RESEARCH ARTICLE

Soft Tissue Sarcoma of Extremities: Descriptive Epidemiological Analysis According to National Population-based Study

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Abstract

Background: Soft-Tissue Sarcoma (STS) is a heterogeneous group of neoplasms of mesenchymal origin, occurring in connective tissues. According to previously conducted studies, STS accounts for approximately 1% and 7-%15% of adult and pediatric malignancies, respectively. Almost 50%-60% of sarcomas arise from extremities and usually present as a large painless or rarely painful soft-tissue mass. The present study aimed to describe the epidemiology of soft-tissue sarcomas, especially in the Iranian population.

Methods: This epidemiological study of limb soft-tissue sarcoma was conducted based on Iran National Cancer Registry data (INCR) between 2009 and 2014. Patients with soft-tissue sarcoma confirmed by histopathological studies were included, and data were classified based on the International Classification of Diseases for Oncology (first revision-third edition [ICD-O-3]) and analyzed. Descriptive analysis was performed to extract age-standardized and age-specific incidence rates.

Results: A total of 2, 593 patients (1,476 males and 1,117 females) were enrolled and assessed in the present study. The age-standardized incidence rate(ASIR) of total soft tissue sarcomas was 6.34 per million person-years. In addition, the highest and lowest ASIR scores stratified by age were observed in patients aged above 65 and under 0 with the value of 19.61 (95% CI:17.91-21.30) and 1.91 (95% CI 1.69, 2.13) per million, respectively. Limb soft tissue sarcomas stratified by gender were dominant in males, and it was statistically significant (P<0.05). The most common extremity soft tissue sarcomas subtypes were mesenchymal tumor (12.26%), spindle cell sarcoma (12.18%), and malignant fibrous histiocytoma (11.45%).

Conclusion: As evidenced by the results of the present study, the ASIR of soft tissue sarcoma dramatically increased with age, and the peak ASIR occurred in the age range of above 65 years. The incidence rate of soft tissue sarcomas analyzed by disease site was higher in hip and lower limb than upper limb and pelvis region, and it was detected consistently in all age groups and both genders.

Level of evidence: IV

Keywords: Sarcoma, Soft Tissue, Extremities, Soft Tissue Neoplasm

Introduction

Soft-Tissue Sarcoma (STS) is a heterogeneous group of neoplasms occurring in connective tissues. According to previous studies, STS accounts for 1% and 7%-15% of adult and pediatric malignancies, respectively (1,2). Almost 50%-60% of sarcomas arise from extremities and usually present as a large painless or rarely painful soft-tissue mass (2,3). About 8,000 new STS cases occur each year in the United States, leading to a higher death rate, as compared to testicular cancer, Hodgkin's disease, and

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thyroid cancer (3,4). These tumors are challenging to treat due to recurrences and metastases despite apparently complete resection with negative margins, bringing about devastating results (2).

A better appreciation of incidence and treatment patterns of STS is critical to consider the impact of STS on public health. Due to its exiguity, a few cases of STS are referred to and diagnosed even in specialized sarcoma centers. Therefore, a large population-based study would be of great help in the evaluation of its incidence and treatment pattern. On the other hand, inattention to these lesions can end in limb loss, morbidity, and even mortality

There are a few population-based studies on STS, reporting the incidences between 1.8 and 5.0 cases per 100,000 people per year (5–9). Nevertheless, the majority of these studies were based on Western populations, and there is a paucity of information about the Asian population, particularly in middle-east people. Furthermore, most of the studies included the STS of all anatomical sites, whereas the treatment and prognoses of STS differ according to the anatomical location (e.g., head and neck, viscera, retroperitoneum, and extremity) (9). In Iran, there is no population-based study on the incidence of soft tissue tumors; therefore, it is required to investigate the incidence and treatment patterns of extremity STS in Iran according to a population-based study. The knowledge of local epidemiologic parameters of these tumors can be effective in better diagnosis and treatment of extremity tumors, and accordingly, the improvement of the general health of the Iranian population.

Materials and Methods

This population-based epidemiological study of limb soft-tissue sarcoma was conducted based on the Iranian National Cancer Registry (INCR) data between January 2009 and December 2014. Patients with soft-tissue sarcoma confirmed by histopathological studies were included and data were classified and analyzed. In addition, data were categorized based on the International Classification of Diseases for Oncology (first revision-third edition [ICD-O-3]) and M-Codes.

All the recorded cases in INCR with a diagnosis of limb soft-tissue sarcoma between 2009 and 2014 were collected. Out of the 2,913 subjects, 103 cases were ruled out due to incorrect histology codes, missing data, and non-Iranian nationality. Furthermore, 217 cases were excluded after duplicate extraction [Table 1].

Table1. Percentage of Data Extraction

Year	Before Duplicate Extraction	After Duplicate Extraction	Percentage
2009	379	379	0.00
2010	339	339	0.00
2011	512	465	9.18
2012	578	492	14.88
2013	534	455	14.79
2014	468	463	1.07
Total	2810	2593	7.72

A number of 2,593 cases (1,476 men and 1,117 women) were included in the study and categorized into histopathological groups and subgroups based on their M-codes [Table 2]. We did not consider histological assessments and grading due to incomplete histopathological records and the lack of histology codes on INCR.

The histopathological name of tumors was extracted from M-Codes. Due to incomplete histopathology registration of the patients and lack of histology codes on INCR, histology evaluation was completely excluded from this study. For each tumor subtype, the patients were classified based on age and gender. In each subgroup, the crude incidence rate, age-specific incidence rate, male to female standardized incidence rate ratio, and truncated Age-Standardized Incidence Rate (ASIR) with 95% confidence interval were calculated and recorded. All analyses were performed using R (version 3.6.3) and SPSS software (version 26) programs. A p-value less than<0.05 was considered statistically significant.

Results

In general, limb soft-tissue sarcomas were dominant in males. The ASIR was 7.19 in males versus 5.47 per million person-years (95% C. I: 0.20-0.30) in females, and the male-to-female standardized incidence rate ratio (SRR) was 1.31 per million person-years, and it was statistically significant (P<0.05) [Table 2]. The overall male gender dominancy was observed in most age subgroups with the most considerable difference in age subgroups 80-84 years [Figure 1]. As illustrated in Table 2, the female higher prevalence was observed in a few groups; nonetheless, none of them was statistically significant.

The male-to-female SRR was statistically significant in five groups of sarcomas, including soft tissue sarcomas Not Otherwise Specified (NOS), fibromatous sarcomas, synovial sarcomas, blood vessels sarcomas, and malignant nerve sheath tumors. Among the major groups, the highest SRR belonged to malignant nerve sheath tumors (2.09 cases per million person-years). Among the subgroups, Kaposi sarcoma, malignant giant cell tumor of soft parts, pleomorphic rhabdomyosarcoma, and malignant peripheral nerve were more significant in male prevalence with SPR of more than 2 per million person-years [Table 2].

Among the major groups, after the group "NOS sarcomas (32.39%), the most common limb soft tissue sarcomas were Fibromatous sarcomas (18.74%), Lipomatous sarcomas (14.26%), Synovial like sarcomas (13.61%), and myomatous sarcomas (9.17%). In the group of NOS sarcomas, Mesenchymal tumors and Spindle cell sarcomas were more common than other subgroups, accounting for 12.26% and 12.18% of all soft tissue sarcomas, respectively. Fibrous histiocytoma and fibrosarcoma were the most common fibromatous sarcomas. Leiomyosarcoma and myxoid liposarcoma were more prevalent sequentially in myomatous and lipomatous sarcomas groups.

The obtained results pointed to an exponential increase in the incidence rate of soft tissue sarcoma with age. The same results were obtained in the four most common major groups [Figure 1]. In both males and females, the highest incidence rates of soft-tissue sarcoma per million person-years were reported as at 19.61 during 2009-2015 (95% CI 17.91-21.30) [Table 3].

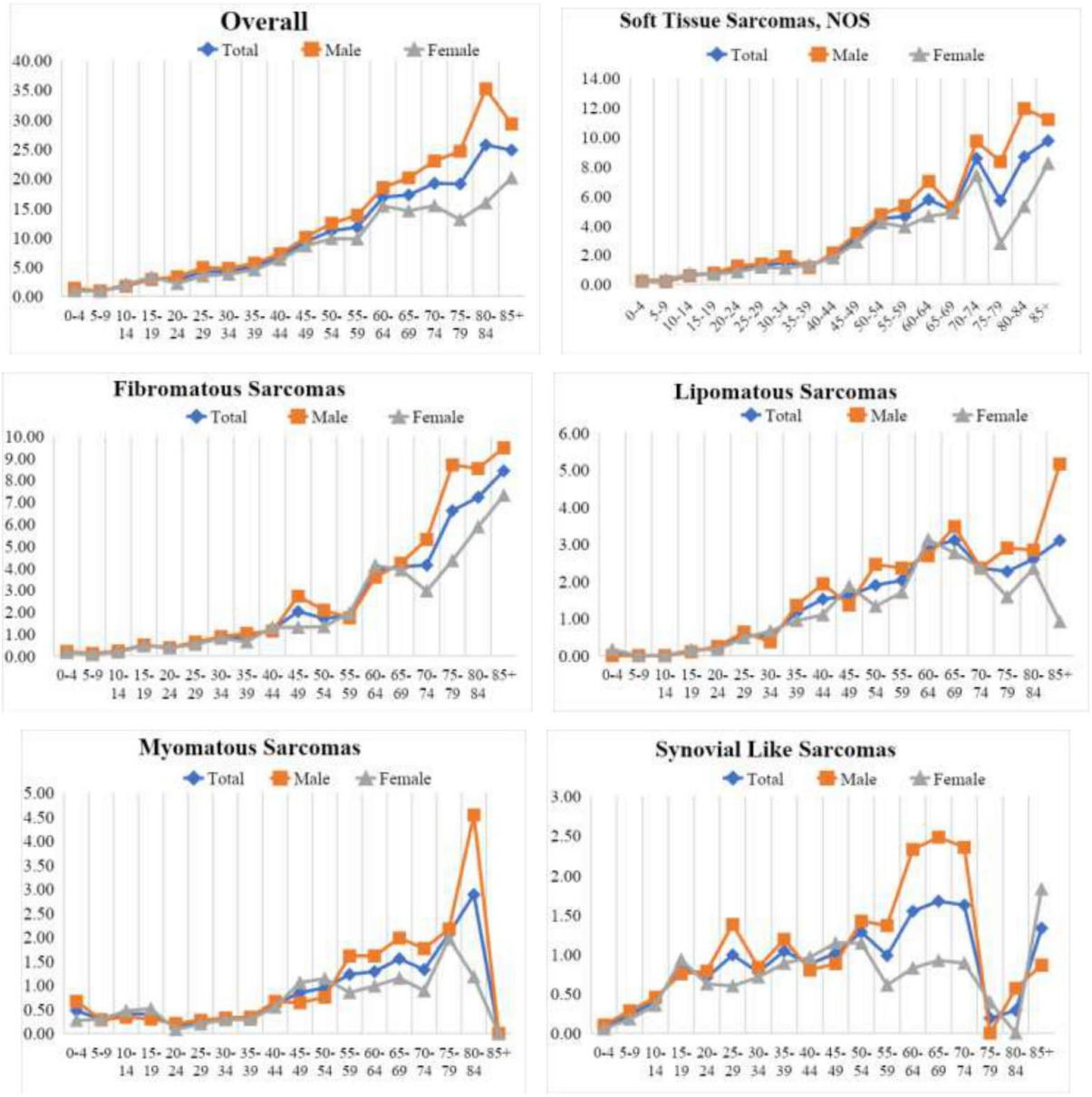

Figure1. Incidence rates (per million) of primary soft tissue cancers in special age groups with topography subtypes and by gender in Iran from 2009 to 2014

Table 2. Incidence (per million person-years) of Primary Soft Tissue Sarcomas by Sex and Histologic Subtype, Iran (2009-2014)

Histologic Subtype	Sex	n	Crude Rate	ASR*	95% CI	SRR	95% CI
Total	Both sexes	2593	5.73	6.34	6.09-6.59		
	Male	1476	6.45	7.19	6.82-7.57	1.31**	1.21-1.42
	Female	1117	4.99	5.47	5.15-5.80		
Paragangliomas and Glomous Tumors	Both sexes	1	<0.01	<0.01	-----		
	Male	1	<0.01	0.01	-----	-----	-----
	Female	0	<0.01	<0.01	-----		

Table 2 continued.

	Both sexes	1	<0.01	<0.01	-----		
Glomangiosarcoma	Male	1	<0.01	0.01	-----	-----	-----
	Female	0	<0.01	<0.01	-----		
	Both sexes	840	1.86	2.08	1.94-2.23		
Soft Tissue Sarcomas, NOS	Male	475	2.08	2.35	2.14-2.57	1.30**	1.13-1.49
	Female	365	1.63	1.81	1.62-2.00		
	Both sexes	318	0.70	0.81	0.71-0.90		
Mesenchymal tumor	Male	174	0.76	0.88	0.75-1.02	1.21	0.96-1.52
	Female	144	0.64	0.73	0.61-0.85		
	Both sexes	316	0.70	0.78	0.69-0.86		
Spindle cell sarcoma	Male	190	0.83	0.94	0.80-1.07	1.53**	1.21-1.92
	Female	126	0.56	0.61	0.50-0.72		
	Both sexes	113	0.25	0.30	0.24-0.35		
Giant cell sarcoma/pleomorphic cell sarcoma	Male	60	0.26	0.32	0.24-0.40	1.18	0.18-1.72
	Female	53	0.24	0.27	0.20-0.34		
	Both sexes	17	0.04	0.04	0.02-0.06		
Small cell sarcoma/round cell sarcoma	Male	10	0.04	0.05	0.02-0.08	1.37	0.51-3.73
	Female	7	0.03	0.03	0.01-0.06		
	Both sexes	38	0.08	0.08	0.05-0.11		
Epithelioid sarcoma	Male	23	0.10	0.09	0.05-0.13	1.33	0.69-2.56
	Female	15	0.07	0.07	0.03-0.10		
	Both sexes	20	0.04	0.05	0.02-0.07		
Undifferentiated sarcoma	Male	10	0.04	0.05	0.02-0.08	0.86	0.35-2.12
	Female	10	0.04	0.05	0.02-0.09		
	Both sexes	18	0.04	0.04	0.02-0.06		
Desmoplastic round cell tumor	Male	8	0.03	0.03	0.01-0.06	0.79	0.30-2.05
	Female	10	0.04	0.04	0.02-0.07		
	Both sexes	486	1.07	1.23	1.12-1.35		
Fibromatous Sarcomas	Male	274	1.20	1.38	1.22-1.55	1.28**	1.07-1.54
	Female	212	0.95	1.08	0.93-1.23		
	Both sexes	114	0.25	0.26	0.21-0.31		
Fibrosarcoma	Male	61	0.27	0.29	0.21-0.36	1.20	0.82-1.75
	Female	53	0.24	0.24	0.17-0.31		
Fibromyxosarcoma	Both sexes	24	0.05	0.06	0.03-0.08		
	Male	8	0.03	0.04	0.01-0.08	0.61	0.26-1.40
	Female	16	0.07	0.07	0.04-0.11		
Infantile/congenital fibrosarcoma	Both sexes	6	0.01	0.01	0.00-0.03		
	Male	3	0.01	0.01	0.00-0.03	-----	-----
	Female	3	0.01	0.01	0.00-0.03		
Solitary fibrous tumor	Both sexes	3	0.01	0.01	0.00-0.02		
	Male	1	<0.01	<0.01	0.00-0.01	-----	-----
	Female	2	0.01	0.01	0.00-0.03		

Table 2 continued.

Fibrous histiocytoma/fibroxanthoma	Both sexes	297	0.66	0.80	0.71-0.89		
	Male	177	0.77	0.93	0.79-1.08	1.42**	1.12-1.79
	Female	120	0.54	0.66	0.54-0.78		
Dermatofibrosarcoma	Both sexes	42	0.09	0.09	0.06-0.12		
	Male	24	0.10	0.10	0.06-0.14	1.26	0.68-2.34
	Female	18	0.08	0.08	0.04-0.12		
Myxomatous Sarcomas	Both sexes	5	0.01	0.01	0.00-0.03		
	Male	3	0.01	0.02	0.00-0.04	-----	-----
	Female	2	0.01	0.01	0.00-0.02		
Myxosarcom	Both sexes	5	0.01	0.01	0.00-0.03		
	Male	3	0.01	0.02	0.00-0.04	-----	-----
	Female	2	0.01	0.01	0.00-0.02		
Lipomatous Sarcomas	Both sexes	370	0.82	0.92	0.83-1.02		
	Male	203	0.89	1.01	0.87-1.15	1.21	0.98-1.49
	Female	167	0.75	0.83	0.70-0.96		
Liposarcoma/fibroliposarcoma	Both sexes	77	0.17	0.19	0.15-0.24		
	Male	39	0.17	0.20	0.14-0.27	1.09	0.69-1.72
	Female	38	0.17	0.18	0.12-0.24		
Liposarcoma, well differentiated	Both sexes	50	0.11	0.13	0.09-0.17		
	Male	24	0.10	0.12	0.07-0.17	0.92	0.52-1.63
	Female	26	0.12	0.13	0.08-0.19		
Myxoid Liposarcoma	Both sexes	163	0.36	0.39	0.33-0.45		
	Male	93	0.41	0.44	0.35-0.53	1.28	0.93-1.76
	Female	70	0.31	0.34	0.26-0.42		
Round cell liposarcoma	Both sexes	19	0.04	0.04	0.02-0.06		
	Male	12	0.05	0.06	0.02-0.09	1.86	0.72-4.81
	Female	7	0.03	0.03	0.01-0.05		
Pleomorphic liposarcoma	Both sexes	40	0.09	0.11	0.08-0.15		
	Male	22	0.10	0.12	0.07-0.18	1.23	0.68-2.42
	Female	18	0.08	0.10	0.05-0.14		
Mixed liposarcoma	Both sexes	11	0.02	0.03	0.01-0.04		
	Male	8	0.03	0.04	0.01-0.06	2.30	0.64-8.23
	Female	3	0.01	0.02	0.00-0.04		
Fibromyxosarcoma	Both sexes	24	0.05	0.06	0.03-0.08		
	Male	8	0.03	0.04	0.01-0.08	0.61	0.26-1.40
	Female	16	0.07	0.07	0.04-0.11		
Infantile/congenital fibrosarcoma	Both sexes	6	0.01	0.01	0.00-0.03		
	Male	3	0.01	0.01	0.00-0.03	-----	-----
	Female	3	0.01	0.01	0.00-0.03		
Solitary fibrous tumor	Both sexes	3	0.01	0.01	0.00-0.02		
	Male	1	<0.01	<0.01	0.00-0.01	-----	-----
	Female	2	0.01	0.01	0.00-0.03		
Fibrous histiocytoma/fibroxanthoma	Both sexes	297	0.66	0.80	0.71-0.89		

Table 2 continued.

	Male	177	0.77	0.93	0.79-1.08	1.42**	1.12-1.79
	Female	120	0.54	0.66	0.54-0.78		
Dermatofibrosarcoma	Both sexes	42	0.09	0.09	0.06-0.12		
	Male	24	0.10	0.10	0.06-0.14	1.26	0.68-2.34
	Female	18	0.08	0.08	0.04-0.12		
Myxomatous Sarcomas	Both sexes	5	0.01	0.01	0.00-0.03		
	Male	3	0.01	0.02	0.00-0.04	-----	-----
	Female	2	0.01	0.01	0.00-0.02		
Myxosarcom	Both sexes	5	0.01	0.01	0.00-0.03		
	Male	3	0.01	0.02	0.00-0.04	-----	-----
	Female	2	0.01	0.01	0.00-0.02		
Lipomatous Sarcomas	Both sexes	370	0.82	0.92	0.83-1.02		
	Male	203	0.89	1.01	0.87-1.15	1.21	0.98-1.49
	Female	167	0.75	0.83	0.70-0.96		
Liposarcoma/fibroliposarcoma	Both sexes	77	0.17	0.19	0.15-0.24		
	Male	39	0.17	0.20	0.14-0.27	1.09	0.69-1.72
	Female	38	0.17	0.18	0.12-0.24		
Liposarcoma, well differentiated	Both sexes	50	0.11	0.13	0.09-0.17		
	Male	24	0.10	0.12	0.07-0.17	0.92	0.52-1.63
	Female	26	0.12	0.13	0.08-0.19		
Myxoid Liposarcoma	Both sexes	163	0.36	0.39	0.33-0.45		
	Male	93	0.41	0.44	0.35-0.53	1.28	0.93-1.76
	Female	70	0.31	0.34	0.26-0.42		
Round cell liposarcoma	Both sexes	19	0.04	0.04	0.02-0.06		
	Male	12	0.05	0.06	0.02-0.09	1.86	0.72-4.81
	Female	7	0.03	0.03	0.01-0.05		
Pleomorphic liposarcoma	Both sexes	40	0.09	0.11	0.08-0.15		
	Male	22	0.10	0.12	0.07-0.18	1.23	0.68-2.42
	Female	18	0.08	0.10	0.05-0.14		
Mixed liposarcoma	Both sexes	11	0.02	0.03	0.01-0.04		
	Male	8	0.03	0.04	0.01-0.06	2.30	0.64-8.23
	Female	3	0.01	0.02	0.00-0.04		
Carcinosarcoma	Both sexes	1	<0.01	<0.01	------		
	Male	0	<0.01	<0.01	------	------	------
	Female	1	<0.01	<0.01	------		
Mixed mesenchymal sarcoma	Both sexes	6	0.01	0.02	0.00-0.03		
	Male	4	0.02	0.02	0.00-0.04	------	------
	Female	2	0.01	0.01	0.00-0.02		
Synovial Like Sarcomas	Both sexes	353	0.78	0.79	0.71-0.88		
	Male	205	0.90	0.92	0.79-1.06	1.40**	1.13-1.74
	Female	148	0.66	0.66	0.55-0.77		
Synovial sarcoma, NOS	Both sexes	184	0.41	0.42	0.35-0.48		
	Male	106	0.45	0.48	0.39-0.58	1.38**	1.02-1.86

Table 2 continued.

	Female	78	0.35	0.35	0.27-0.43		
Synovial sarcoma, spindle cell	Both sexes	79	0.17	0.17	0.13-0.21		
	Male	49	0.21	0.22	0.16-0.29	1.72**	1.08-2.75
	Female	30	0.13	0.13	0.08-0.18		
Synovial sarcoma, epithelioid cell	Both sexes	4	0.01	0.01	0.00-0.02		
	Male	1	<0.01	<0.01	0.00-0.01	------	------
	Female	3	0.01	0.01	0.00-0.03		
Synovial sarcoma, biphasic	Both sexes	60	0.13	0.13	0.10-0.16		
	Male	33	0.14	0.14	0.09-0.19	1.19	0.71-2.01
	Female	27	0.12	0.12	0.07-0.16		
Clear cell sarcoma of tendons and aponeuroses, melanoma	Both sexes	26	0.06	0.06	0.04-0.08		
	Male	16	0.07	0.07	0.04-0.11	1.51	0.67-3.39
	Female	10	0.04	0.05	0.02-0.08		
Blood Vessels Sarcomas	Both sexes	61	0.13	0.16	0.12-0.21		
	Male	38	0.17	0.21	0.14-0.28	1.72**	1.02-2.91
	Female	23	0.10	0.12	0.07-0.17		
Haemangiosarcoma	Both sexes	22	0.05	0.06	0.03-0.09		
	Male	8	0.03	0.04	0.01-0.08	0.57	0.24-1.38
	Female	14	0.06	0.08	0.04-0.12		
Hemangioendothelial sarcoma	Both sexes	3	0.01	0.01	0.00-0.02		
	Male	2	0.01	0.01	0.00-0.02	------	------
	Female	1	0.00	<0.001	------		
Kaposi sarcoma	Both sexes	29	0.06	0.08	0.05-0.11		
	Male	24	0.10	0.13	0.08-0.19	5.32**	2.15-13.15
	Female	5	0.02	0.03	0.00-0.05		
Malignant Haemangiopericytoma	Both sexes	7	0.02	0.02	0.00-0.03		
	Male	4	0.02	0.02	0.00-0.04	1.43	0.31-6.60
	Female	3	0.01	0.01	0.00-0.03		
Lymphatic Vessels Sarcomas	Both sexes	2	<0.001	0.01	0.00-0.01		
	Male	1	<0.001	0.01	0.00-0.02	------	------
	Female	2	0.01	0.01	0.0-0.03		
Lymphangiosarcoma	Both sexes	2	<0.001	0.01	0.00-0.01		
	Male	1	<0.001	0.01	0.00-0.02	------	------
	Female	2	0.01	0.01	0.0-0.03		
Giant Cell Tumors-Malignant	Both sexes	44	0.10	0.10	0.07-0.14		
	Male	23	0.10	0.11	0.06-0.15	1.03	0.56-1.88
	Female	21	0.09	0.10	0.06-0.15		
Malignant giant cell tumor of soft parts	Both sexes	19	0.04	0.04	0.02-0.06		
	Male	14	0.06	0.06	0.03-0.10	2.83**	1.04-7.72
	Female	5	0.02	0.02	0.00-0.04		
Malignant tenosynovial giant cell tumor	Both sexes	25	0.06	0.06	0.04-0.09		
	Male	9	0.04	0.04	0.01-0.07	0.52	0.23-1.19

Table 2 continued.							
	Female	16	0.07	0.08	0.04-0.12		
Nerve Sheath Tumors-Malignant	Both sexes	96	0.21	0.22	0.18-0.27		
	Male	66	0.29	0.30	0.22-0.37	2.09**	1.36-3.21
	Female	30	0.13	0.14	0.09-0.20		
Malignant peripheral nerve sheath tumor	Both sexes	91	0.20	0.21	0.17-0.25		
	Male	63	0.28	0.28	0.21-0.36	2.10**	1.35-3.26
	Female	28	0.13	0.14	0.08-0.19		
malignant schwannoma, Neurilemmosarcoma	Both sexes	3	0.01	0.01	0.00-0.02		
	Male	1	<0.001	<0.001	------	------	------
	Female	2	0.01	0.01	0.00-0.02		
Malignant peripheral nerve sheath tumor	Both sexes	2	<0.001	<0.001	------		
	Male	2	0.01	0.01	0.00-0.02	------	------
	Female	0	<0.001	<0.001	------		
Granular cell and Alveolar Soft Tissue Sarcoma	Both sexes	21	0.05	0.04	0.02-0.06		
	Male	10	0.04	0.04	0.01-0.06	0.82	0.34-1.97
	Female	11	0.05	0.05	0.02-0.08		
Alveolar soft part sarcoma	Both sexes	21	0.05	0.04	0.02-0.06		
	Male	10	0.04	0.04	0.01-0.06	0.82	0.34-1.97
	Female	11	0.05	0.05	0.02-0.08		
Ewing tumor and Askin tumor of soft tissue	Both sexes	68	0.15	0.14	0.11-0.17		
	Male	42	0.18	0.17	0.12-0.22	1.44	0.88-2.35
	Female	26	0.12	0.12	0.07-0.16		

ASIR = age-standardized incidence rate, CI = confidence interval, NOS = not otherwise specified
SRR = male-to-female standardized incidence rate (ASIR) ratio
*ASRs were age-standardized to the new world health organizing (WHO) standard population
** Indicates statistical significance at the 0.05 level

Table3. Incidence rates of soft-tissue sarcoma per million person-years during 2009-2015 in Iran, stratified by age and gender (CI: confidence interval, ASR*: truncated age-standardized incidence rate)

Age (Years)	n	Crude Rate	ASR* (95% CI)
Both Sexes			
<20	286	1.95	1.91 (1.69-2.13)
20-44	931	4.52	4.64 (4.34-4.94)
45-64	855	11.57	11.81 (11.01-12.60)
65+	521	19.88	19.61 (17.91-21.30)
Male			
<20	143	1.91	1.87 (1.56-2.18)
20-44	537	5.167	5.26 (4.81-5.71)
45-64	472	12.84	13.15 (11.96-14.35)
65+	324	24.69	24.12 (21.47-26.77)
Female			
<20	143	1.99	1.94 (1.63-2.26)
20-44	394	3.87	4.00 (3.61-4.40)
45-64	383	10.32	10.49 (9.43-11.54)
65+	197	15.07	15.03 (12.92-17.13)

The age-standardized incidence rates in the five most common major groups were reported as 2.08, 1.23, 0.92, 0.79, 0.59 for soft tissue NOS, fibromatous, lipomatous, synovial like, and myomatous sarcomas per million person-years, respectively.

In the soft tissue sarcomas NOS group, the highest ASIR belonged to mesenchymal tumors and spindle cell sarcomas with ratios of 0.81 and 0.78 per million person-years. In the fibromatous sarcomas group, malignant fibrous histiocytoma had a higher rate with an ASIR of 0.8 per million person-years. Myxoid liposarcoma with an ASR of 0.39 per million person-years was more frequent than the other subgroups. In synovial like sarcoma, synovial sarcoma NOS was more common with an ASR of 0.42, followed by synovial sarcoma spindle cell and biphasic synovial sarcoma. Finally, in the myomatous sarcomas group, leiomyosarcoma had the highest ASIR which was 0.378 per million person-years.

The incidence of soft-tissue sarcomas was assessed in three regions, including upper limb (C 49.1), hip and lower limb (C 49.2), as well as the pelvis (C 49.5) [Table 4]. The incidence rate in the hip and lower limb was totally higher, as compared to that in the upper limb and pelvis region, and it was confirmed in all gender and age groups. Especially in lipomatous sarcomas, the incidence rate of tumors in the lower limb was more than four times higher than that in the upper limb. On the contrary, the incidence rate of malignant giant cell tumors in the upper limb was higher than that in other areas [Table 4].

Table 4. Incidence (per million person-years) of Primary Soft Tissue by Histologic Subtype and Topography subgroup, Iran (2009-2014)

Histology Subgroup	C49.1	C49.2	C49.5
Total	15.41 (15.28-15.53)	36.70 (36.51-36.89)	10.30 (10.20-10.41)
Paragangliomas and Glomous Tumors	0.00 (0.00-0.00)	0.03 (0.02-0.03)	0.00 (0.00-0.00)
Soft Tissue Sarcomas, NOS	5.24 (5.17-5.31)	11.17 (11.06-11.27)	4.24 (4.18-4.31)
Fibromatous Sarcomas	3.32 (3.26-3.37)	7.45 (7.36-7.54)	1.41 (1.38-1.45)
Myxomatous Sarcomas	0.05 (0.04-0.05)	0.10 (0.08-0.11)	0.00 (0.00-0.00)
Lipomatous Sarcomas	1.34 (1.30-1.37)	6.09 (6.02-6.17)	1.72 (1.68-1.76)
Myomatous Sarcomas	1.31 (1.27-1.35)	2.68 (2.63-2.73)	1.54 (1.50-1.58)
Complex Mixed Sarcomas	0.05 (0.04-0.05)	0.13 (0.12-0.15)	0.02 (0.01-0.02)
Synovial Like Sarcomas	1.84 (1.80-1.88)	5.35 (5.28-5.42)	0.65 (0.63-0.67)
Blood Vessels Sarcomas	0.67 (0.64-0.70)	0.90 (0.86-0.93)	0.08 (0.07-0.09)
Lymphatic Vessels Sarcomas	0.03 (0.03-0.04)	0.03 (0.02-0.03)	0.00 (0.00-0.00)
Giant Cell Tumors-Malignant	0.73 (0.70-0.76)	0.22 (0.21-0.24)	0.03 (0.02-0.03)
Ewing tumor and Askin tumor of soft tissue	0.30 (0.29-0.32)	0.77 (0.74-0.79)	0.30 (0.28-0.31)

Discussion

Soft tissue sarcomas are rare neoplastic lesions accounting for 1% of adult malignancies (1). Limb soft tissue sarcomas are even less frequent. According to previous studies, malignant fibrous histiocytoma was the most common soft tissue sarcoma in extremities with an incidence of 23%-24% (10–13). In another study, leiomyosarcoma was recognized as the most common and malignant fibrous histiocytoma as the second most common soft tissue sarcomas (8). According to a recent population-based study in Australia in 2019, leiomyosarcoma (20.43%), malignant fibrous histiocytoma (16.14%), and soft tissue tumors/sarcomas, and NOS (10.18%) were the most common STS subtypes(14).

In the present study, the most common soft tissue sarcomas of the extremities were mesenchymal tumor (12.26%), spindle cell sarcoma (12.18%), and malignant fibrous histiocytoma (11.45%) [Table 2]. This discrepancy in the results can be attributed to inaccurate and un-detailed histopathological classifications in the noted studies. In these studies, soft tissue sarcomas were not classified according to ICD-O3, and the major group of soft tissue sarcoma NOS were ignored. According to our database analysis, soft tissue sarcoma NOS include 32.39% of all extremity soft tissue sarcomas which was more frequent than other histopathological major groups. In their study, A. Gingrich et al. pointed out that most extremity soft tissue sarcomas in both nonelderly adult and elderly adult populations were soft tissue sarcoma NOS (15). They also used ICD-O3 to classify the tumors (15). In the current study, ignoring soft tissue sarcoma NOS, malignant fibrous histiocytomas (MFH) included 11.45% of soft tissue sarcomas. The other probable cause of contradictory results can be racial differences.

Gender dominancy was also observed in most groups and their subgroups, with men suffering much more often soft-tissue sarcomas [Table 2]. In some of the groups, this dominant ratio was statistically significant. Although

female predominancy in the incidence ratio of tumors was detected in a few groups, they were not statistically significant. In general, the SRR was 1.31 in a total of 2,593 cases of soft-tissue sarcoma. Although some reports indicated that STS involved both genders with approximately equal ratios (13,16), some other studies revealed male dominancy among STS patients (13,16). According to Parker et al., soft-tissue sarcoma was more frequent in men, and deaths due to STS were more frequent in females (17). On the contrary, Reshadi et al. reported a higher prevalence of STS in the female population(10).

As illustrated by the results, the incidence rates (per million) of soft-tissue sarcoma increased with age in total cases and by subgroups [Table 3]. The incidence rates (per million) of STS in the age range of above 65 years was higher than other age groups. This finding is comparable to most of the results obtained in previously conducted studies (13,15). On the other hand, Reshadi et al. reported the peak age of incidence between 30-59 years of age (10).

The majority of soft-tissue sarcomas in the Iranian population were detected in the hip and lower extremities [table 4]. As an exception, malignant giant cell STS were more frequent in the upper limbs. The findings in the Iranian population are comparable to the published studies reporting that 75% and 33% of soft-tissue sarcomas of extremities occur in lower limbs and thighs, respectively (10,18).

The present investigation was the first epidemiological study on the soft-tissue sarcoma of the extremities based on Iran National Cancer Registry (INCR) data. Herein, we gathered precious epidemiological findings which can be used in further investigations. Among the notable limitations of the present study, we can refer to incomplete recorded data and a lack of insight into the geographic distribution of tumors in the country. Furthermore, in this registry, due to incomplete histopathology registration of the patients and lack of histology codes, we had no information about histology codes and staging of the lesions. Moreover, no information was available regarding the type of treatment and patient surveillance. The International Classification of Diseases for Oncology, third edition (ICD-03), was used to identify patients with soft tissue sarcomas (2009 to 2014) according to INCR. Although it was better to use the new version of ICD-09 or ICD-10, the data was gathered according to (ICD-03). It is suggested that further studies be conducted to complete the database and analyze this information.

In conclusion, soft-tissue sarcomas of extremities are rare neoplastic lesions. The incidence rate of these tumors in the Iranian population increases with age, and they are more frequent in patients older than 65 years of age; moreover, most of these tumors are more common in males. The three most common histopathological types of soft-tissue sarcomas in extremities include mesenchymal tumor, spindle cell sarcoma and leiomyosarcoma. Among the Iranian population, the majority of soft-tissue sarcomas in extremities occur in the lower limbs and hip region. The three most common soft tissue sarcomas based on (M-codes) in extremities were mesenchymal tumor (M-code: 8800), spindle cell sarcoma (M-code: 8801), and malignant fibrous histiocytoma tumor (M-code: 8800) according to INCR. Most soft tissue sarcomas were detected in the lower limbs and pelvis region.

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