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The Profile of Soft Tissue Sarcoma Patients who Undergo Radiotherapy in Dr. Hasan Sadikin General Hospital Bandung

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ABSTRACT

Background: Soft Tissue Sarcoma is one of the rare cancers that increased in number in the last few years, but information about soft tissue sarcoma patients was still limited, especially in West Java, Indonesia. This study aimed to find out the patient profile and the histopathological cell distribution of soft tissue sarcoma patients who undergo radiotherapy.

Methods: The study design was retrospective descriptive quantitative with the total sampling method. This study was done by observing all patients' medical records registered from January 1, 2018, until December 31, 2019, in the Hospital-Based Cancer Registry of Radiology Department of Dr. Hasan Sadikin General Hospital Bandung, with the inclusion criterion of patients diagnosed with soft tissue sarcoma.

Results: A total of 5% (n = 75) from 1,388 cases registered were soft tissue sarcoma. The most common patient profile was female (57.3%) and age group 45–54 years (21.3%). The chief complaint was dominated by a painless mass (56.0%) at the lower limb (37.8%) with the most frequent cell of fibrosarcoma (17.3%), the most intention of the radiotherapy of curative adjuvant (78.7%).

Conclusions: The number of soft tissue sarcoma is small compared to other malignancies. It is more common in women, the most age group is from 45 to 54 years with the median of 47 years old, ranging from 9 to 90 years, it tends to occur in the lower limb with a chief complaint of a painless mass, and the most frequent cell is fibrosarcoma. The common treatment combination is surgery with radiotherapy.

INTRODUCTION

Soft tissue sarcoma is one of the solid tumors and a malignancy that comes from the mesenchymal layer. Soft tissue sarcoma grows from connective tissue throughout the body from head-neck to toe. There are more than 50 subtypes of histopathological soft tissue sarcoma. The most frequent types of sarcoma are sarcoma Not Otherwise Specified (NOS), liposarcoma, fibrosarcoma, leiomyosarcoma, and rhabdomyosarcoma [1,2].

The standard treatment for soft tissue sarcoma used to be amputation, but the patient could still die due to metastasis. After some studies, radiotherapy was found to be helpful. Instead of doing an amputation procedure, clinicians could perform limb-sparing resection only by performing radiotherapy before surgery was done or defined as neoadjuvant indication or intention. Radiotherapy also reduces the chance of recurrence in patients and local control if the radiotherapy is done after surgery or adjuvant intention [3].

The information about profiles and distributions of soft tissue sarcoma in Indonesia is limited. The rarity of sarcoma makes it difficult to be studied. In addition, there are differences in frequencies of soft tissue sarcoma amongst countries from the information of sex, age, topography, and cell type [1,2,4–6]. This study aimed to find out the patient's profile and the histopathological cell distribution of soft tissue sarcoma patients who undergo radiotherapy at Dr. Hasan Sadikin General Hospital Bandung from 2018 to 2019.

METHODS

This study design was a descriptive retrospective quantitative using total sampling method and was done by observing the patients' status/medical records from January 1, 2018, to December 31, 2019, which were registered based on the Hospital-Based Cancer Registry (HBCR) in the Department of Radiology of Dr. Hasan Sadikin General Hospital Bandung. The inclusion criterion

was patients diagnosed who have soft tissue sarcoma and have undergone radiotherapy.

For each case, there were view variables that were observed. The variables are sex, age, chief complaint, cell morphology or histopathologic, sites (topography), the intention of radiotherapy, completeness, delivery equipment, and management(s). Cell morphology and sites of tumor were taken as a result in the pathology anatomy form based on the International Classification of Diseases for Oncology, 3rd edition (ICD-O-3). Management was based on the previous history of management of patients consisting of surgery, radiotherapy, and/or chemotherapy.

The data was recaptured and processed with Microsoft® Excel 2019 and IBM® SPSS® version 25 software. This study had been approved by the Research Ethics Committee of Universitas Padjadjaran number 801/UN6.KEP/EC/2020 and Dr. Hasan Sadikin General Hospital number LB 02.01/X.2.2.120543/2020.

RESULTS

In total, there were 75 cases of soft tissue sarcomas of the 1,388 cases recorded in HBCR medical records of the Department of Radiology from 2018 to 2019. The data were presented in **Table 1**.

The profiles of soft tissue sarcoma patients vary greatly. Soft tissue sarcoma is more common in women than men of 43 (57.3%) and 32 cases (42.7%), respectively. The median age is 47 years and ranges from 9 to 90 years. The most common age group is the 45–54 years (21.33%).

The most common to least chief complaints by patients were painless mass (58.7%), post-surgery mass (24.0%), pain (9.3%), mass and pain (2.7%), and others. Other complaints include decreased hearing function, hoarseness, and a history of fractures. Based on the location of the chief complaint, the most common site was in the lower extremities (37.8%). Histopathological cell types obtained were 25 from 70 types of cells that exist. The most common to least common were fibrosarcoma (17.3%), dermatofibrosarcoma (13.3%), undifferentiated pleomorphic sarcoma (UPS) (10.7%), and myxoid liposarcoma (9.3%). Other cell types consisted of myofibroblastic sarcoma, plexiform fibrohistiocytic sarcoma, myxosarcoma, spindle cell rhabdomyosarcoma, alveolar rhabdomyosarcoma, synovial sarcoma, chondroblastic osteosarcoma, myxoid chondrosarcoma, chondromyxoid fibroma, giant cell sarcoma, and alveolar soft part sarcoma.

Based on the radiotherapy status, the most common intention was curative adjuvant (78.7%). There were 3 types of treatment delivery equipment used; from the most often to least often used, they were External Beam Radiotherapy (EBRT) Linac (60,0%), EBRT Cobalt-60 (38.7%), and brachytherapy (1.33%). The number of patients who completed their radiotherapy was 64 (85.3%) and did not complete was 11 (14.6%).

Table 1. Distribution of sarcoma soft tissue patient

Categories	n = 75	%
Sex		
Male	32	42.7
Female	43	57.3
Age groups (years)		
9–14	4	5.3
15–24	5	6.7
25–34	14	18.7
35–44	13	17.3
45–54	16	21.3
55–64	12	16.0
65–74	8	10.7
>75	3	4.0
Chief Complaints		
Mass (painless)	42	56.0
Pain	7	9.3
Post-surgery mass	20	26.7
Mass and pain	2	2.7
Other	4	5.4
Chief complaints sites		
Head-neck	19	25.3
Upper extremities and shoulder	7	9.3
Lower extremities	28	37.8
Thorax	6	8
Abdomen-peritoneal	3	4.0
Pelvic-buttocks	7	9.3
Trunks (Including flank and back)	5	6.7
Morphology (ICD-M)		
Undifferentiated Pleomorphic Sarcoma (8802.3)	8	10.7
Fibrosarcoma (8810.3)	13	17.3
Fibromyxosarcoma (8811.3)	3	4.0
Malignant Fibrous Histiocytoma (8830.3)	3	4.0
Dermatofibrosarcoma (8832.3)	10	13.3
Liposarcoma Atypical Lipomatous; Well-Differentiated (8851.3)	2	2.7
Myxoid Liposarcoma (8852.3)	7	9.3
Leiomyosarcoma (8890.3)	3	4.0
Rhabdomyosarcoma (8900.3)	3	4.0
Pleomorphic Rhabdomyosarcoma (8901.3)	2	2.7
Clear Cell Sarcoma (9044.3)	2	2.7
Angiosarcoma (9120.3)	2	2.7
Osteosarcoma, Osteoblastic; NOS (9180.3)	3	4.0
Chondrosarcoma (9220.3)	3	4.0
Others	11	14.7
Radiotherapy intent		
Curative definitive	10	13.3
Curative adjuvant	62	82.7
Palliative	3	4.0
Treatment delivery equipment		
EBRT* Cobalt-60	29	38.7
EBRT* Linac	45	60.0
Brachytherapy	1	1.3
Completeness		
Complete	64	85.3
Incomplete	11	14.7
Management type		
Radiotherapy	13	17.3
Surgery-radiotherapy	54	72.0
Radiotherapy-chemotherapy	1	1.3
Surgery-radiotherapy-chemotherapy	7	9.3

Table 2. Histopathological cells by patient profile

Morphology	Sex		Age Category		
	Male n= 32	Female n= 43	Children n= 7	Adult n= 52	Elderly n= 16
Undifferentiated Pleomorphic Sarcoma	3	5	0	3	5
Fibrosarcoma	7	6	1	10	2
Fibromyxosarcoma	0	3	0	3	0
Myofibroblastic Sarcoma	0	1	0	1	0
Malignant Fibrous Histiocytoma	1	2	0	3	0
Dermatofibrosarcoma	6	4	2	8	0
Plexiform Fibrohistocytic Sarcoma	0	1	1	0	0
Myxosarcoma	1	0	0	0	1
Liposarcoma Atypical Lipomatous; Well-Differentiated	1	1	0	2	0
Myxoid Liposarcoma	4	3	2	5	0
Leiomyosarcoma	0	3	0	2	1
Rhabdomyosarcoma	1	2	0	2	1
Pleomorphic Rhabdomyosarcoma	1	1	0	0	2
Spindle Cell Rhabdomyosarcoma	1	0	0	1	0
Alveolar Rhabdomyosarcoma	1	0	0	0	1
Synovial Sarcoma	0	1	0	1	0
Clear Cell Sarcoma	0	2	0	1	1
Angiosarcoma	0	2	0	1	1
Osteosarcoma	2	1	0	3	0
Chondroblastic Osteosarcoma	1	0	1	0	0
Chondrosarcoma	2	1	0	2	1
Myxoid Chondrosarcoma	0	1	0	1	0
Chondromyxoid Fibroma	0	1	0	1	0
Giant Cell Sarcoma	0	1	0	1	0
Alveolar Soft Part Sarcoma	0	1	0	1	0
Total in percentage	42.7%	57.3%	9.33%	69.34%	21.33%

Table 3. Distribution of body regio and topography

ICD-C	Topography	Male n=32	Female n=43
44.3	Skin of other and unspecified parts of face	1	0
44.4	Skin of scalp and neck	2	0
44.5	Skin of trunk	3	3
44.7	Skin of lower limb and hip	0	2
48.0	Retroperitoneum	0	2
49.0	Soft tissue of Head-Neck	6	10
49.1	Soft tissue of upper limb and shoulder		
49.11	Right Upper limb and shoulder	1	3
49.12	Left Upper limb and shoulder	2	1
49.2	Soft tissue of lower limb and hip		
49.21	Right lower limb and hip	7	9
49.22	Left lower limb and hip	2	8
49.3	Soft tissue of thorax	5	0
49.4	Soft tissue of abdomen	0	1
49.5	Soft tissue of pelvis	3	2
49.6	Soft tissue of trunks NOS	0	1
49.9	Soft tissue NOS	0	1

NOS, not otherwise specified

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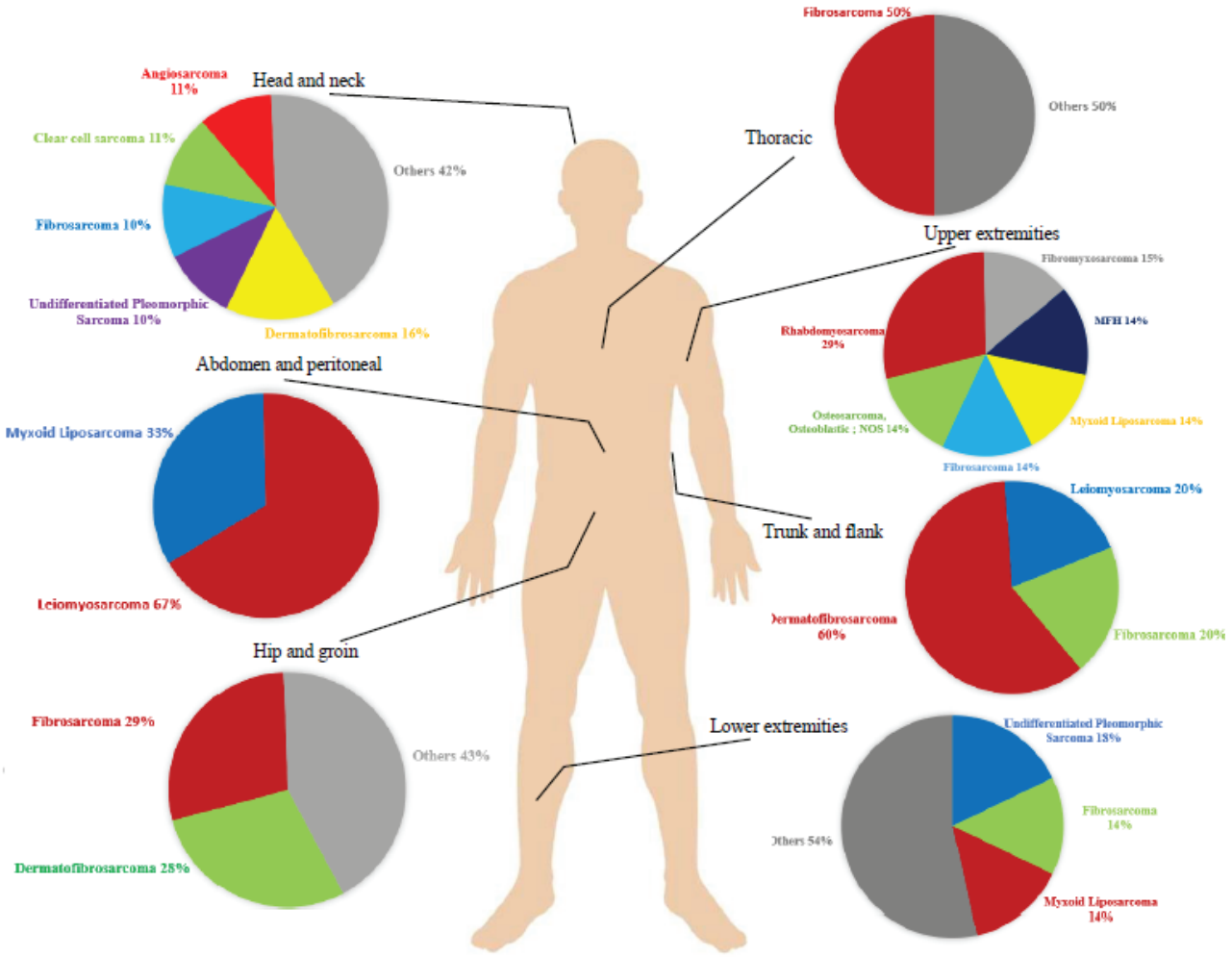

Figure 1. Histopathologic distribution based on site

DISCUSSION

This study found a male-to-female ratio of 1 to 1.3 in 2018 and 2019. The results are in line with previous research done by Yang et al. [1] in China, Arfiana et al. [6] in Pekanbaru, and Bhatt et al. [7] in Ireland but differs from the research results in some countries conducted by Liu et al. [8] in Taiwan, Fabiano et al. [2] in Italy, Stiller et al. [9] in Europe, and a book written by Goldblum et al. [10] on Soft Tissue Tumors which states that the incidence in men is more common than in women. The incidence of soft tissue sarcoma was thought to be due to the role of female hormones, but based on the research conducted by Fioretti et al. [11] in Italy, there was no significant relation between soft tissue sarcoma incidence with hormone factors based on menstrual cycle pattern, menopausal age, the number of parity, and the number of abortions, except the risk for women with a history of later age pregnancy.

Although soft tissue sarcoma was more common in women, several types of cells were more numerous in men (**Table 2**). The most common in both sexes of both females and males was fibrosarcoma (14% and 21.9%) in line with Folpe et al. [12] study about fibrosarcoma. The second and third most cell types in women were undifferentiated pleomorphic sarcoma (11.6%) and dermatofibrosarcoma (9.3%) while in men were dermatofibrosarcoma (18.8%) and myxoid liposarcoma (12.5%). There were more various cell types in women than men, namely 21 variations in women and only 14 variations of histopathological cells in men.

The incidence gradually increased with age, from 9 to 14 years with a peak at 44–54 years and decreased again to the lowest point at the age range of > 75 years; this is in line with the research conducted by Arfiana et al. [6] in Pekanbaru and Sajjad et al. [13] in India. In contrast to the study conducted by Yang et al. [1] in China, Bessen et al. [14] in Australia, and Bhatt et al. [7] in Ireland said that the peak was in the age range of 75–84 years. This could be due to the differences in life expectancy between Indonesia and the country from previous research, but there was a piece of in-line information that the increase in cases happened after the age of 35 years [1,6,7,13,14].

The age ranges were divided into three based on the age group, children (0–19 years), adults (20–59 years), and elderly (> 60 years). Based on **Table 2**, the most common cell in children was dermatofibrosarcoma (28.6%), in adults was fibrosarcoma (19.8%), and in the elderly was UPS (31.3%). Although soft tissue sarcoma is rare cancer, its mortality rate was high enough about 1.3 per 100,000 and 5,000 to 6,000 deaths in America [15]. It was also responsible for 6% to 15% of cancer incidence in children under 15 years old [8,16].

We found the most frequent sites for both women and men were lower limbs (21.3% right lower limb and 12.0% left lower limb) and the head-neck (20.0%), in line with other studies [1,2,7,10]. In addition to the diverse cell types, women also had various tumor locations that were more diverse than men (**Table 3**). In women, it occurred throughout all regions except the thoracic region while, in men, it occurred throughout all regions except the abdominal-peritoneal and trunks region (including flank and back). Every site of the body had its most frequent and less frequent cell type (**Figure 1**). The most frequent in head-neck was dermatofibrosarcoma (15.8%), in upper limb was Rhabdomyosarcoma (28.6%), and in lower limb was UPS (17.9%) followed by fibrosarcoma and myxoid liposarcoma (14.3%) in line with previous research [4]. In the thorax, there was fibrosarcoma (50.0%), in abdomen-peritoneal was leiomyosarcoma (67%), in pelvic-buttocks were dermatofibrosarcoma and fibrosarcoma (28.6%), and in the trunk was dermatofibrosarcoma (60.0%). In contrast to previous studies that cited the upper limb as one of the most sarcoma locations, this study found that the incidence of sarcoma in the upper extremity region was relatively low (8.0%) [1,2,10].

This study found that major complaints in medical records are painless mass, followed by pain, postoperative mass, mass and pain, and others. The patient's chief complaint was dominated by painless mass [3,4,10]. The most complaints in the most consecutive were painless mass (58.7%), post-operative mass (24.0%), pain (9.3%), mass and pain (2.7%), and others. Most postoperative mass complaints appeared in fibrosarcoma cells. A study suspected the involvement of stem cancer cells that initiated the growth and proliferation of fibrosarcoma [17]. Complaints of lumps and pain appeared in osteosarcoma cells [15].

In 2018, there were 33 cases handled, and the most used equipment was Linac; meanwhile, in 2019, there were 42 cases, and the most used equipment was Cobalt-60. Most cases in 2018 were handled by Linac due to the limited equipment caused by cobalt-60's damage, so the number of patients that could be handled decreased. It was also marked that no patients were treated with Cobalt-60 from March to July 2018.

Patients who registered and did not complete their radiation therapy could be due to various factors either from the patient's issue or health facilities' issue. In terms of patients, it could be due to fear or occurring side effects and complications that can arise from therapy such as radiation dermatitis, not having enough money for non-medicine costs like transportation and inn, and the condition of patients who have been too weak or already died before receiving therapy or completing the therapy [3,18,19]. The health facility is also responsible for the large number of patients who do not get radiotherapy. The cause was an imbalance of supply (competent human resources and adequate facilities or equipment both number and quality) and demand (increasing number and complexity of cancer patients every year) of health facility sources [20,21].

Intentions of radiotherapy given to patients depend on the decisions made by the oncology team involving multidisciplinary. The intention of curative adjuvant was the highest because based on the standard treatment for soft tissue sarcoma was surgery then followed by additional therapy like radiotherapy to maintain local control and eradicate the rest of the tumor if the site was not free-tumor yet [4,10]. Radiotherapy is used as the main treatment or indicated as curative definitive treatment if surgery could not be done due to patient's condition like low Hb levels, patient's condition that is too weak, the location or size of the tumor that already invades the neurovascular region and may affect patient's quality of life, or the patient that refuses to perform surgery [3,4,22].

Management combinations from the most to least were surgery-radiotherapy (72.0%), radiotherapy (17.3%), surgery-radiotherapy-chemotherapy (9.33%), and radiotherapy-chemotherapy (1.33%). The case which was given radiotherapy and chemotherapy was only rhabdomyosarcoma located at two different sites at the same time with indications of chemoradiation as proposed in Europe [10]. The cases treated with a combination of surgery, radiotherapy, and chemotherapy are fibrosarcoma, chondroblastic, clear cell sarcoma, and leiomyosarcoma that tend to be sensitive for chemotherapy, which has undergone metastasis, are located in the head or need to be sensitized according to the agreement and recommendations of the oncology group [3,4].

However, this study has several limitations. The statistical analysis was not done due to the small size of the acquired data. This study cannot state the outcome of patients after radiotherapy treatment. It is also hard to compare the data with the international data due to broad incidence results amongst countries.

CONCLUSIONS

The number of soft tissue sarcoma compared to other malignancies is low, approximately 5% of the entire malignancy cases. Soft tissue sarcoma could happen to anyone. This study found it was more

common in women than in men (1:0.7) and the most age group was from 45 to 54 years (21.3%) with the median of 47 years ranging from 9 to 90 years. The distribution of soft tissue sarcoma varied. In this study, it tends to occur in lower limbs followed by head-neck, with a chief complaint of a painless mass and the most frequent cell was fibrosarcoma. The most common treatment combination was surgery with radiotherapy.

DECLARATIONS

Ethics Approval

This study had been approved by the Research Ethics Committee of Universitas Padjadjaran number 801/UN6. KEP/EC/2020 and Dr. Hasan Sadikin General Hospital number LB 02.01/X.2.2.120543/2020..

Competing of Interest

The authors declare no competing interest in this study.

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