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Epidemiological Study of Head and Neck Sarcomas

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Abstract

Introduction:

Head and neck sarcomas are uncommon tumors that account for less than 1% of head and neck malignancies and fewer than 5% of all sarcomas. This study aims to assess the head and neck sarcomas pattern in Isfahan, Iran, compare its results with previous findings, and investigate treatment methods and the recurrence and survival rate.

Materials and Methods:

This study was done on 160 patients diagnosed with head and neck sarcomas between 2001 and 2020 in four medical centers in Isfahan, Iran. The patients with head and neck sarcoma confirmed by biopsy were included. Patient information included sex, age at diagnosis, and full characteristics of the mass. Disease recurrence and 2-year and 5-year overall survival (OS) were investigated by phone.

Results:

Among 160 patients, 94 (58.8%) were male. The mean age was 36.9 ± 23.2 years. The neck was the most reported location for sarcomas (N=34, 21.3%). Undifferentiated pleomorphic sarcoma was the most frequent histopathologic pattern (N=48, 30.0%). The brain and lungs were the most common destinations for metastasis. “Surgery and adjuvant therapy together” was the most common type of treatment (N=108, 68.8%). The 2-year and 5-year recurrence rates were N=100, 62.5%, and N=110, 68.8%, respectively. The 2-year and 5-year OS was N=103, 64.4%, and N=58, 36.6%, respectively. Eighty-nine patients have had metastasis (55.6%).

Conclusions:

Both 2-year and 5-year recurrence rates and OS were significantly correlated with metastasis. The OS within two years and five years were significantly higher in those treated only by “Surgery”.

Keywords: Epidemiology, Head and Neck, Sarcoma

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Introduction

Sarcomas are malignancies with transformed mesenchymal cells originating from bone, cartilage, muscle, blood vessels, fat, fibrotic, and nerve tissue (1,2). The exact etiology of head and neck sarcoma is still unclear (3). Less prevalent than other head and neck tumors, head and neck sarcomas are uncommon tumors that make up less than 1% of head and neck malignancies and fewer than 5% of all sarcomas (4). The rate of morbidity and mortality in these tumors is significantly high (5). Most head and neck sarcomas are seen in anatomical locations where other tumors usually do not occur, and for this reason, they are more challenging to diagnose (4). The usual symptoms of head and neck sarcoma are painless swelling in soft tissue sarcomas and pain in hard tissue sarcomas. Other symptoms are visual disturbance, sinusitis, and motor and sensory disturbances (3).

Diagnostic methods include computed tomography scan, magnetic resonance imaging, and tissue biopsy. Positron emission tomography (PET) scan studies are useful for evaluating distant metastasis. Known risk factors for head and neck sarcomas are Li-Fraumeni syndrome, neurofibromatosis type 1, genetic abnormalities, lymphedema, infections like human immunodeficiency virus, Epstein-Barr virus and human herpes virus-8 in Kaposi sarcoma, and history of radiation or chemotherapy (5-7). Head and neck sarcomas can metastasize to distant areas such as the liver, lung, and bone (2).

Decision-making for treating head and neck sarcomas depends on histological type, location, disease stage, tumor size, and age (3). Surgery with the removal of the wide margins of the tumor is considered the most important treatment process; however, radiation therapy and chemotherapy are used as adjuvant treatments (8).

Radiotherapy is used for the treatment of all high-grade and large tumors (tumor size ≥5 cm). Furthermore, it is used when resection margins are microscopically involved (9,10). Chemotherapy is used in the systemic treatment of those who are at risk of metastatic disease and for palliative purposes (11). However, chemotherapy's efficacy in patients' overall survival is still unclear. The treatment methods differ case by case depending on the features of the disease, and multidisciplinary settings are needed for the best treatment outcomes (12, 13). Early detection, diagnosis, and treatment in patients with head and neck sarcoma are very important in improving the outcome of treatment (13). Prognostic factors of the disease include age, gender, tumor size, histology, and tumor grade (9). Surgery with complete removal of tumor margins is also a very important prognostic factor in the appropriate rehabilitation of patients (2).

Better outcomes in treatment are strongly relative to the skill and knowledge of pathologists, surgeons, radiotherapists, oncologists, and other multidisciplinary settings existing in medical centers(9). Because of their unique anatomical location and difficulty during excision, head and neck sarcomas have a higher local recurrence rate and a worse prognosis than sarcomas in other body parts (9).

Many studies have been conducted on the prevalence of head and neck sarcomas. However, their results were in terms of disease subtypes, the average age of onset, the relationship between gender and the disease, and the most common sites of primary involvement, which appear to be distributed differently depending on race and location. As a result, it is necessary to conduct new epidemiological studies regionally (14).

Previous studies in Isfahan, Iran, did not evaluate different types of treatment, recurrence, and disease survival; they were only about the epidemiological aspects of head and neck sarcomas (4). This study aimed to assess the head and neck sarcomas pattern in Isfahan, Iran, compare the results with previous findings, and investigate treatment methods and the recurrence, survival, and metastasis rate.

Materials and Methods

This census cross-sectional study was done on 160 patients with head and neck sarcomas between 2001-2020 in Al-Zahra, Kashani, Omid, and Imam-Hossein medical centers of Isfahan, Iran. The study design was approved by the Ethics Committee of Isfahan University of Medical Sciences (IR.MUI. MED. REC. 1401.127). The patients with primary head and neck sarcoma between 2001 and 2020, confirmed by biopsy, were included in the range of the clavicle bone and above. Patients

with missing data, including pathology reports and contact information, were excluded from the study. In Isfahan, head and neck surgery was performed only by a small number of surgeons in university hospitals. Every surgeon had experience. The same settings were used for each surgery. Standard radical resection with free margin was the technique that was taken into consideration for these procedures. The key finding of this study is that it is descriptive, and as such, the influence of surgeons is not taken into account. Clinical trial studies take into account the influence of surgeons' skills.

Patient information, including sex, age at diagnosis, and full characteristics of the mass (the primary location of the involvement, the tissue subtype, and the type of treatment), was collected through patients' documents. Additionally, further information, including disease recurrence and 2-year and 5-year overall survival (OS), was investigated through a phone call. The data are analyzed using IBM SPSS Statistics, version 26.0.0.1. Quantitative data are reported by mean ± standard deviation, and qualitative data by frequency and percentage. The statistical tests used for quantitative data were the student's t-test if the data was normally distributed and the Mann-Whitney test if the data was non-normally distributed. The statistical test used for qualitative data was the chi-square test. Logistic regression was used to assess the overall survival rate.

Results

Among 160 patients, 94 patients (58.8%) were male. Male to female ratio is 1.42. The mean age was 36.9 ± 23.2 years. Table 1 indicates the prevalence of sarcomas in different locations. So, the most common place for head and neck sarcoma was the neck specifically (N=34, 21.3%).

Table 1: The prevalence of sarcomas in different locations of the head and neck region (analyzed by incident frequency– No statistical test is used.)

Neck and Nose	Thyroid	Tonsil	Palate	Parotid	Tongue	Nose	Nasopharynx	Cervical vertebrae	Larynx	Nose and Sinus	Orbit	Cheek	Brain	Eye	Ear	Sinus	Scalp	Mandible	Neck	Tumor location
1	1	1	1	2	3	3	4	4	5	6	6	7	8	11	11	13	16	23	34	Frequency
0.6	0.6	0.6	0.6	1.3	1.9	1.9	2.5	2.5	3.1	3.8	3.8	4.4	5.0	6.9	6.9	8.1	10.0	14.4	21.3	Percentage %

Undifferentiated pleomorphic sarcoma (UPS) and rhabdomyosarcoma were the most frequent histopathologic patterns that were seen among the tumors (N=48, 30.0% and N=32, 20.0%, respectively) (Table 2).

Table 2: Distribution of different histopathologic types of head and neck sarcomas (analyzed by frequency of incident – No statistical test is used.)

Kaposi Sarcoma	Angiosarcoma	Fibrosarcoma	Dermatofibrosarcoma	Leiomyosarcoma	Spindle Cell Sarcoma	Fibromyxoid Sarcoma	Chondrosarcoma	Osteosarcoma	Ewing Sarcoma	Rhabdomyosarcoma	Undifferentiated Pleomorphic Sarcoma	Tumor type
1	2	3	4	6	8	9	12	14	21	32	48	Frequency
0.6	1.3	1.9	2.5	3.8	5.0	5.6	7.5	8.8	13.1	20.0	30.0	Percentage %

The present study investigated the association between gender and metastasis, 2-year OS, 5-year OS, 2-year recurrence, and 5-year recurrence in Table 3. Gender and the prognosis of the disease were not related (P-Value > 0.05). The current study compared several age groups, as shown in Table 4. Our patients were split up into three groups. The first group consisted of those under 20 and 20. Individuals aged 20 to 40 comprised the second group, while those aged 40 and older comprised the third. Results showed no significant link between age and 2-year recurrence, 5-year recurrence, 2-year OS, 5-year OS, or metastasis (P-Value > 0.05).

Table 3: Relationship between gender and prognosis of the disease (P-Value ≥ 0.05, Analyzed by Chi-squared test)

		Gender		
		Male	**Female**	**p-value**
2-year recurrence	Frequency	64	46	0.864
	Percentage%	68.1%	69.7%	
5-year recurrence	Frequency	56	44	0.409
	Percentage%	59.6%	66.7%	
2-year OS	Frequency	61	42	0.869
	Percentage%	64.9%	63.6%	
5-year OS	Frequency	35	23	0.283
	Percentage%	37.2%	34.8%	
Metastasis	Frequency	54	35	0.629
	Percentage%	57.4%	53.0%	

Table 4: Relationship between different age groups and prognosis of the disease (P-Value ≥ 0.05, Analyzed by Chi-squared test)

		Age			p-value
		≥20	**20-40**	**≥40**	
2-year recurrence	Frequency	29	32	39	0.431
	Percentage%	55.8%	68.1%	63.9%	
5-year recurrence	Frequency	32	32	46	0.283
	Percentage%	61.5%	68.1%	75.4%	
2-year OS	Frequency	36	30	37	0.635
	Percentage%	69.2%	63.8%	60.7%	
5-year OS	Frequency	18	19	21	0.778
	Percentage%	34.6%	40.4%	34.4%	
Metastasis	Frequency	27	29	33	0.592
	Percentage%	51.9%	61.7%	54.1%	

The most common type of treatment was "surgery and adjuvant therapy together", "adjuvant therapy only," and "surgery only", respectively (N=108, 68.8%, and N=35, 21.2% and N=17 10.0%). The 2-year and 5-year recurrence rate was N=100, 62.5% and N=110, 68.8%, respectively. The 2-year and 5-year OS was N=103, 64.4%, and N=58, 36.6%, respectively. Eighty-nine patients had metastasis (N=89, 55.6%). Table 5 shows the distribution of metastasis locations. Four patients had metastasis in more than one location.

Table 5: Distribution of metastasis locations for primary head and neck sarcomas incident – No statistical test is used.)

Larynx	**Knee**	**Kidneys**	**Vertebrae**	**GI tract**	**Heart**	**Chest**	**The soft tissue of the Neck**	**Hip**	**Face**	**Other bones**	**Liver**	**Lungs**	**Brain**	**Metastasis location**
4	5	6	7	7	8	8	9	10	11	13	13	43	52	Frequency
2.5	3.1	3.8	4.4	4.4	5.0	5.0	5.6	6.3	6.9	8.1	8.1	26.9	32.5	Percentage%

Metastasis, 2-year and 5-year recurrence, and 2-year and 5-year OS did not show significant differences between male and female gender. Both 2-year (OR 3.76; 95% CI 1.85-7.61; P<0.001) and 5-year recurrence rate (OR 4.67; 95% CI 2.17-10.04; P<0.001) were significantly correlated with metastasis. Also, 2-year (OR 3.23; 95% CI 1.54-6.76; P=0.002) and 5-year OS (OR 7.69; 95% CI 3.60-16.44; P<0.001) were significantly correlated with metastasis (Table 6).

Table 6: The effect of metastasis on the recurrence and OS of patients with head and neck sarcoma (P-Value ≤ 0.05, Analyzed by Chi-squared test)

Variable	Metastasis		P-Value
	Yes	No	
2-year recurrence	66 (74.2%)	34 (47.9%)	0.001
5-year recurrence	72 (80.9%)	38 (53.5%)	0.001
2-year OS	46 (51.7%)	57 (80.3%)	0.001
5-year OS	14 (15.7%)	44 (62.0%)	0.001

Metastasis, 2-year, and 5-year recurrence were not statistically different between different types of treatment, but 2-year and 5-year OS was significantly higher in the "Surgery only" group (Table 7).

Table 7: The effect of type of treatment on the recurrence and OS of patients with head and neck sarcoma (P-Value ≤ 0.05, Analyzed by Chi-squared test)

Variable	Type of treatment			P-Value
	Surgery only	Adjuvant therapy only	Surgery + Adjuvant therapy	
Metastasis	6 (6.9%)	24 (27.6%)	57 (65.5%)	0.066
2-year recurrence	8 (50.0%)	20 (58.8%)	71 (66.4%)	0.381
5-year recurrence	8 (50.0%)	22 (64.7%)	79 (73.8%)	0.124
2-year OS	12 (75.0%)	15 (44.1%)	75 (70.1%)	0.015
5-year OS	10 (62.5%)	7 (20.6%)	40 (37.4%)	0.015

It is clear that one of the most significant factors in determining the prognosis of this illness is the tumor's stage, but we did not have a precise pathological staging of the tumor to mention in our publication, which is recognized as a limitation of our study. We needed comprehensive pathology reports to examine the tumor stage, which were not accurately documented.

Discussion

This research investigated the epidemiologic characteristics of head and neck sarcomas in Isfahan, Iran. The findings of such regional studies can set healthcare policies.

Several studies with epidemiologic evaluations on head and neck sarcomas were done worldwide. The difference between male and female genders was the first epidemiologic factor that should be considered. Most previous studies showed that head and neck sarcomas were significantly higher in male patients (8,13, 15), consistent with our findings. Conversely, in some studies, gender was not considered a statistically significant factor (4,16,17).

In Guevara-Canales et al. (18) and Singh et al. (13) studies, the percentage of male patients was higher. Surprisingly, Peng et al. (19) reported that the male gender worsens cause-specific survival in multivariable analysis.

Many studies have found that increasing age is an important risk factor for head and neck sarcomas. The mean age of our patients was 36.9 years old, like a previous study in Isfahan (4), while other studies reported different means in the range of 30-50 years old (9,13,20). We did not compare different age groups and their effect on sarcoma incidence.

In our study, the neck was the most common region in head and neck sarcomas, similar to the Singh et al. study (13). Past research introduced many different parts, like the skin, larynx, mandible and oral cavity, as the most involved regions (4,8,9,15,21,22). The different points of view regarding the involved organs caused the heterogeneity of these findings. In the related studies, osteosarcoma (4,18), undifferentiated pleomorphic sarcoma (UPS) (8,19), and rhabdomyosarcoma were the most frequent histopathologic subtypes of resected sarcomas. We found undifferentiated pleomorphic sarcoma (UPS) and rhabdomyosarcoma to be the most reported tumor cell types (3,9). The difference between epidemiologic studies in such characteristics is rational, as the purpose of the study is to investigate them. Similar to our study,

surgical resection with negative margins plus radiation therapy (as adjuvant therapy, especially in the case of R1 or R2 margins) was the preferred type of management for head and neck sarcomas in many studies (3,12,17) while in Mücke et al. (20) and Peng et al. (19) studies surgery without adjuvant therapy was the most frequent type of treatment. The propensity-matched model by Peng et al. (19) showed no significant efficiency in cause-specific survival. Surgical treatment without adjuvant therapy appeared to improve the prognosis and OS in our study, but it did not affect the recurrence rate and metastasis status. The beneficence of chemotherapy is not well recognized yet (12). Galy-Bernadoy et al. (12) reported a 5-year OS of 60% in head and neck sarcomas. In 1992, Wanebo et al. (23) reported a percentage of 70% for 5-year OS. The results mentioned above were outside our findings for 5-year OS (36.6%). Many factors, such as the level of care and patient follow-up, can cause this discrepancy. Our estimation of metastasis rate (55.6%) was higher than previously reported percentages (10%-40%) (9). The distribution of metastasis locations for primary head and neck sarcomas and recurrence rate was rarely investigated in sarcomas specifically. Like Tejani et al. (9) and Singh et al. results (13), we found the brain and lungs as the most common destinations for head and neck sarcoma metastasis. As a fact, the significant correlation between OS and recurrence rate with metastasis was reconfirmed. Metastasis and recurrence rates were not statistically different between male and female patients or different types of treatments.The current study had some limitations. The retrospective nature of the study and its related biases can decrease the stability of the data. However, the long period in which patients were reviewed due to the need to check survival causes undeniable heterogeneity of results. We did not include some other important risk factors like smoking and tumor grade. The number of patients could have been more than 160 if database facilities at Isfahan Medical Center had collected patients' data more accurately. Also, many pathologic reports needed to be completed, making us exclude patients from our study. On the other hand, the specialized examination of head and neck sarcoma and its characteristics was the strength of our study, and the information obtained in this study can be used in other regions with similar facilities and conditions. Unlike previous studies in this region, we evaluate the relationship between different types of treatment, metastasis, recurrence, and overall disease survival. As mentioned, epidemiological studies aim to express the differences of various regions so that regional policies can be corrected and updated to make appropriate patient decisions. Future studies are needed to evaluate more details and wider areas and to clarify the cause and how to deal with these differences.

Conclusion

The current epidemiologic survey in Isfahan, Iran, showed that the neck is the most common place for sarcoma in the head and neck region. Undifferentiated pleomorphic sarcoma (UPS) and rhabdomyosarcoma were the most frequent histopathologic patterns. “Surgery and adjuvant therapy together” was the most common type of treatment. Both 2-year and 5-year recurrence rates and OS were significantly correlated with metastasis. The OS within two and five years was significantly higher in those treated only by “Surgery.” The probable reason is that surgical treatment without adjuvant therapy indicates when the tumor is at an early stage, small size, low grade, and with defined margins; therefore, the survival rate is subsequently higher in these patients. However, further studies on a larger group of patients are necessary to evaluate and affirm this hypothesis.

Limitations

It is clear that one of the most significant factors in determining the prognosis of this illness is the tumor's stage, but we did not have a precise pathological staging of the tumor to mention in our publication, which is recognized as a limitation of our study. We needed comprehensive pathology reports to examine the tumor stage, which were not accurately documented.

Authors' Contributions

A.E. and N.B. designed the study. A.A. and F.A. collected the data. N.M. analyzed the data. All the Authors contributed to the submitted manuscript.

Ethical Statement

The study design was approved by the Ethics Committee of Isfahan University of Medical Sciences (IR.MUI.MED.REC.1401.127).

Conflict of Interest

The authors declare no conflict of interest.

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