RESEARCH ARTICLE

Increasing Frequency of Soft Tissue Sarcomas in Vojvodina - Comparison with the Literature

Tihomir Dugandzija*, Marica Miladinov Mikov, Nenad Solajic, Borislava Nikolin, Jasna Trifunovic, Maja Ilic

Abstract

Background: Soft tissue sarcomas (STS) represent 1% of all malignant lesions. In this study the authors analyzed the incidence of STS in Vojvodina (the north region of Serbia) in the period from 1985 to 2009. A number of studies conducted worldwide indicate that STS incidence rates are tending to increase. Materials and Methods: On the basis of data from the Cancer Registry of Vojvodina, age standardized STS incidence rates were established as well as their linear trend, with data on histological structure, age, gender and STS distribution at specific locations. Results: The total number of registered patients was 1,308. Average age standardized rate was 1.90/100,000 per year. The investigated period showed a slight increase in the incidence rate (average annual percent increase=0.77%). The most frequent histological type was sarcoma not otherwise specified-NOS (27%), followed by leiomyosarcoma (21%), liposarcoma (14%), rhabdomyosarcoma (11%) and malignant fibrous histiocytoma (9%). The male/female ratio was 0.73:1. Every fifth patient was younger than 39. Conclusions: Comparison among eight international STS epidemiology studies show that the incidence rate range is between 1.4/100,000-5.0/100,000, though our finding is closer to the lower limit. Furthermore, the incidence rate increase was lower than that characteristic for the half of the analyzed studies. A partial explanation for that should be looked for among changes in diagnostic criteria and STS classifications.

Keywords: Epidemiology - soft tissue sarcoma - incidence - trend - Serbia - international comparison

Asian Pac J Cancer Prev, **15 (2)**, 1011-1014

Introduction

Soft tissue sarcoma (STS) includes extraoseal malignant tumors of mesenchymal origin.They represent 1% of all malignant tumors (Fletcher et al., 2002). Age standardized incidence rate in the world falls within the range between 1.4/100,000 and 5/100,000 (Schuurman et al., 1992; Ross et al., 1993; Gustafson 1994; Storm et al., 1994; Levi et al., 1999; Toro et al., 2006; Wibmer et al., 2010). STS etiology is mostly unknown. Small number of STS is associated with inherited syndromes such as Familial Adenomatous Polyposis (FAP), neurofibromatosis 1, Li-Fraumeni syndrome and retinoblastoma (Latchford et al., 2007; Ji et al., 2008; Aqaimy et al., 2012; Svajdler et al., 2012). Certain number of STS may be associated with ionizing radiation (Gladdy et al., 2010; Samartzis et al., 2013). Chemical substances such as some kinds of herbicides, arsenic, dioxin, phenol derivatives and polyvinyl chloride are considered to be the STS risk factors (Zamh et al., 1997; Hoppin et al., 1998; Steenland et al., 1999). Epstein-Barr virus and Human Herpes Virus 8, combined with immunosuppression, are also significant for development of some types of STS (Bhatia et al., 2012; Radu et al., 2013). Finally, there are assumptions that lymphedema and trauma may also be possible etiological factors (Muller et al., 1987; Visuri et al., 2003).

The objective of this work was to analyze the incidence rate and trend of STS in Vojvodina in the period between 1985-2009, its localization and histological structure as well as distribution of new cases by gender and age.

Materials and Methods

By using the retrospective approach, this work included the analysis of STS incidence rate and trend in Vojvodina (the north region of Serbia) compared to other analyses of STS incidence rate and trends in the world. The Province of Vojvodina has around 2 million citizens (population censuses 1991, 2002, 2012). Data have been obtained from the Cancer Registry of Vojvodina, established in 1967, and operating as a part of Vojvodina Institute of Oncology, located in Sremska Kamenica. The Registry has been a member of the International Association of Cancer Registries (IACR) since 1989. The method used in the study was the descriptive epidemiological method. Besides demographic data, data on clinical localization and histology of tumor were used as well. Data processing was carried out in compliance with the third revision of the International Classification of Diseases for Oncology, ICD-O-3. The study included all cases of STS defined as such according to criteria

*Oncology Institute of Vojvodina, Sremska Kamenica, Serbia *For correspondence: dugandzija.tihomir@onk.ns.ac.rs*

of „Pathology and genetics of tumors of soft tissue and bones“ published by the International Agency for Research of Cancer (IARC) from Lion (France), at recommendation of World Health Organization (WHO) for classification of tumors (1). Statistica (version 10) software was used for statistical analysis and Annual Percent Change (APC) was calculated by fitting a least square regression line on the natural logarithm of the rates, using the calendar year as a regressor variable (Neter et al., 1985).

Results

Age standardized incidence rates

Average age standardized incidence rates of STS in Vojvodina in the period from 1985 to 2009 was 1.90/100,000 (Figure 1). The lowest rate was calculated in 1991 (1.42/100 000), and the highest in 1997 (2.47/100 000). The trend shows the tendency of increase, and the linear correlation coefficient was 0.34 (p>0,05). Average Annual Percent Change (APC) was 0.77%. Percentage of STS in the total number of new cases, for the investigated period, was 0.67%.

Histological structure

Within the investigated period (25 years) 1308 STS patients were registered, i.e. 52 per year. Table 1 shows the aggregate results of histological structure (Table 1). The most frequent histological type was NOS sarcoma , (i.e., at that moment, not included in the existing, precisely defined classifications) which developed in every fourth patient (27%). It was followed by leiomyosarcoma (21%), liposarcoma (14%), rhabdomyosarcoma (11%) and malignant fibrous histiocytoma (9%).

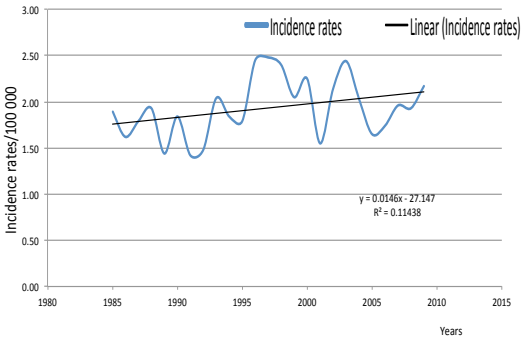

Figure 1. Age Standardized Incidence Rates and Trend of STS in Vojvodina in the Period 1987-2006

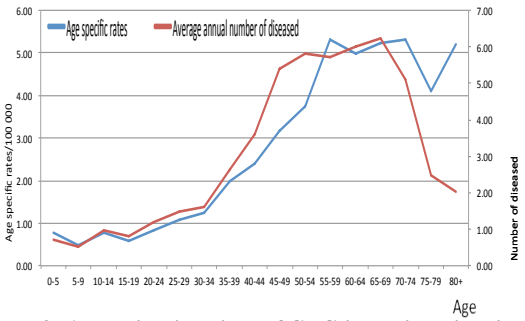

Figure 2. Age Distribution of STS in Vojvodina in the Period 1987-2006

Table 1. Histological Distribution of STS in Vojvodina in the Period 1987-2006

Morphology code ICD-O-3	Histotype	n	(%)
8800	Sarcoma NOS	351	26.83
8890	Leiomyosarcoma	279	21.33
8850	Liposarcoma	186	14.22
8900	Rhabdomyosarcoma	139	10.63
8830	Malignant fibrous histiocytoma	120	9.18
8810	Firbrosarcoma	91	6.96
9120	Angiosarcoma	71	5.43
9040	Synovial sarcoma	34	2.60
9140	Kaposi's sarcoma	14	1.07
8990	Malignant mesenchymoma	14	1.07
9364	Peripheral primitive neuroectodermal tumor	3	0.23
9260	Extrasceletal Ewing tumor	3	0.23
8804	Epithelioidsarcoma	3	0.23

Table 2. Topography Distribution of STS in Vojvodina in Period 1985-2009

Morphology code ICD-O-3	Histotype	n	(%)
C00-C14	Oral cavity and pharynx	9	0.69
C15-26	Digestive system	83	3.34
C30-C39	Respiratory system	72	5.50
C46-C49	Soft tissue	66	50.92
C50	Breast	45	3.44
C51-C58	Female genital system	265	20.25
C60-C63	Male genital system	17	1.29
C64-C68	Urinary system	26	1.98
C69-C72	Eye and central nervous system	13	0.99
C73-C75	Endocrine system	9	0.69
C76-C80	Unspecified localisation	129	9.86

Table 3. Five Most Common Histotypes of STS

Author (country)	Distribution the most common histotypes of STS in %				
	Sarcoma NOS	Leimyo-sarcoma	Lipo-sarcoma	MFH	Fibro-sarcoma
Schuurman (The Netherlands)	4.4	20.1	13.8	16.2	5.7
Gustafson (Sweden)	6.0	13.0	10.0	41.0	3.0
Ross (USA)	5.4	17.7	5.5	10.0	3.7
Levi (Switzerland)	7.6	25.4	8.5	n.s.	19.2
Toro (USA)	12.0	23.9	11.5	17.1	3.3
Wibmer (Austria)	36.0	24.0	12.0	9.0	5.0
This studia (Serbia)	26.8	21.3	14.2	9.2	7.0

Table 4. Male/Female Ratio of STS

Author (country)	Male/Female ratio
Zahm (USA)	1.42
Storm (Denmark)	>1
Schuurman (The Netherlands)	1.17
Gustafson (Sweden)	not specified
Ross (USA)	0.93
Levi (Switzerland)	0.88
Toro (USA)	>1
Wibmer (Austria)	0.8
This studia (Serbia)	0.73

Age and gender structure

Distribution of STS by age shows that almost every fifth STS occurs at the age younger than 39 (248 cases, i.e. 19%). In general, STS mostly occurs at the older age (Figure 2). The highest age-specific rates occur in two moderate peaks, the first one between 55-59 (5.31/100 000), and the second one between 70-74 (5.32/100 000).

Data analyses show that STS was more frequent in

females than in males. Male/female ratio was 0.73:1, i.e. there are 551 registered STS males and 757 females.

Distribution of tumor by localisation

Analysis of tumor by localisation shows that every second tumor (51%), is registered by clinical diagnosis C46-C49 (Table 2). Every fifth STS is located in the female genital system (20%), and not rarely they are found in digestive (6%) and respiratory system (5%). Almost ten percent of STS are not precisely enough defined and miscellaneous (C76-C80).

Discussion

STS average age standardized incidence rates of 1.90/100,000 fits into the range of STS values in the world, which is from 1.4/100,000 to 5/100,000 (Ross et al., 1993; Gustafson 1994; Storm et al., 1994; Levi et al., 1999; Toro et al., 2006; Wibmer et al., 2010). Differences among countries can be explained by different criteria for defining something as STS, by different classification of STS in various points of time and in various countries, by different diagnostic capacities and finally, by the small absolute number of STS.

Incidence rates in three studies conducted in the USA, are higher than in this study and fall in the range between 4/100,000 and 5/100,000 (Ross et al., 1993; Toro et al., 2006; Zahm et al., 1997). High STS incidence rate in the USA are the result not only of wider criteria they apply for defining something as STS, but also of significant frequency of Kaposi's sarcoma and generally higher rates of new patients among Afro-American population. The data in the USA have been obtained from 9 American states and they are collected and included together in SEER (Surveillance, Epidemiology and End Results) and refer to 10% of American population. Some states (like California), compared to other American states, have the significant part in total number of sarcoma, because of their influence to the number of AIDS-related Kaposi sarcomas. The number of STS shows the increasing tendency in all these studies, except in the study conducted by Ross. Zahm collected data for the period from 1935 to 1989, Ross for the period from 1973 to 1987 and Toro for the period from 1978 to 2001.

In Austria, STS incidence rates are similar to those obtained in our study and are equal to 2.4/100,000 (Wibmer et al., 2010). During the observed period (from 1984 to 2004) no statistical change was identified in the number of new STS patients. The data have been obtained from the Austrian National Cancer Registry.

Lower STS incidence rates were obtained by an author from Sweden (1.80/100,000) based on data from the south part of Sweden(Gustafson 1994). The study was conducted for the period from 1964 to 1989. The important information is that this study included only persons older than 16. The same as with our study, the authors from Sweden and Austria did not include cases of dermatofibrosarcomas in STS (Gustafson 1994; Wibmer et al., 2010).

STS incidence rates obtained in Switzerland are higher than those from our study and are equal to 3.6/100,000 for the period from 1974 to 1994 (Levi et al., 1999). The data were obtained from the Cancer Registry of Vaud Canton which covers almost 10% of the whole Swiss population. Excluding Kaposi's sarcoma, the number of new cancer cases during the observed period has not significantly changed.

Based on data from the National Cancer Registry, Danish authors established STS incidence rates in their country of 3.2/100,000, which number was not the subject of significant oscillations during the observed period of four decades (from 1948 to 1987) (Storm et al., 1994).

High STS incidence rates were discovered in Holland (4.7/100,000) in the period from 1950 to 1988 (Schuurman et al., 1992). Together with incidence rates from the American study Toro (5.0/100,000), these are, in general, the highest STS incidence rates. One of the reasons for high value of incidence rates in the Holland study is the presence of Kaposi's sarcoma of 13.9%. The observed period shows the increasing number of STS new patients.

Half of all studies, such as our study, Holland study (Schuurman) and two American ones (Zahm and Toro), show the increasing number of new STS patients. However, the said increase is much lower in our study (APC 0.77%) than in others where it exceeds 1% (Schuurman et al., 1992; Toro et al., 2006). Various factors are stated to be the reasons for such STS incidence rate increase (Fletcher et al., 2002). In our study the reason is not related to a different number of Kaposi's sarcoma, but one can assume that it may be related to frequent and quick changes in diagnostic criteria and STS classification (Fletcher et al., 2002).

Analysis of histological structure of new STS patients shows significant differences among countries. The most frequent sarcoma (excluding NOS sarcomas), in all studies, is leiomiosarcoma (Table 3). The exception is a Swedish study (Gustafson 1994) where the presence of MFH (Malignant fibrous histiocytoma) is extremely high, even 41% is the result of changes in classification of this sarcoma. Our study, as well as the Austrian one (Wibmer et al., 2010), which is, in geographic terms, the closest to Vojvodina, which territory is the subject of the study, distribution of histological structure is very similar. The presence of NOS sarcomas is smaller in older studies (studies in Table 3 are given in chronological order).

None of the stated studies included, nor did the Swedish one (Gustafson, 1994), dermatofibrosarcoma metastasing in less than 5%. The presence of dermatofibrosarcoma in other studies is between 5% and 10%. Except for the Swedish and American study (Gustafson 1994; Toro et al., 2006), other studies included Kaposi's sarcoma. In this study and in Austria (Wibmer et al., 2010), the presence of this type is small (2% and 1%, respectively), while in Switzerland, Holland and USA (Schuurman et al., 1992; Ross et al 1993; Levi et al., 1999), it is around 15%. According to WHO classification (Fletcher et al., 2002), gastointestinal stromal cancer (ICO-O-3 code 8936/3) was not included in this study, although in the past years ectodermal origin (neural crest) of this tumor was denied and its mesodermal origin proved. Following the same principles of WHO classification, this study does not include nerve sheath tumors (ICO-O-3 codes from

9540/3 to 9571/3) which are assumed to be of ectodermal origin (neural crest). Based on recommendations of the stated classifications, the study also excludes endometrial stromal sarcomas (ICO-O-3 code 8930/3), the total registered number of which, within the observed period, was 29, which is slightly more than 2% of the total number of all STS cases.

The fact that every fifth new patient is younger than 40 may be explained by high presence of rhabdomiosarcoma in this study of almost 11%, which is the most characteristic for the youngest age groups (Zahm et al., 1997; Wibmer et al., 2010). The ratio between males and females in this study is the closest to that in Austria (Wibmer et al., 2010) (Table 4). Not including the American study (Toro et al., 2006), the latest studies show more STS cases in females than in males, and vice verse in older studies (Table 4). Studies in this table are given in chronological order, as well.

This study shows high i.e. almost 10% presence of sarcomas classified in groups of not precisely defined and not defined by location. This can be partly explained by classifying tumor in group C76 (other locations) instead of group C49 (STS). The leading location in this study as well as in most of other studies refers to C49 group and participates with around half of all cases (Toro et al., 2006; Wibmer et al., 2010).

In conclusion, STS average age standardized incidence rate of 1.90/100,000 fits into the range of STS values in the world (from 1.4/100,000 to 5/100 000). A small increase in number of new STS patients was identified in the observed period. Such increase has also been identified in half of analyzed studies conducted worldwide. The partial explanation for these differences among studies result from applying different criteria for identifying STS cases, changes in STS classification made in time and among countries, different diagnostic capacities as well as small absolute number of STS.

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