Costs and quality indicators of soft tissue sarcoma clinical pathway

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Objective

Soft tissue sarcomas (STS) are rare malignances accounting for less than 2% of all tumors in adults. They comprise a wide range of different malignancies classified according to their cell lineage (adipocytic, chondro-osseous, fibroblastic or myofibroblastic, fibro-histiocytic, nerve sheath tumors, pericytic, skeletal muscle, smooth muscle, vascular, tumors of uncertain differentiation, undifferentiated/unclassified sarcoma). Inside these main lineage classes, histological phenotypes, immunohistochemical patterns, and molecular profiling discriminate more than 100 subtypes that differ significantly in their clinical outcome. In western countries, the mean 5-year STS overall survival rate in adults reaches approximatively 65%, however this value considerably varies from 80% to 15% according to histotypes, neoplastic stages, or operative contexts.

In cancer care, adopting standardized diagnostic and therapeutic strategies enables care quality to be monitored consistently, and healthcare system efficiency to be critically assessed. Both these actions are essential to improving patient outcomes and optimizing the allocation of resources. Quality of patient care can be reliably monitored by means of "indicators" addressing a center's performance, and the outcomes of the adopted diagnostic-therapeutic pathway. In oncology, as in other clinical specialties, quality indicators are useful to both identify and quantify:

1. the appropriateness of diagnostic procedures;
2. the efficacy of anticancer therapies and surgical treatments;
3. the critical areas most requiring corrective actions;
4. the sustainability and relative priority of investments directed toward oncological cares.

To promote evidence-based clinical strategies, international agencies and scientific societies in Europe and the USA have developed different clinical practice guidelines (CPGs) for STS managing. However, the rate of adherence to these guidelines remains unsatisfactory (partly due to the changing diagnostic criteria), resulting in a significant variability in how the disease is diagnosed and treated, and also making it difficult to estimate the costs of care for patients with STS.

In an effort to support the best care strategies and the most rational allocation of resources, the Veneto (North-East Italy) Oncology Network (ROV) formally proposed standard diagnostic and therapeutic procedures to be implemented in cancer care units throughout the region.

This population-based study critically addresses the clinical management of STS patients resident in the Veneto in the year 2018. Quality of care was ranked thon the strength of a set of internationally-acknowledged clinical indicators selected by a multidisciplinary regional working group (RWG) of specialists with expertise in soft tissue malignancies. This research also aimed to estimate the direct costs sustained by the Veneto's regional healthcare system for the care of adults with STS in the first two years after their diagnosis.

Materials and Methods

In 2015, the Veneto's Regional Oncology Network defined a comprehensive document detailing the clinical procedures to be applied in each step of the clinical management of STS patients, from their initial diagnosis to their end-of-life care. The Network's document, now under update, was based on current national and international literature.

The cohort of the present study was extracted from

- the Veneto Cancer Registry, a high-resolution population-based database which covers the inhabitants of the whole region (4.9 million residents
- the regional health service records.

This work concerns all incident cases of STS documented by the Registry in the year 2018. Recording procedures rely on various informative sources such as pathology reports, clinical charts, death certificates, and health service administrative records. In detail, the available features include: age and sex; tumor site; diameter of the primary tumor (mm); depth; histological subtype (ICD-O-3 code); tumor grade; combined clinical-pathological TNM stage at diagnosis; treatments; and status of resection margins. The results of diagnostic imaging (ultrasound [US], computerized tomography [CT], MRI [magnetic resonance imaging], Positron Emission Tomography [PET]); the identification code of the institution(s) delivering the treatment; and the timing of therapeutic procedures (surgery, chemotherapy [ChT]; radiation [RT]) were also available.

In 2021, a RWG of epidemiologists, healthcare managers, oncologists, pathologists, radiologists, radiotherapists, statisticians, and surgeons established a list of indicators to monitor the care quality in adult STS patients (Table 2). Reference or threshold values were also defined for each indicator to better evaluate how centers performed in real-world clinical practice compared to theoretical expectation.

All regional public health institutions potentially involved in STS care were included in this quality assessment (QA) project.

Variable	Total STS patients: 214 (%)	
Sex	Male	124 (57.9)
	Female	90 (42.1)
Age Mean = 65.9 (SD = 15.3) Median = 67	20-29 (M:F=0:1)	1 (0.5)
	30-39 (M:F=4:9)	13 (6.1)
	40-49 (M:F=17:8)	25(11.7)
	50-59 (M:F=16:18)	34 (15.9)
	60-69 (M:F=24:20)	44 (20.6)
	70-79 (M:F=42:16)	58 (27.1)
	80-89 (M:F=20:13)	33 (15.4)
	≥90 (M:F=1:5)	6 (2.8)
Primary site	Limbs	81 (37.9)
	Trunk	56 (26.2)
	Retroperitoneum	50 (23.4)
	Head-neck	24 (11.2)
	Unknown	3 (1.4)
Lineage of cell differentiation	Uncertain differentiation	60 (28.0)
	Liposarcoma	55 (25.7)
	Fibroblastic/myofibroblastic sarcoma	43 (20.1)
	Leiomyosarcoma	34 (15.9)
	Vascular sarcoma	12 (5.6)
	Others	10 (4.7)
TNM stage at initial diagnosis (AJCC 7th edition)	I	46 (21.5)
	II	67 (31.3)
	III	51 (23.8)
	IV	29 (13.6)
	Unknown	21 (9.8)

Table 1. Demographics and clinico-pathological profile of the adult STS cohort.

Based on the principal steps of a patient's clinical management, the RWG identified six main phases, each of which was evaluated by means of a variable number of indicators: diagnosis (2 indicators); process performance (2 indicators); surgical treatments (4 indicators); combined surgical and medical treatments (3 indicators); medical treatments (3 indicators); and end-of-life management (1 indicator).

The costs were estimated considering only the incident cases of STS in 2018, as recorded by the regional cancer registry.

The cost analysis was conducted from a health system perspective. Data on visits to outpatient clinics, specialist services, drug prescriptions, hospital or hospice admissions, treatments at the emergency department, and the use of medical devices were obtained from the regional administrative subject-level databases. The cost of any diagnostic, therapeutic (surgical or other) interventions was based on the reimbursement rates established by the Veneto Regional Authority. Each patient was linked via an anonymous unique identification code to all administrative data. All costs sustained over two years after STS was diagnosed were included. The average real-world costs per patient (total and by single item of expenditure) were calculated and stratified by TNM stage at initial cancer assessment. The mean total survival-weighted costs were calculated by summing the average cost at first year plus the average cost at second year calculated including only those patients survived at first year.

All costs were calculated in euros.

Operative Phase	Indicators	Threshold	Estimated percentage (95% CI)
Diagnosis	**1.** Proportion (%) of deep STS (any size), or superficial STS (> 5 cm) without MRI/CT before biopsy	<5%	10.59 (5.44, 19.26)
	2. Proportion (%) of second opinions obtained for STS diagnostic biopsy	>90%	45.40 (37.70, 53.10)
Process performance	**3.** Proportion (%) of surgical or medical treatments administered within 90 days after diagnostic biopsy	>90%	90.30 (84.04, 94.57)
	4. Proportion (%) of patients given at least one surgical treatment at non-reference STS centers in the region out of total STS patients treated surgically in Veneto	<30%	70.59 (63.26, 77.11)
Surgical therapy	**5.** Proportion (%) of superficial small-size and/or low-grade STS (excluding lipoma-like) in head-neck, trunk or limbs that were treated appropriately (Figure 1)	>80%	92.98 (82.73, 97.57)
	6. Proportion (%) of low-grade, lipoma-like STS in head-neck, trunk or limb, that were treated appropriately (all types of surgery, including enucleation)	>80%	100.00 (63.54, 100.00)
	7. Proportion (%) of medium- or high-grade STS of head-neck, trunk or limbs showing clear margins after surgical treatment	>90%	80.00 (72.06, 86.29)
	8. Proportion (%) of retroperitoneal STS treated with multivisceral surgery	>80%	36.59 (22.91, 52.46)
Surgical-medical therapy	**9.** Proportion (%) of large-sized and/or deep, medium- or high-grade STS in head-neck or trunk that were treated appropriately (Figure 1)	>80%	34.62 (18.81, 54.21)
	10. Proportion (%) of large-sized and/or deep, medium- or high-grade STS in limbs that were treated appropriately (Figure 1)	>80%	70.00 (51.69, 83.68)
	11. Proportion (%) of STS in head-neck, trunk or that were treated appropriately (cumulative value of indicators 5, 6, 9 and 10)	>80%	75.00 (66.30, 82.18)
Medical therapy	**12.** Proportion (%) of medium- or high-grade STS of head-neck, trunk or limbs, deep and >5 cm in diameter, radically removed with conservative surgery and treated with RT within 90 days before or after surgery	>90%	66.67 (45.76, 83.09)
	13. Proportion (%) of STS of limbs, deep and >5 cm in diameter, grade G3, radically removed with conservative surgery and treated with ChT within 60 days before or after surgery	>90%	36.36 (13.51, 66.71)
	14. Proportion (%) of patients withdrawn from ChT due to toxicity	No threshold	1.96 (0.10, 10.44)
End of life care	**15.** Proportion (%) of patients treated with ChT within 30 days before their death	<10%	31.43 (18.25, 48.56)

Table 2. Regional working group quality indicators on soft tissue sarcoma. Threshold values were based on the current literature. Estimated percentage and 95%CI were calculated on data obtained from the regional health service administration (year 2018).

Results

In 2018, the regional population-based cancer registry recorded 214 incident cases of adult STS. Table 1 shows the demographics and clinico-pathological profile of these STS patients.

Table 2 lists the measured 15 indicators by clinical pathway phase: diagnostic, process performance, therapeutic (surgical and non-surgical) and end of life care. The table also reports the indicators threshold values established by the RWG, and the real-world estimates.

Pre-biopsy imaging, as recommended by the international and regional guidelines, was available for 89% of patients. The initial diagnosis of STS was supported by a second opinion in 45% of cases. Both these indicators do not satisfy the established thresholds.

Indicators 3 and 4 measure whether and when the activities recommended to accomplish the strategic objectives of the integrated care processes actually took place. More than 90% of STS patients received a treatment within 90 days from their histological diagnosis (indicator 3), and 71% of patients were at least partially treated with surgical procedures at non-reference centers (indicator 4).

Two of the four indicators concerning surgical therapies (5, 6, 7 and 8) were consistent with the thresholds. Among the 2018 incident cases of retroperitoneal STS, however, only 37% were treated with multivisceral surgery (well below the threshold of >80%; indicator 8).

None of the indicators relating to combined therapies (surgery plus other treatments; indicators 9, 10, 11), or medical therapies (indicators 12, 13) satisfy the thresholds. The best performance (75% versus 80%) was achieved for indicator 11, which measure how multimodal therapies were administered for head-neck, trunk, or limb STS of any size or histological grade.

The prevalence of ChT suspension due to toxicity was 2%.

More than 30% of patients were given ChT within 30 days before their death (indicator 15).

The survival weighted mean total cost per patient, into two years from diagnosis, amounted to €22,183. A higher TNM stage at diagnosis was associated with higher healthcare costs: a mean expense of €10,379 was estimated for I staged cases, €40,042 for IV staged subjects.

The highest cost item consisted in hospitalization.

		Mean	Median	SD	[Min; Max]
TNM stage	I	10,379	5,992	11,162	[7,153; 13,605]
	II	21,729	16,213	13,949	[18,389; 25,070]
	III	30,320	22,729	18,856	[25,145; 35,495]
	IV	40,042	23,935	56,621	[19,781; 60,304]
All cases		22,183	14,523	18,951	[19,650; 24,717]

Table 3. Survival-weighted total costs (€) into two years after diagnosis.

Conclusion

The present study results can estimate population based both direct costs of illness of incident cases of STS into two year from diagnosis and give an overview on quality of care of sarcoma clinical pathways.

The high proportion of STS patients who underwent imaging only after a biopsy is a concern as the lack of information from propaedeutic imaging data significantly limits the pathologist's assessment. The low incidence of STS, and the variety of histological subtypes, meaningfully limit operators' diagnostic experience, resulting in high variability. A second opinion would be hence preferable.

Among indicators 5, 6, 7, 8, two were totally consistent with the thresholds: superficial, small-sized or low-grade STS received appropriate surgical treatment, while surgery for medium- or high-grade STS of the head-neck, trunk or limbs was radical only in 80% of cases. Concerning surgery for retroperitoneal STS, the widest gap between the threshold and the actual value was observed (respectively 80% and 37%). This poor result may be partially explained considering that multivisceral surgery has been adopted only recently. The indicators referring to the treatment of large-size STS (9 and 10) showed a suboptimal care management, demanding a critical reassessment of either the diagnostic-therapeutic procedures implemented or the consistency of the indicators' thresholds. This need is reinforced by the unsatisfactory values in indicators 12 and 13, which address the timely treatment of large-sized STS after surgery.

In the terminal phase of their disease, 31% of the patients considered were given chemotherapy (threshold <10%). This finding prompts both clinical and ethical considerations: corrective action should be prioritized to ensure the cost-effectiveness of anticancer drugs, clinicians' empathy when dealing with patients' wishes in the advanced phase of their illness could have negative impacts.