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Incidence of soft tissue sarcoma in Taiwan: A nationwide population-based study (2007–2013)

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ABSTRACT

Background: Asian studies on soft tissue sarcoma (STS) incidence, irrespective of the primary site, are scant.
Methods: STS data were acquired from the population-based 2007–2013 Taiwan Cancer Registry of the Health and Welfare Data Science Center, Taiwan. Histological subtype-, site-, sex-, and age-specific STS incidence rates were analyzed according to the 2013 classification of the World Health Organization.
Results: In total, 11,393 patients with an age-standardized incidence rate (ASIR) of 5.62 (95% confidence interval, 5.51–5.73) per 100,000 person-years were identified. Overall, a male predominance (sex-standardized incidence rate ratio, 1.2) was noted, and the rate increased with age, peaking at > 75 years. Approximately 30% of STSs occurred in connective, subcutaneous, and other soft tissues and 70% in other sites. In addition to connective, subcutaneous, and other soft tissues, the three most common primary sites were the stomach (15.9%), skin (14.3%), and small intestines (10.5%). Gastrointestinal stromal tumor was the most common subtype (29.2%; ASIR, 1.55/100,000 person-years), followed by liposarcoma (11.5%; ASIR, 0.63/100,000 person-years) and leiomyosarcoma (9.7%; ASIR, 0.53/100,000 person-years). Compared with relevant data from Western countries, the incidence rate of angiosarcomas was higher than that in other regions, whereas the incidence rates of leiomyosarcoma and Kaposi sarcoma were lower than those in other regions.
Conclusion: STS incidence varied by histological subtype, sex, age, and primary site in an Asian population. Our results suggested regional and racial discrepancies in the incidence rates of certain STS subtypes.

1. Introduction

Soft tissue sarcoma (STS) is a rare and complex disease with > 100 histological subtypes, heterogeneous in terms of location, histology, molecular profile, and prognosis [1,2]. The 2013 edition of the World Health Organization (WHO) classification of soft tissue tumors [2], revised from the previous 2002 version [3], includes molecular characterization of these tumors as well as entities that were previously

Abbreviations: STS, Soft tissue sarcoma; GIST, gastrointestinal stromal tumor; WHO, World Health Organization; TCR, Taiwan Cancer Registry; DFSP, Dermatofibrosarcoma protuberans; ICD-O-3, *International Classification of Diseases for Oncology* Third Edition; IARC, International Agency for Research on Cancer; MV%, percentage of microscopy-verified registration; DCO%, percentage of death certificate only; HWDC, Health and Welfare Data Science Center; UPS, undifferentiated pleomorphic sarcoma; MFH, malignant fibrous histiocytoma; NOS, not otherwise specified; CI, confidence interval; SIRR, standardized incidence rate ratio; ASIR, age-standardized incidence rate; APC, annual percentage change; HIV, human immunodeficiency virus

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Table 1
Soft tissue sarcoma by histologic subtype (and primary site for GIST and leiomyosarcoma) during 2007–2013 in Taiwan.

		All primary sites excluding bones and joints					
		n	%	Rate[†]	95% CI	SIRR	95% CI
Histotype	**Morphology code ICD-O-3[$]**						
GIST[#(f)]	8936	3332	(29.2)	1.55	(1.50, 1.61)	1.2[*]	(1.10, 1.26)
Stomach		1764	(15.5)	0.82	(0.78, 0.86)	1.05	(0.96, 1.16)
Small intestine		1135	(10)	0.53	(0.50, 0.56)	1.36[*]	(1.21, 1.53)
Esophagus/others		252	(2.2)	0.12	(0.10, 0.13)	1.18	(0.92, 1.51)
Colon/rectum		181	(1.6)	0.09	(0.07, 0.10)	1.33	(0.99, 1.79)
Liposarcoma	8850-8855, 8857-8858	1312	(11.5)	0.63	(0.59, 0.66)	1.7[*]	(1.56, 1.95)
Well differentiated	8851	468	(4.1)	0.22	(0.20, 0.24)	1.7[*]	(1.37, 2.00)
Dedifferentiated	8858	286	(2.5)	0.13	(0.12, 0.15)	1.8[*]	(1.45, 2.34)
Myxoid/round cell[#(b)]	8852, 8853	267	(2.3)	0.14	(0.12, 0.15)	1.9[*]	(1.44, 2.39)
Liposarcoma NOS	8850	155	(1.4)	0.07	(0.06, 0.09)	1.8[*]	(1.31, 2.54)
Pleomorphic	8854	91	(0.8)	0.04	(0.03, 0.05)	1.7[*]	(1.13, 2.68)
Mixed type[#(c)]	8855	45	(0.4)	0.02	(0.01, 0.03)	1.5	(0.83, 2.74)
Leiomyosarcoma	8890, 8891, 8894-8896	1102	(9.7)	0.53	(0.50, 0.56)	0.3[*]	(0.26, 0.34)
Excluding uterus		605	(5.3)	0.29	(0.27, 0.32)	0.69[*]	(0.59, 0.81)
Uterus (Female only)		497	(4.4)	0.47[@]	(0.42, 0.51)		
DFSP[#(d)]	8832, 8833	953	(8.4)	0.51	(0.48, 0.55)	1.1	(1.00, 1.29)
Angiosarcomas	9120, 9130, 9133, 9150, 9170	701	(6.2)	0.34	(0.31, 0.36)	1.6[*]	(1.37, 1.86)
Kaposi sarcoma	9140	576	(5.1)	0.27	(0.25, 0.29)	5.4[*]	(4.41, 6.63)
Fibrosarcoma[#(e)]	8810-8811, 8813-8815, 8840	444	(3.9)	0.22	(0.20, 0.24)	1.4[*]	(1.15, 1.69)
UPS/MFH[#(a)]	8830	395	(3.5)	0.19	(0.17, 0.20)	1.6[*]	(1.32, 1.99)
Malignant nerve sheath tumors (including MPNST)	9540, 9560-9561, 9571, 9580	282	(2.5)	0.15	(0.13, 0.17)	1.2	(0.95, 1.54)
Rhabdomyosarcoma	8900-8902, 8910, 8912, 8920, 8921	238	(2.1)	0.17	(0.14, 0.19)	1.3	(1.00, 1.73)
Rhabdomyosarcoma NOS	8900	72	(0.6)	0.05	(0.03, 0.06)	1.2	(0.75, 2.05)
Embryonal	8910	67	(0.6)	0.06	(0.04, 0.07)	1.1	(0.67, 1.83)
Pleomorphic	8901	44	(0.4)	0.02	(0.02, 0.03)	1.2	(0.63, 2.12)
Alveolar	8920, 8921	41	(0.4)	0.03	(0.02, 0.04)	1.5	(0.81, 2.92)
Mixed type	8902	7	(0.1)	0.00	(0.00, 0.01)	6.3	(0.95, 41.45)
Spindle cell/sclerosing	8912	7	(0.1)	0.01	(0.00, 0.01)	3.7	(0.63, 21.82)
Ewing sarcoma/PNET[#(g)]	9260, 9364, 9365, 9473	192	(1.7)	0.13	(0.11, 0.15)	1.1	(0.82, 1.50)
Synovial sarcoma	9040-9043	188	(1.7)	0.11	(0.09, 0.12)	1.0	(0.74, 1.34)
Chondrosarcoma	9220, 9231, 9240	59	(0.5)	0.03	(0.02, 0.04)	2.1[*]	(1.19, 3.54)
Alveolar soft part sarcoma	9581	37	(0.3)	0.03	(0.02, 0.03)	0.8	(0.43, 1.60)
Osteosarcoma	9180, 9181	30	(0.3)	0.01	(0.01, 0.02)	0.7	(0.32, 1.38)
Clear cell sarcoma	9044	22	(0.2)	0.01	(0.01, 0.02)	1.7	(0.56, 5.23)
Other specified sarcomas	8711, 8806, 8963, 9251, 9252, 8940, 8982, 8990	192	(1.7)	0.10	(0.09, 0.12)	1.2	(0.92, 1.67)
Sarcoma NOS	8800-8805	1338	(11.7)	0.65	(0.61, 0.68)	1.3[*]	(1.15, 1.43)
Total		11393	(100)	5.62	(5.51, 5.73)	1.2[*]	(1.16, 1.25)

Abbreviations: CI, confidence interval; DFSP, dermatofibrosarcoma protuberans; GIST, gastrointestinal stromal tumor; ICD-O-3, *International Classification of Diseases for Oncology, Third Edition*; MFH, malignant fibrous histiocytoma; MPNST, malignant peripheral nerve sheath tumor; NOS, not otherwise specified; PNET, primitive neuroectodermal tumor; SIRR, standardized incidence rate ratio; UPS, undifferentiated pleomorphic sarcoma.

[$] The fifth digit of the codes (behavior code) is "3," which indicates malignancy.

[†] Rates were per 100,000 person-years and age-adjusted to the 2000 world standard population.

[*] This value reflects a statistically significant difference at the $p < 0.05$ level. The male-to-female SIRRs and 95% CIs were calculated to compare the cancer incidences by sex. The SIRRs were considered significantly different if the estimated 95% CI did not contain one.

[@] Female incidence rate.

[#] Updated in the 2013 World Health Organization classification of tumors of soft tissue. [(a)] Malignant fibrous histiocytoma (ICD-O-3 88303) was removed and unclassified/undifferentiated sarcomas (undifferentiated pleomorphic sarcoma or UPS) was classified separately; [(b)] round cell liposarcoma was removed as a synonym for high-grade myxoid liposarcoma; [(c)] mixed type liposarcoma was removed; [(d)] DFSP was included in the soft tissue volume for the first time. [(e)] Hemangiopericytoma was removed as a synonym for malignant solitary fibrous tumor (ICD-O 88153); [(f)] GIST was included in the soft tissue volume for the first time; [(g)] PNET removed as a synonym for Ewing sarcoma.

ignored [4]. Among these, the inclusion of gastrointestinal stromal tumors (GISTs) was a major change that can significantly affect overall STS incidence. Similarly, dermatofibrosarcoma protuberans (DFSP)—previously classified under skin cancer—was also included in the 2013 WHO STS classification for the first time [2,4]. Grouping of STSs has varied widely among relevant reports, mainly because of these tumors' complexity and difficulties in classification [5–7].

According to the American Cancer Society, STS can arise in any part of the body, including the extremities, trunk, head, neck, retroperitoneum, and internal organs [8]. However, in standard reports from most cancer-reporting authorities, including the Taiwan Cancer Registry (TCR) [9], tumors of the soft tissue are confined to STSs in "peripheral nerves and autonomic nervous system" and "connective, subcutaneous, and other soft tissues" [*International Classification of Diseases for Oncology, Third Edition* (ICD-O-3) topography codes C47 and C49]. STSs arising in sites other than ICD-O-3 C47 and C49, including the retroperitoneum, peritoneum, and internal organs, are attributable to the site of origin, without considering the histology [10,11]. Because those arising from only ICD-O-3 C47 and C49 are considered STSs, the incidence of STS reported by cancer-reporting authorities has always

Table 2
Soft tissue sarcoma by primary site during 2007–2013 in Taiwan.

Topography	Topography code ICD-O-3 (excluding C40-C41)	*n*	%
Connective, subcutaneous and other soft tissues	C47, C49	3402	(29.9)
Stomach	C16	1810	(15.9)
Skin	C44	1630	(14.3)
Small intestine	C17	1192	(10.5)
Retroperitoneum and peritoneum	C48	713	(6.3)
Uterus	C53-C55	585	(5.1)
Liver and intrahepatic bile ducts, gallbladder and extrahepatic bile ducts	C22, C23-24	260	(2.3)
Colon, rectum, rectosigmoid junction and anus	C18, C19-21	224	(2)
Lip, oral cavity, salivary glands and pharynx	C00, C01-C14	223	(2)
Pancreas and other and ill-defined sites within digestive organs and peritoneum	C25, C26	166	(1.5)
Brain, and other and unspecified parts of nervous system	C70, C71, C72	155	(1.4)
Larynx, trachea, bronchus, and lung	C32-C34	153	(1.3)
Thymus, heart and mediastinum	C37-C383, C388	112	(1)
Nasal cavity, accessory sinuses, middle ear and inner ear	C30-C31	108	(0.9)
Breast	C50	98	(0.9)
Kidney, renal pelvis, ureter and other urinary system	C64, C65, C66, C68	89	(0.8)
Other male genital organs	C61, C60, C63	79	(0.7)
Ovary, fallopian tube and broad ligament, and other female genital organs	C56, C570-C574, C51-C52, C577-C579, C58	73	(0.6)
Urinary bladder	C67	34	(0.3)
Esophagus	C15	41	(0.4)
Pleura, and other and ill-defined sites within respiratory system and intrathoracic organs	C384, C39	24	(0.2)
Testis	C62	24	(0.2)
Eye and lacrimal gland	C69	17	(0.1)
Others		181	(1.6)
Total		11393	(100)

Abbreviations: ICD-O-3, International Classification of Diseases for Oncology, Third Edition.

been underestimated. Taken together, the aforementioned factors have impeded the global comparison of STS incidence rates.

Most population-based studies on STS incidence have been conducted in Western countries [5,7,12–16], and information relevant available in Asia has been limited [17–19]. The population in Taiwan is approximately 23.4 million, of which 95% is Han Chinese. By using data from the nationwide population-based TCR, we analyzed the incidence of STS as per the 2013 WHO classification, irrespective of the primary site, to provide the most comprehensive picture of the STS burden in an Asian population.

2. Material and methods

2.1. TCR

The data for STS registered in the nationwide TCR database during 2007–2013 were acquired from the Health and Welfare Data Science Center (HWDC), Ministry of Health and Welfare, Taiwan. The TCR is organized and funded by the Ministry of Health and Welfare, Taiwan, and has been collecting cancer data since 1979. Beginning with 2002 incidence data, the ICD-O-3 replaced the ICD-O, Field Trial Edition, for coding in the TCR. In 2003, the Cancer Control Act was enacted; it mandates that all hospitals with > 50 beds, which provide outpatient and hospitalized cancer care, must submit cancer data to the central registry. The completeness and data quality of TCR database has been excellent since then. For the latest data (2015), the completeness of the TCR database was 98.17% [9]. Regarding the indices of data quality defined by the International Agency for Research on Cancer (IARC), an increased percentage of microscopy-verified registration (MV%) and decreased percentage of death certificate only (DCO%) have already been demonstrated [20,21]. STS diagnoses were made by specialist pathologists with board certification. For regional and district general hospitals without pathologists specializing in STS classification, the diagnoses were made by consulting the STS Committee of the Taiwan Society of Pathology, Taiwan Division of the International Academy of Pathology. TCR is one of the population-based cancer registries worldwide, with 100% coverage, and has been used in large-scale international studies for global surveillance of trends in cancer incidence and survival [22].

2.2. Ethical approval

The Institutional Review Board of Taipei Veterans General Hospital, Taiwan approved the protocol for this retrospective observational study (IRB-TPEVGH No.: 2016-11-003CC#1).

2.3. Data acquisition

STS data of all primary sites were extracted according to the ICD-O-3 morphology and topography codes of the tumor [23]. This study excluded cancers of bones and joints (ICD-O-3 C40 and C41), as well as lymphoma and multiple myeloma. The ICD-O-3 topography codes of the sites including “peripheral nerves and autonomic nervous system” and “connective, subcutaneous and other soft tissues” (C47 and C49), and all other primary sites (C00–C80, except C47, C49, C40, and C41) are listed in Table 2. Hereafter, we use “connective, subcutaneous, and other soft tissues” to indicate C47 and C49. The data of STSs are tabulated according to the 2013 WHO classification of tumors of soft tissue [2], with some modification, which includes subgroups of leiomyosarcoma, undifferentiated pleomorphic sarcoma [UPS; including those formerly called malignant fibrous histiocytoma (MFH)], liposarcoma, DFSP, rhabdomyosarcoma, angiosarcomas, Kaposi sarcoma, fibrosarcoma (fibroblastic and myofibroblastic tumors), GIST, malignant nerve sheath tumors, Ewing sarcoma, chondrosarcoma, osteosarcoma, clear cell sarcoma, alveolar soft part sarcoma, other specified sarcomas, and sarcoma not otherwise specified (NOS). The codes used to identify the study population are given in Tables 1 and 2.

2.4. Data analysis

The incidence rates of STS were analyzed according to histotype, sex, age, and primary site. This study employed the IARC’s methods to calculate the incidence, standard errors, 95% confidence intervals (CIs), and standardized incidence rate ratios (SIRRs) [24]. Age-specific

Table 3
Comparison of incidence rates of soft tissue sarcomas irrespective of the primary site in different regions.

	Rate per 100,000 persons			
Region	Switzerland/Vaud,	Three European regions,	USA/SEER,	Taiwan,
Study period	1990-1994[#,a]	2005-2008[b]	1978-200[c]	2007-2013[#]
Total no. of patients	212	1558	26758	11393
Histotype				
GIST	Not included	1.36	Not included	1.55
Liposarcoma	0.32	0.99	0.59	0.63
Leiomyosarcoma	1.10	0.93	1.23	0.53
Uterus (F)				0.47
Excluding uterus (Both sexes)				0.29
Excluding uterus (M)				0.24
Excluding uterus (F)				0.35
African American/Caucasian American				
Uterus (F)			0.92/0.55	
Excluding uterus (M)			1.21/1.01	
Excluding uterus (F)			1.43/0.8	
DFSP	–	0.36	0.5	0.51
Angiosarcomas	0.19	0.23	0.21	0.34
Kaposi sarcoma	1.74	0.37	Not included	0.27
Fibrosarcoma*	0.84	0.3	0.19	0.22
UPS/MFH	–	0.37	0.88	0.19
Malignant nerve sheath tumors (including MPNST)	–	0.07	0.19	0.15
Rhabdomyosarcoma	0.23	0.19	0.21	0.17
Synovial sarcoma	0.17	0.13	0.11	0.11
Sarcoma, NOS	0.42	0.35	0.65	0.65
Total (except GIST and Kaposi)	3.81	4.4	5.03	3.8

Abbreviations: DFSP, dermatofibrosarcoma protuberans; F, female; GIST, gastrointestinal stromal tumor; M, male; MFH, malignant fibrous histiocytoma; MPNST, malignant peripheral nerve sheath tumor; NOS, not otherwise specified; SEER, Surveillance, Epidemiology and End Results program; UPS, undifferentiated pleomorphic sarcoma.
-Data not shown in the original reports.
[#] Rates were age-standardized to the world standard population.
[a] Levi et al. (1999).[13].
[b] Mastrangelo et al. (2012).[6] Only crude rates were reported. There were methodological differences among the 3 regions: Rhone-Alps, 2005–2006; Veneto, 2007–2008; and Aquitaine.2007–2008.
[c] Toro et al. (2006).[5] Rates are age-adjusted to the 2000 US (19 age groups) standard.
* Different grouping method of this group of tumors between studies. The original report by Mastrangelo et al.[6] showed rates of "fibrosarcoma" ($0.05/10^5$ persons), "low-grade fibromyxoid sarcoma" (0.04), "malignant solitary fibrous tumor" (0.04), and myxofibrosarcoma (0.17), respectively. A sum of these tumors (0.3) was showed in this table for comparison. Similarly, the report by Toro et al.[5] demonstrated rates of "fibrosarcoma" ($0.18/10^5$ persons) and "myxosarcoma" (0.01), respectively. A sum of these tumors (0.19) was showed in this table for comparison.

incidence rates were stratified into 18 subgroups by 5-year age intervals (0–4 to ≥85 years). Census data were obtained from the Department of Statistics, Ministry of the Interior, Taiwan. The world standard population in 2000 was used to calculate age-standardized incidence rates (ASIRs). Here, ASIRs are expressed per 100,000 person-years. All computations were performed on Microsoft Office Excel 2016, Microsoft Corporation, Washington, D.C., USA.

To identify significant changes in incidence rates, the joinpoint regression model (Joinpoint Regression Program, version 4.0.4; Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute, Bethesda, MD, USA) and permutation tests were used [25,26], in which up to one joinpoint (two line segments) were produced to express the annual percentage change (APC). The software takes ASIRs and selects the best-fitting trend lines and tests the significance level using the Monte Carlo permutation method. APC was considered significant if the 95% CI did not include zero ($p < 0.05$). The male-to-female SIRRs and 95% CIs were calculated to compare the cancer incidence by sex. The SIRRs were considered significantly different if the estimated 95% CI did not contain one ($p < 0.05$).

3. Results

In 2013, 1.66% of all newly diagnosed cancer cases in Taiwan were of STS. Tables 1 and 2 list the case numbers, and percent distributions of STS during 2007–2013 by histologic types and primary sites, respectively. In total, 11,393 patients were diagnosed as having STS during the study period [annual average, 1627.6 persons; crude incidence rate, 7.02/100,000 person-years; ASIR, 5.62 (95% CI, 5.51–5.73) per 100,000 person-years]. The cumulative risk of developing STS from 0 to 74 years of ager was 0.54%. The average MV% for all STS was 97.6% (range, 97.0%–98.3%, 2007–2013). GIST was the most common histologic subtype (29.2%; ASIR, 1.55 per 100,000 person-years), followed by liposarcoma (11.5%; ASIR, 0.63), and leiomyosarcoma (9.7%; ASIR, 0.53). The three subtypes comprised half of all STSs diagnosed in the Taiwanese population. Approximately 30% (3,402/11,393) of STSs occurred in "connective, subcutaneous and other soft tissues," whereas 70% occurred in all other sites. The three most common sites other than "connective, subcutaneous and other soft tissues" were the stomach (15.9%), skin (14.3%), and small intestines (10.5%; Table 2).

3.1. Subtype-specific incidence rates

Subtype-specific incidence rates are listed in Table 1. For GIST, the most common primary sites included the stomach (52.9%) and small intestines (34.1%). These two sites comprised > 80% of all GISTs; others included the colon and rectum (5.4%) and the esophagus and other sites (7.9%).

For liposarcoma, the most common histopathologic subtypes were well differentiated (35.7%), dedifferentiated (21.8%), and myxoid/round cell (20.4%).

Approximately half (45.1%; n = 497) of the 1,102 leiomyosarcomas

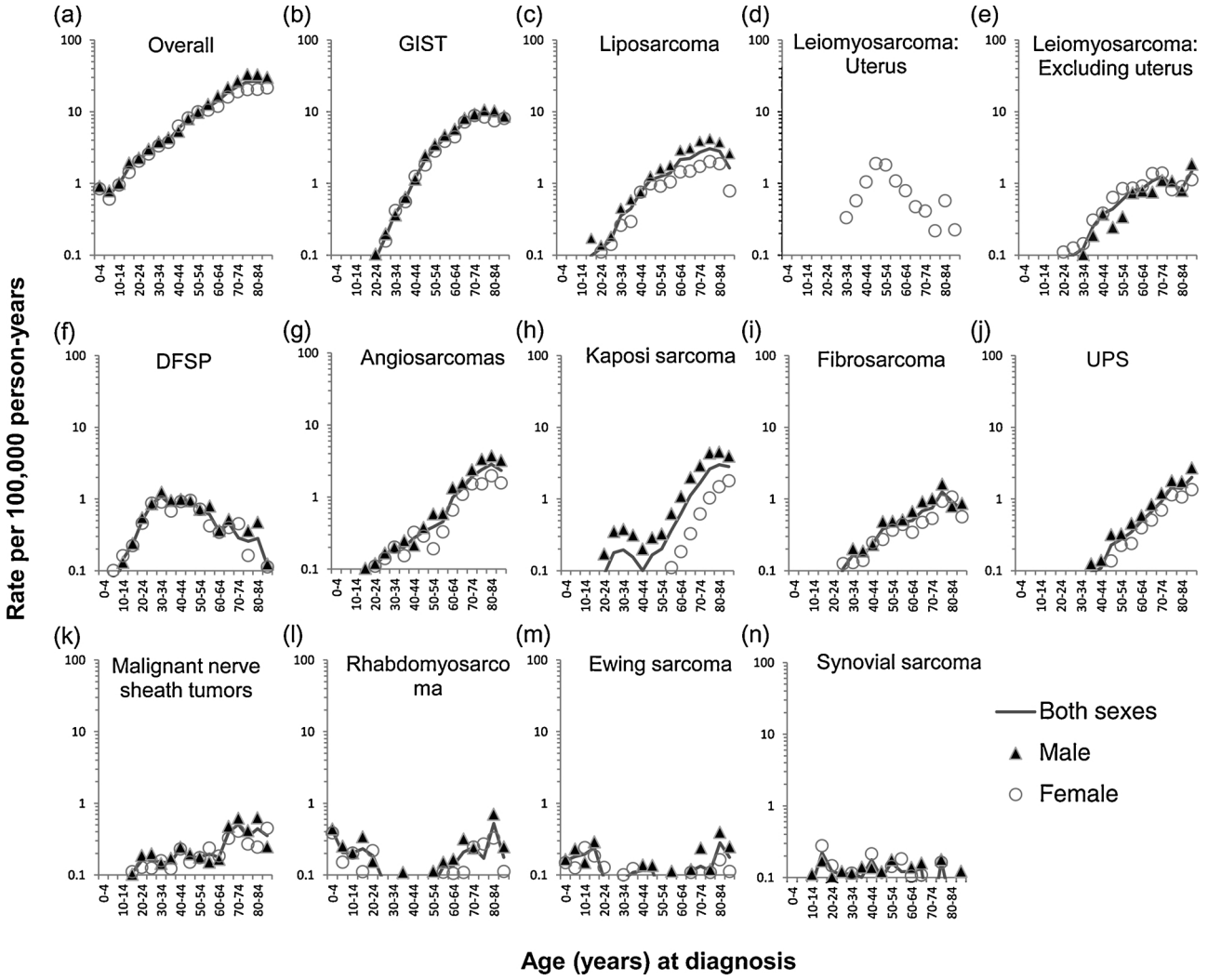

Fig. 1. Age-specific incidence rates of STS by histologic subtype and sex during 2007–2013.

were of uterine origin (ASIR, 0.47 per 100,000 females) and the remaining arose in primary sites excluding the uterus (54.9%; ASIRs, 0.29/100,000 person-years, 0.24/100,000 person-years, and 0.35/100,000 person-years for both, male, and female sexes, respectively, Table 3).

For rhabdomyosarcoma, the most common histopathologic subtypes were rhabdomyosarcoma NOS (30.3%), followed by embryonal (28.2%), pleomorphic (18.5%), and alveolar (17.2%). Mixed type and spindle cell or sclerosing type were rare, each comprising only 3%.

3.2. Sex-specific incidence rates

Difference in sex was noted for overall STS, with a significant male predominance (SIRR, 1.2; 95% CI, 1.16–1.25, $p < 0.05$). Male-to-female SIRRs are shown in Table 1. The subtype with the most significant male predominance was Kaposi sarcoma (SIRR, 5.4; 95% CI, 4.41–6.63, $p < 0.05$); other subtypes also exhibiting male predominance were UPS, liposarcoma, angiosarcomas, fibrosarcoma, GIST, chondrosarcoma, and sarcoma NOS, with SIRRs of 1.2–2.1. By contrast, leiomyosarcoma was the only subtype with a female predominance (SIRR, 0.3; 95% CI, 0.26–0.34, $p < 0.05$). For GIST, only those arising in the small intestine exhibited a significant male predominance (SIRR, 1.36; 95% CI, 1.21–1.53, $p < 0.05$); no sex predilection was found for GIST in the other sites.

Of all leiomyosarcoma cases, approximately half occurred in the uterus. For those occurring in sites other than the uterus, a significant female predilection was found (male-to-female SIRR, 0.69; 95% CI, 0.59–0.81, $p < 0.05$).

No sex predilection was found for any histopathologic subtypes of rhabdomyosarcoma.

3.3. Age-specific incidence rates

Fig. 1 illustrates the age-specific incidence rates of STS by histotype (and primary site for leiomyosarcoma). For overall STS, the incidence rate increased with age and peaked at > 75 years (Fig. 1a). The subtypes, which mainly occurred in adults and exhibited increasing rates with age, were GIST (Fig. 1b), liposarcoma (Fig. 1c), leiomyosarcoma excluding the uterus (Fig. 1e), angiosarcomas (Fig. 1g), fibrosarcoma (Fig. 1i), UPS (Fig. 1j), and malignant nerve sheath tumors (Fig. 1k). Incidence rates of leiomyosarcoma in the uterus and DFSP significantly increased in the middle-aged patients (Fig. 1d and f, respectively). The incidence rate of Kaposi sarcoma reached its first peak for young adults at the age of 30–34 years, but only in male patients (Fig. 1h). At the age of 40–44 years, these rates increased sharply and then increased with age, but with a significant male predilection; however, the proportion of female patients increased with age beginning at the age of 55–59 years. The incidence rates of rhabdomyosarcoma and Ewing sarcoma were bimodal, peaking during childhood and old age (Fig. 1l and m, respectively). The rates of synovial sarcoma showed modest increased

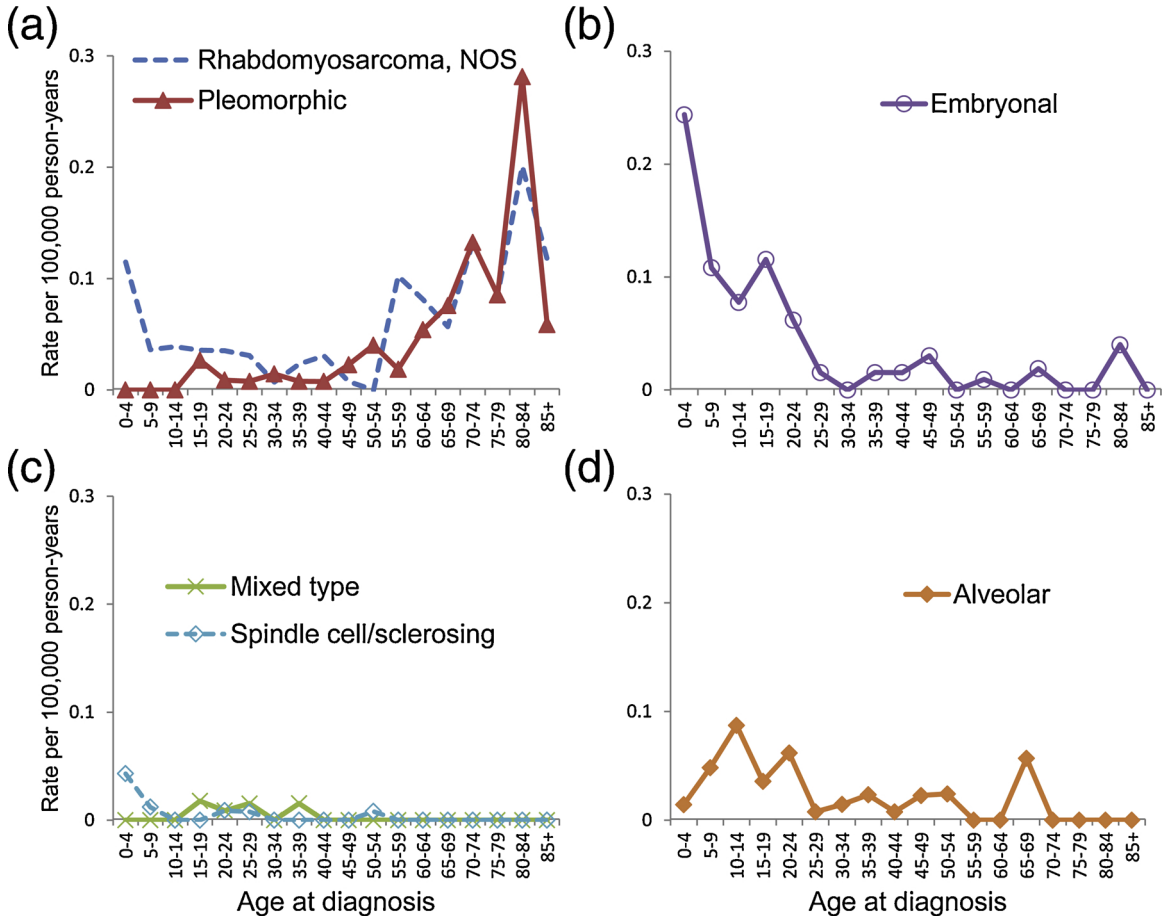

Fig. 2. Age-specific incidence rates of rhabdomyosarcoma by histopathologic subtype. (a) Rhabdomyosarcoma NOS, and pleomorphic; (b) embryonal; (c) mixed type and spindle cell/sclerosing; and (d) alveolar.

in adolescent, middle-aged, and older patients (Fig. 1n). Age-specific rates of rhabdomyosarcoma by cell type (Fig. 2) revealed significant age variations; rhabdomyosarcoma NOS and pleomorphic subtypes were predominant in older adults (Fig. 2a), whereas the embryonal cell type was mainly found in children, adolescents, and young adults (Fig. 2b).

3.4. Temporal trends

Table A.1 in Supplementary material demonstrates the time trends of the STS incidence rates by histologic subtype (and primary site for GIST and leiomyosarcoma) during 2007–2013. For overall STS, no significant incidence trend was identified. However, a significantly declining trend of the incidence of UPS was found (APC, −7.8%; 95% CI, −14.6% to −0.5%, $p < 0.05$). The dedifferentiated cell type of liposarcoma and alveolar cell type of rhabdomyosarcoma exhibited upward incidence trends. The incidence of GIST of the small intestine significantly increased (APC, 2.5%; 95% CI, 0.7%–4.5%, $p < 0.05$), particularly in male patients.

3.5. STS incidence by region

The results from Vaud, Switzerland; three European regions (Rhone-Alps, Veneto, and Aquitaine); and Surveillance, Epidemiology and End Results (SEER) program, the United States are compiled in Table 3 and Fig. 3 for comparison [5,6,13]. Overall, the STS incidence excluding that of GIST and Kaposi sarcoma (3.8/100,000 person-years) in Taiwan was similar to that in Vaud, Switzerland (3.81/100,000 person-years) [13], but it was lower than that in the United States (5.03/100,000 person-years) and the three European regions (4.4/100,000 person-years) [5,6]. The incidence of angiosarcomas was higher than that in other regions (Fig. 3a); whereas that of leiomyosarcoma, Kaposi sarcoma, and UPS was significantly lower than that in other regions. Moreover, significant racial variation in leiomyosarcoma incidence was found for either sites, including the uterus, or excluding the uterus (to include both male and female patients; Fig. 3b), with the highest rates observed in African Americans, followed by Caucasian Americans and finally Taiwanese patients [5].

4. Discussion

The current population-based study revealed site-specific STS incidence in Taiwan for 2007–2013, based on the 2013 WHO classification of STS. Improvements in classification changes must be considered when interpreting these STS incidence rates. An issue associated with the new WHO classification was the addition of GISTs—nearly 30% of all STSs according to the results of the current study. Moreover, because Kaposi sarcoma is associated with human immunodeficiency virus (HIV), the incidence rates varied by HIV endemism, which could confound the interpretation of the variations in STS incidence between countries. When comparing STS incidence rates between studies, excluding GIST and Kaposi sarcoma to prevent misinterpretations was reasonable. After this exclusion, the rate of overall STS (3.8/100,000 person-years) in Taiwan was close to that in Vaud, Switzerland (3.81/100,000 person-years) but lower than that in the United States (5.03/100,000 person-years) and the three European regions (4.4/100,000 person-years; Table 3). Further comparison of the subtypes revealed a higher incidence rate for angiosarcomas and lower incidence rates for leiomyosarcoma and Kaposi sarcoma in Taiwan compared with other

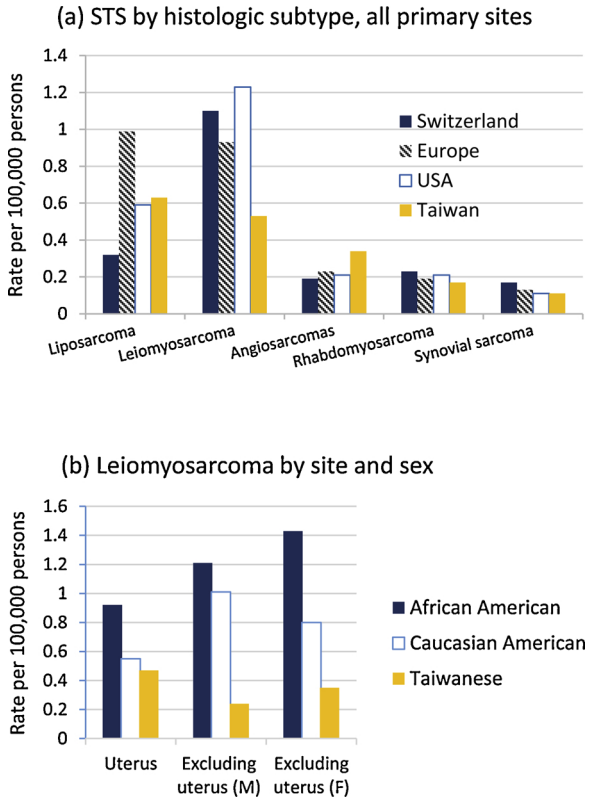

Fig. 3. Comparison of the incidence rate of STSs among different regions (a) and races (b, leiomyosarcoma).

series. This evidence suggested geographical variations among the incidence of certain STS subtypes.

In our analysis, the incidence of Kaposi sarcoma (0.27/100,000 person-years) was less than half of the worldwide average (0.6/100,000 person-years) [10,11]; this is potentially attributable to the relatively low HIV endemism in Taiwan. Moreover, this study demonstrated that GIST incidence rate in Taiwan (1.55/100,000 person-years) represented the upper half of the global rates (0.43–2.2/100,000 persons) [27]. A study of GIST incidence in Taiwan revealed an upward trend of GIST during 1998–2008 (from 1.13/100,000 persons in 1998 to 1.97/100,000 persons in 2008) [28], and attributed the cause partially to the advancement of diagnostic methods and increased physician awareness. The current study presented more recent (2007–2013) data and provided new information by revealing a significant male predilection (male-to-female SIRR, 1.36) and an upward trend for GIST in males, but confined to the small intestines only (APC, 2.9%, Table A.1 in Supplementary material). Additional studies are required to explore the possible environmental risk factors for this trend in men.

The evidence on racial disparity in STSs has been limited. A report on overall STS incidence rates during 1973–2008 from the SEER program revealed that African Americans had the highest incidence rate (5.1/100,000 persons), followed by Caucasian Americans (4.5/100,000 person-years) and finally Native Americans and Asia Pacific Islanders (2.8/100,000 person-years) [29]. Another report on the overall STS data of 15–29-year-old patients from SEER (1995–2008) revealed the highest incidence rate in African Americans (2.99/100,000 person-years), followed by Latin Americans (2.00/100,000 person-years) and finally Caucasian Americans (1.87/100,000 person-years) [30]. In the current analysis, angiosarcoma had a higher incidence rate in Taiwan than in Western countries (Table 3). However, no reports on the racial difference in angiosarcoma incidence have been published thus far. Nevertheless, we found the evidence of racial variation in leiomyosarcoma incidence when comparing our results with data from the United States (African and Caucasian Americans) [5], with the highest incidence rates in African Americans, followed by Caucasian Americans and Taiwanese people—for primary sites either including or excluding the uterus (Fig. 3b). Taken together, this limited evidence suggested racial variations in the incidence of certain STS subtypes, particularly leiomyosarcoma.

This study revealed that all STS subtypes represented “rare cancers” in Taiwan, based on the definition of either the National Cancer Institute (< 15/100,000 individuals per year) or RARECAREnet working group (< 6/100,000 individuals per year) [1,31]. Thus far, collaborative network on information and research of rare cancers remains lacking in Asia, particularly Taiwan. The paucity of epidemiological data regarding rare cancers renders planning research or clinical trials difficult, particularly in regions other than the United States and Europe. The present analysis, including cases of STSs in any part of the body, presents the most comprehensive statistics of STS by primary site and can contribute to the understanding of the real burden of STS in Asian populations.

This study has several limitations. To prevent presenting unstable data, the overall STS incidence was slightly underestimated because some STS subtypes with extremely low incidence were omitted. Because STS is rare and heterogeneous, we expanded the study period to 7 years to enroll a sufficient number of cases; however, the factors associated with the retrospective study design—such as improvements in pathological diagnostic technology, improvements in cancer registration, and changes in cancer classification over the study period—may have influenced the incidence rates and trends.

In conclusion, this study revealed that STS incidence rates in Taiwan varied by subtype, sex, age, and primary site. The strengths of this study are the use of nationwide, high-quality population-based data in a defined population, including STSs arising in any part of the body, as well as the presentation of STSs according to the latest 2013 WHO STS classification. Incidence rate standardization in this analysis and homogeneous Taiwanese ethnicity rendered the results comparable with those from other countries or ethnic groups. Our results demonstrated a higher incidence rates for angiosarcomas but lower rates for leiomyosarcoma and Kaposi sarcoma in Taiwan compared with other series. Significant racial variation was found for leiomyosarcoma incidence rates when comparing Taiwanese with Caucasian and African Americans. These population-based data are extremely important in enhancing our understanding of this rare cancer among Asian people. In the future, more population-based studies should be conducted in Asia for comparison with the results from Western countries and for further clarification of geographical and racial variation in STS subtype incidence.

Contribution Author(s)

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Declarations of interest

None.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.canep.2019.04.007.

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