoux received institutional honoraria for participation to advisory boards from Astra Zeneca, Nanobiotix, and Roche; institutional honoraria for participation to educational meetings from Amgen, Astra Zeneca, Medscape, and Lilly; and personal honoraria from PrimeOncology for participation to educational meetings. The other authors declare that there are no conflict of interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of the study are available in the public domain and have been cited in the reference section.

ORCID

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