

Intra-abdominal and Retroperitoneal Soft Tissue Sarcomas Survey in Iranian Patients; A Population-Based Study

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ABSTRACT

Background:

To the best of our knowledge, we do not have enough data on the rate of intra-abdominal sarcoma (IaS) and retroperitoneal sarcoma (RPS) in Iran compared to other countries. We aimed to report a 10-year survey on the incidence and demographic characteristics or potential risk factors of RPS and IaS in Iranian patients in a population-based study setting.

Materials and Methods:

This descriptive-analytic, cross-sectional study was performed during 2009-2014 to evaluate the incidence of sarcomas in Iranian patients in different provinces under the supervision of the Cancer Research Center of Shahid Beheshti University of Medical Sciences. 2142 patients were included in this study. Demographic data of the patients including age, sex, and year of diagnosis, as well as primary tumor location and recurrence tumor site, tumor morphology, and tumor grade after clinical and pathological examinations were collected. Six-digit codes for histological grading and differentiation were used to evaluate the tumor grade. Data were entered into SPSS software, version 22, and analyzed.

Results:

In this study, data of 2142 patients were included and evaluated. Of the patients with soft tissue sarcoma, 993 (46.4%) were women and 1149 (53.6%) were men. Among the patients, 109 (5.1%) were children, 1450 (67.7%) were adults, and 583 (27.2%) were in the elderly age group. The peak frequency of soft tissue sarcoma was 237 (11.1%) in the 50-54 year-old age group, with the highest rate in 40-69 year-olds and the lowest in the age range of 5 to 14 years. The morphology of soft sarcomas was evaluated, gastrointestinal stromal sarcoma (16.9%, n = 362) being the most common, followed by sarcoma (9.9%, n = 212), spindle cell sarcoma (9.9%, n = 211), leiomyosarcoma (7.7%, n = 166%) and liposarcoma not otherwise specified (6.2%, n = 133) were the four most common types. The morphology of the tumors was also evaluated by age and sex, which was statistically significant. gastrointestinal stromal sarcoma has the highest sex-specific incidence in patients with sarcoma, in other words, during the six years of our study, the sex-specific incidence rate for gastrointestinal stromal sarcoma were 163.14 cases per 1000 patients with sarcoma for women, and the sex-specific incidence was 174.6 for men. In patients less than 15 years old, the desmoplastic small round cell tumor morphology had the highest specific incidence, which was 201.83 per 1000 patients with soft tissue sarcoma in this age group.

Conclusion:

Our study data show that the four most common types of soft tissue sarcomas in our country are gastrointestinal stromal sarcoma, followed by sarcoma, spindle cell sarcoma, leiomyosarcoma, and liposarcoma NOS and The peak age range of this sarcomas was 50-54 years.

Keywords: Population-based study, Soft tissue sarcoma, Intra-abdominal sarcoma, Retroperitoneal sarcoma

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INTRODUCTION

Mesenchymal tumors include two broad categories of soft tissue sarcomas (STSs) and bone sarcomas based on the World Health Organization (WHO) classification (1,2). STSs are responsible for about 1% of malignant tumors, which may occur in all ages and any location in the body (3,4). In 2016 in the United States, 12310 new cases of STSs and 4990 deaths were documented (1). In general, from all soft-tissue sarcomas, 60% are related to the extremity (most commonly, the thigh), 19% originate from the

Table 1: Sixth Digit Code for Histological Grading and Differentiation

Code	Grade	Differentiation
1	Grade I	Well-differentiated Differentiated, not otherwise specified
2	Grade II	Moderately differentiated Moderately well differentiated Intermediate differentiation
3	Grade III	Poorly differentiated
4	Grade IV	Undifferentiated Anaplastic
9		Grade or differentiation not determined, not stated or not applicable

trunk wall, 15% are located in the retroperitoneum and 9% involve the head and neck tissue. Intra-abdominal STSs consist of liposarcoma and leiomyosarcoma, which often occur in the retroperitoneum (1,3).

Retroperitoneal sarcoma (RPS) and intra-abdominal sarcoma (IaS) are related to various soft tissue tumors with a variety of prognostic values (5). Nearly 12-15% of all STSs are retroperitoneal sarcomas. The annual incidence rates of RPS is 2.7 cases per million (6). The annual prevalence of RPS in the USA is about 1250 new cases (6). They occur more in men with a ratio of ~1.3:1 and commonly diagnosed during 54 to 65 years of age (4,6).

IaS is among the peritoneal cavity sarcomas or intraperitoneal sarcomas in the medical literature, which includes visceral sarcomas as well. Approximately 15-20% of STSs originate from the intra-peritoneal space or gastrointestinal tract (6,7). Gastrointestinal stromal tumors (GISTs) are accountable for the most IaSs. In this regard, strict anatomical definitions divided them into two groups of GISTs and IaSs other than GISTs. IaSs other than GISTs included about 5-10% of all mesenchymal tumors and GISTs for more than 90% of them, which are located within the peritoneal cavity (6-8).

The diagnosis of intra-abdominal and retroperitoneal sarcomas (IaRSs) is often challenging since they often involve significant visceral structures and greater lesions at diagnosis (9). Moreover, their signs and symptoms are not usually distinctive and discrete (10,11). The tumor site, hemorrhage, ascites, pressure symptoms, and pain could influence IaRS symptoms. IaRS should be diagnosed by MRI, CT, or ultrasound scans when the tumor has reached an appropriate size (10,11).

Treatment strategy for IaRS is influenced by

Table 2: Frequency of the Primary Tumor site

Tumor site	Frequency	Percentage
Antrum of stomach	15	0.7
Anus and anal canal	4	0.2
Appendix	4	0.2
Ascending colon	6	0.3
Body of stomach	13	0.6
Cardia	9	0.4
Cecum	10	0.5
Cervical esophagus	2	0.1
Colon	29	1.4
Connective tissue of pelvis	417	19.5
Connective tissues of abdomen	280	13.1
Descending colon	3	0.1
Esophagus	15	0.7
Fundus of stomach	6	0.3
Greater curvature of stomach	1	0.01
Hepatic flexure of colon	1	0.01
Ill-defined sites of abdomen	182	8.5
Ill-defined sites of pelvis	152	7.1
Lesser curvature of stomach	7	0.3
Lower third of esophagus	4	0.2
Middle third of esophagus	3	0.1
Overlapping lesion of colon	1	0.01
Overlapping lesion of retro Peritoneum	5	0.2
Overlapping lesion of stomach	4	0.2
Peritoneum	121	5.6
Pylorus	2	0.1
Rectosigmoid junction and retroperitoneum	31	1.4
Retroperitoneum	406	19.0
Sigmoid	7	0.3
Small intestine	181	8.5
Stomach	213	9.9
Thoracic esophagus	2	0.01
Transverse colon	5	0.2
Upper third of esophagus	1	0.01
Total	2142	100.0

precise diagnosis, especially for compartment resection (5,12). The recurrence rate for RPS is 22-84% which is related to difficulties for obtaining a complete surgical resection and recurrence of histological subtypes (9,12). The long-term survival rate for RPS is 50-66% (13).

To the best of our knowledge, we do not have enough data related to IaRS rate in Iran in contrast with

Table 3: Frequency of recurrence tumor site

Recurrence tumor site	Frequency	Percentage
Abdomen and retro peritoneum	1229	57.4
Antrum of stomach	15	0.7
Anus and anal canal	4	0.2
Appendix	4	0.2
Ascending colon	6	0.3
Body of stomach	13	0.6
Cardia	9	0.4
Cecum	10	0.5
Cervical esophagus	2	0.1
Colon	29	1.4
Descending colon	3	0.1
Esophagus	15	0.7
Fundus of stomach	6	0.3
Greater curvature of stomach	1	0.01
Hepatic flexure of colon	1	0.01
Ill-defined sites of abdomen	182	8.5
Ill-defined sites of pelvis	152	7.1
Lesser curvature of stomach	7	0.3
Lower third of esophagus	4	0.2
Middle third of esophagus	3	0.1
Overlapping lesion of colon	1	0.01
Overlapping lesion of stomach	4	0.2
Pylorus	2	0.1
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Stomach	213	9.9
Thoracic esophagus	2	0.1
Transverse colon	5	0.2
Upper third of esophagus	1	0.01
Total	2142	100.0

other countries such as Italy (4), Taiwan (14), Tanzania (15), Australia (3), Germany (16), etc. and there are only some case reports on Iranian patients (17-20). We aimed to report a 10-year survey on the prevalence and demographic characteristics or potential risk factors of RPS and IaS in Iranian patients in a population-based study setting.

MATERIALS AND METHODS

This descriptive-analytic, cross-sectional study was done during 2009-2014 to evaluate the incidence

Table 4: Frequency of tumor morphology

Tumor morphology	Frequency	Percentage
Adenosarcoma	2	0.1
Alveolar rhabdomyosarcoma	10	0.5
Alveolar soft part sarcoma	4	0.2
Atypical fibrous histiocytoma	1	0.01
Carcinosarcoma	9	0.4
Chondroblastic osteosarcoma	2	0.1
Chondrosarcoma	10	0.5
Chordoma	13	0.6
Clear cell sarcoma, NOS	4	0.2
Dedifferentiated liposarcoma	15	0.7
Dermatofibrosarcoma	13	0.6
Desmoplastic small round cell tumor	110	5.1
Embryonal rhabdomyosarcoma	23	1.1
Embryonal sarcoma	1	0.01
Endometrial stromal sarcoma	2	0.1
Endometrial stromal sarcoma, low gr	2	0.1
Epithelioid hemangioendothelioma	1	0.01
Epithelioid leiomyosarcoma	2	0.1
Epithelioid sarcoma	9	0.4
Ewing sarcoma	20	0.9
Fibro myxo sarcoma	8	0.4
Fibro sarcoma	40	1.9
Fibrous mesothelioma malignant, sarcoma	3	0.1
Gastrointestinal stromal sarcoma	362	16.9
Gastrointestinal stromal tumor, NOS	1	0.01
Giant cell sarcoma except of bone	44	2.1
Giant cell tumor of bone malignant	1	0.01
Hemangioendothelial sarcoma	1	0.01
Hemangiopericytoma malignant	5	0.2
Hemangiosarcoma	6	0.3
Infantile fibro sarcoma	1	0.01
Kaposi sarcoma	16	0.7
Leiomyosarcoma	166	7.7
Liposarcoma not otherwise specified	133	6.2
Liposarcoma well differentiated	71	3.3
Lymphangiosarcoma	1	0.01
Malignant fibrous histiocytoma	109	5.1
Malignant giant cell tumor of soft	1	0.01
Malignant histiocytosis	1	0.01
Malignant peripheral nerve sheath t	61	2.8
Malignant rhabdoid tumor, rhabdoid	2	0.1
Malignant tumor Giant cell type	7	0.3
Malignant tumor spindle cell type	79	3.7

Tumor morphology	Frequency	Percentage
Mast cell sarcoma	1	0.01
Meningeal sarcomatosis	1	0.01
Mesenchymal chondrosarcoma	4	0.2
Mesothelioma malignant	37	1.7
Mixed liposarcoma	12	0.6
Mixed tumor, malignant	11	0.5
Mixed type rhabdomyosarcoma	1	0.01
Mullerian mixed tumor	4	0.2
Myeloid sarcoma	4	0.2
Myosarcoma	1	0.01
Myxoid chondrosarcoma	7	0.3
Myxoid leiomyosarcoma	3	0.1
Myxoid liposarcoma	81	3.8
Myxosarcoma	3	0.1
Neuroilemoma sarcoma	4	0.2
Osteosarcoma	2	0.1
Paraganglioma malignant	5	0.2
Pleomorphic liposarcoma	29	1.4
Pleomorphic rhabdomyosarcoma	11	0.5
Rhabdomyosarcoma	40	1.9
Round cell liposarcoma	8	0.4
Sarcoma	212	9.9
Small cell sarcoma, round cell sarcoma	13	0.6
Solitary fibrous tumor malignant	2	0.1
Spindle cell sarcoma	211	9.9
Stromal sarcoma	3	0.1
Synovial sarcoma	32	1.5
Synovial sarcoma, biphasic	9	0.4
Synovial sarcoma, epithelioid cell	1	0.01
Synovial sarcoma, spindle cell	9	0.4
Telangiectasia osteosarcoma	1	0.01
Undifferentiated sarcoma	8	0.4
Total	2142	100.0

of sarcomas in Iranian patients in different provinces under the supervision of Shahid Beheshti University of Medical Sciences Cancer Research Center. This study has also been approved by the University Ethics Committee (IR.SBMU.CRC.REC.1398.010). The data of this study were collected from 12 medical centers in 30 provinces of Iran, where the data were recorded.

Inclusion criteria were completeness of patient

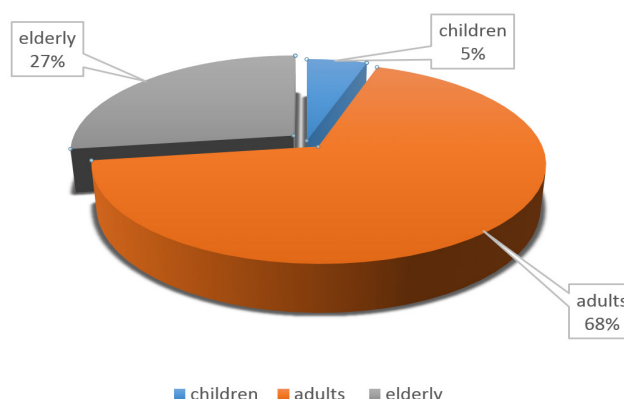


Fig.1: Soft tissue sarcoma according to age category

records and correct data recording and diagnosis of STS. 2142 patients were included in this study. Demographic data of patients including age, sex, year of diagnosis, as well as primary tumor location and recurrence tumor site, tumor morphology, and tumor grade after clinical and pathological examinations, were collected. Six-digit codes for histological grading and differentiation were used to evaluate the tumor grade. ICD-O, (International classification of diseases for oncology) as the sixth digit of the morphology code, includes a single-digit code number designating the grade or differentiation of malignant neoplasms. the code numbers 1 to 4 are used to identify grades I to IV, respectively (21).

Data analysis:

Data were entered into SPSS software, version 22, and then qualitative data were analyzed using frequency tables. Data were also analyzed for age- and sex-specific incidence rates. Crude rates or sex- and age-specific incidence rates were considered equal the total number of new cancer cases diagnosed in a specific year in the population category of interest, divided by the at-risk population for that category and multiplied by 100,000 (cancers by primary site). We compared categorical variables using Chi-square or Fisher's exact tests. $p < 0.05$ was considered as statistically significant.

RESULTS

Demographic information of patients and cancer research centers:

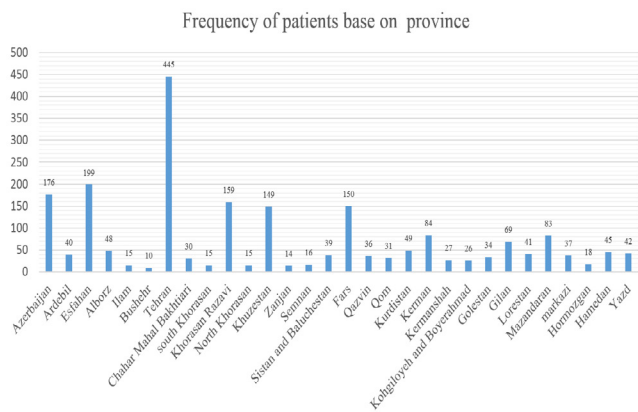


Fig.2: Frequency of soft tissue sarcoma based on the province

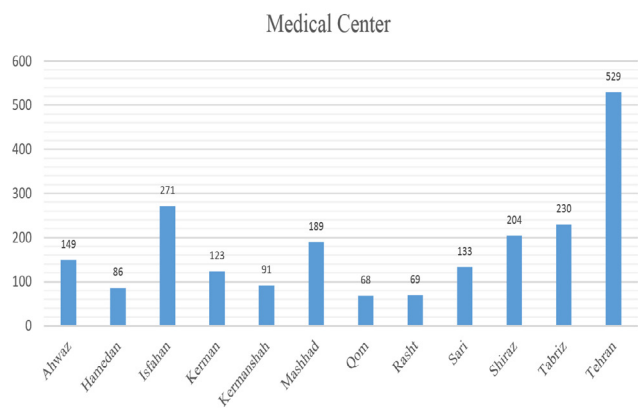


Fig.3: Frequency of soft tissue sarcoma based on medical centers

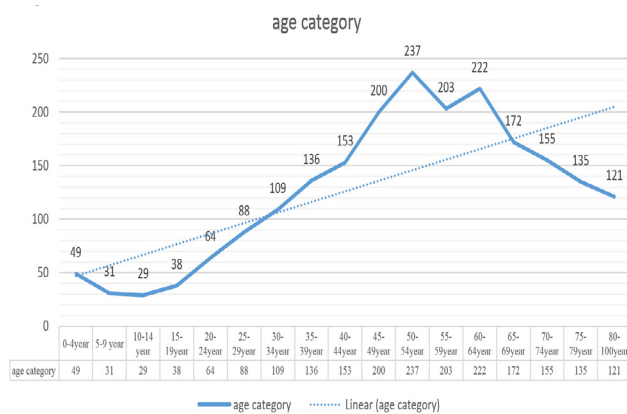


Fig.4: Frequency of soft tissue sarcoma based on age groups

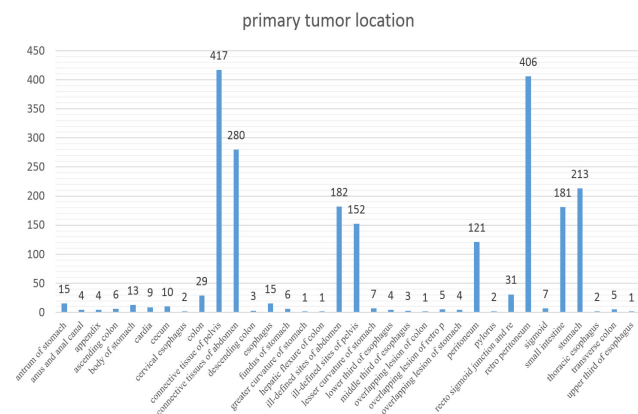


Fig.5: Frequency of primary tumor location

In the present study, the data of 2142 patients were included and evaluated. Of the patients with STS, 993 (46.4%) were women and 1149 (53.6%) were men. The patients were categorized into three groups of children (less than 15 years old), adults (15-65 years old), and the elderly (over 65 years old) according to age. Among the patients, 109 (5.1%) were children, 1450 (67.7%) were adults, and 583 (27.2%) were in the elderly age group.

The data were from 30 provinces of Iran. Most cases of STS (n = 445, 20.8%) were in Tehran province followed by Isfahan (n = 199, 9.3%), Azerbaijan (n = 176, 8.2%), and Khorasan Razavi (n = 159, 7.4%) and the lowest incidence was observed in Bushehr (n = 10, 0.5%) (figure 2). With respect to medical centers, most data were from Tehran (24.7%), Isfahan (12.7%), and Tabriz (10.7%), respectively. In 2012, there were 428 (20%) cases followed by 410 (19.1%) in 2011 and 2013. However, this distribution was not reliable

by year because data entry at the health center may not be accurate enough.

Patients with STS:

As shown in figure 4, the peak frequency of STS was 237 (11.1%) in the age group of 50-54 years, with the highest rate in the age range of 40 to 69 years and the lowest in the age range of 5-4 years. As shown in figure 5, the most frequent primary tumor site was the connective tissue of the pelvis (19.5%) followed by retroperitoneum (19%), the connective tissue of the abdomen (13.1%), and the stomach (9.9%).

Tumor recurrence was also evaluated, with the most common sites being the abdomen and retroperitoneum (n = 1229, 57.4%), stomach (n = 213, 9.9%), ill-defined sites of the abdomen (n = 182, 8.5%), small intestine (n = 181, 8.5%) and ill-defined sites of the pelvis (n = 152, 7.1%).

Soft tissue sarcomas were evaluated on the basis of

Table 5: Frequency of sixth digit code for histological grading and differentiation

	Frequency	Percentage
	(1) Well-differentiated Differentiated, Not otherwise specified	277
(2) Moderately differentiated Moderately well differentiated Intermediate differentiation	95	4.4
(3) Poorly differentiated	234	10.9
Undifferentiated Anaplastic	38	1.8
(9) Grade or differentiation not determined, not stated or not applicable	1498	69.9
Total	2142	100.0

Table 6: Frequency of common tumor morphology based on age category and sex

Tumor morphology		Age category			Sex	
		Children	Adults	Elderly	Female	Male
Desmoplastic small round cell tumor	Count	22	69	19	45	65
	% within Age-Category	20.2%	4.8%	3.3%	4.5%	5.7%
Gastrointestinal stromal sarcoma	Count	1	244	117	162	200
	% within Age-Category	0.9%	16.8%	20.1%	16.3%	17.4%
Leiomyosarcoma	Count	1	120	45	117	49
	% within Age-Category	0.9%	8.3%	7.7%	11.8%	4.3%
Liposarcoma not otherwise specified	Count	5	96	32	59	74
	% within Age-Category	4.6%	6.6%	5.5%	5.9%	6.4%
Liposarcoma well differentiated	Count	0	53	18	32	39
	% within Age-Category	0.0%	3.7%	3.1%	3.2%	3.4%
Malignant tumor spindle cell type	Count	1	47	31	6	6
	% within Age-Category	0.9%	3.2%	5.3%	0.6%	0.5%
Mixed liposarcoma	Count	0	10	2	33	48
	% within Age-Category	0.0%	0.7%	0.3%	3.3%	4.2%
Myxoid liposarcoma	Count	0	59	22	100	112
	% within Age-Category	0.0%	4.1%	3.8%	10.1%	9.7%
Sarcoma	Count	6	139	67	45	65
	% within Age-Category	5.5%	9.6%	11.5%	4.5%	5.7%
Malignant fibrous histiocytoma	Count	1	75	33	44	35
	% within Age-Category	0.9%	5.2%	5.7%	4.4%	3.0%
		$p = 0.0001$			$p = 0.007$	
Fisher's exact test						

incidence of STS was 54-50 years (11.1%), with the highest frequency being in the 40-69 age range and the lowest in the 5-14 year-old age group. According to a study in India, the peak age was in the fourth to fifth decades of life (22). On the other hand, in a study in Australia, the age of diagnosis and peak age were

in the fifth and sixth decades of life(3). The results of this study evaluated the primary location of tumors with the most frequent being pelvic connective tissue (19.5%) followed by retroperitoneal (19%), abdominal connective tissue (13.1%), and stomach (9.9%). Tumor recurrence was also evaluated, with the most

common being the abdomen and the peritoneum.

In terms of pathological grading, the most common finding was not determined, not stated or not applicable, indicating the low accuracy of pathological examination and grading of tumors, which could be attributed to various causes such as inadequate pathological evaluation, inappropriate specimen, and improper registration system. According to our study, morphologically, gastrointestinal stromal sarcoma was the most common type, followed by sarcoma, spindle cell sarcoma, leiomyosarcoma, and liposarcoma not otherwise specified. Significant findings were also found between morphology, age, and sex in our study.

In a ten-year study in Iran, the relative frequency of different types of STS pathology was evaluated in Ahwaz. The results showed that in male adults, the most common sarcomas were MFH, (Malignant fibrous histiocytoma) liposarcoma, synovial sarcoma, fibrosarcoma, and rhabdomyosarcoma, respectively. The most common sarcomas in adulthood in females were liposarcoma, MFH, synovial sarcoma, DFSP (Dermatofibrosarcoma Protuberans), rhabdomyosarcoma, and fibrosarcoma, respectively. In children, the most common type was rhabdomyosarcoma sarcoma (23). The results of the mentioned study were quite different from ours, which could be because the mentioned study was conducted in one center while our data were collected from the whole country, and that adds to the value and generalizability of our study.

In a population-based study, leiomyosarcoma (20.43%), malignant fibrous histiocytoma (16.14%), and soft tissue tumors/sarcomas that were not otherwise identified (10.18%) were the most common STS subtypes), which are somewhat similar to our study. This study was performed in Australia and was a cohort study, and during the study, the patients' serviceability was evaluated, which was not considered in our study, and it is strongly needed to conduct cohort studies similar to this study in our country.

Few studies have been conducted in this area, most of which have been outside Iran, and most have been case reports, making it difficult to analyze our findings. However, a study in India found that 90% of cases belonged to adolescents and adults, and this is consistent with our research. Liposarcoma

(18%) was the most common subtype, followed by leiomyosarcoma and Ewings sarcoma. 66.6% were in the extremities, and the rest were in the abdomen (22). One of the differences between this study and our study was that bone marrow sarcoma was also included in this study, and the review was single-centered, while data from cancer research centers were collected nationwide in our research, and this will increase the value of the study. However, studies have shown that the rarity and heterogeneity of STS, along with other factors, such as clinical inaccuracy, often lead to problems and delays in the accurate diagnosis and improper management of any STS subtype (4). Therefore, this group of tumors needs special attention and approaches to diagnosis and treatment.

On the other hand, review of this study and other studies collectively showed that epidemiological data on STS are limited. Concerns have also been raised about the precise registration of STS in cancer registry and disease history. Solving these problems is very helpful in diagnosing and treating patients correctly.

CONCLUSION

The four most common types of soft tissue sarcomas in our country are gastrointestinal stromal sarcoma, followed by sarcoma, spindle cell sarcoma, leiomyosarcoma, and liposarcoma not otherwise specified and the peak age of these sarcomas is 50-54 years.

CONFLICT OF INTEREST

The authors declare no conflict of interests related to this work.

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