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Histological Grading System for Soft Tissue Sarcoma-A Five Year Study

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Abstract

Background: Sarcoma (Greek origin meaning "flesh") is a heterogeneous group of rare tumors of mesenchymal cell origin affecting approximately 1% of all adult malignancies. Tumour grade has been proposed as an essential factor in the staging of patients with soft tissue sarcomas. Histopathologic grading by French Federation of Cancer Centres (FNCLCC) is widely accepted and applicable to all types of soft tissue sarcomas, it includes criteria for grading tumour differentiation, mitotic count and pattern of tumour necrosis. By this grading system advent of metastasis, prognosis and survival rate can be evaluated.

Aims and objectives: To determine median age, gender, site, histological grades of soft tissue sarcoma according to FNCLCC. To know prevalence of various soft tissue sarcoma in MY hospital. To study the reproducibility of FNCLCC grading system, by comparing results of different pathologist .To get reliable prognostic information by this grading system.

Materials and methods: It is a retrospective and prospective study done over a period of 5 years in M.Y. Hospital. Total 112 cases of soft tissue sarcoma were taken. Soft tissue sarcoma was diagnosed on the basis of CT scan, MRI and were confirmed by histopathological examination and grading was done by FNCLCC. Age, Gender distribution, site, histological type and grading were evaluated and correlated. The results of different observers were compared and evaluated.

Result: In this study we found that the most common age group was 41 yrs-50 yrs with males predominance. The most common site was lower limb and most common type was Osteosarcoma followed by fibrosarcoma, rhabdomyosarcoma, PNET, liposarcoma, mesenchymal sarcoma and others type of soft tissue sarcoma. However, agreement was found in the grading of tumour and commonest grade was Grade II.

Conclusion: French Federation of Cancer Centres (FNCLCC) was better system for grading of soft tissues sarcomas as reproducibility of grading soft tissue sarcomas is good. By this grading system we get reliable information about disease diagnosis, prognosis, advent of metastasis, patient survival rate by post chemo and radio therapy monitoring, risk of relapse assessment and treatment pattern.

Keywords: Soft tissue sarcoma • Histological grades • French Federation of Cancer Centres (FNCLCC) • Prevelance

Introduction

Sarcomas are the malignant tumours of mesenchymal origin accounts for less than 1 percent of all adult malignancies and 12 percent of paediatric cancers among them most of the cases are arise from soft tissue [1].

STS usually present as painless soft tissue masses, often large at the time of diagnosis and them metastasize hematogenously, mainly to the lung. For the initial assessment of the lesion imaging should be done before biopsy, artifacts may be produced, but more importantly because imaging features can be used to choose the near exact biopsy location [2].

The concept of grading in STS was first properly introduced by Russell et al in 1977 and was the most important factor of their clinico-pathological classification [3].

Currently the most common systems used are the French grading and the National Cancer Institute grading [4].

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The NCI system uses a combination of histological type, cellularity, pleomorphism and mitotic rate for attributing grade 1 or 3 [5,6].

In 2002 the World Health Organization (WHO) gave a new classification of soft tissue tumors (9) for the uniform and comprehensive nomenclature of the soft tissue tumor subtypes.

The final diagnosis of STS is made histologically, allowing differentiation between benign and malignant masses and, in case of malignancy, to establish the histological grade and subtype of sarcoma. Treatment of STS requires a multidisciplinary approach [7].

Rhabdomyosarcoma is the most common type of soft tissue sarcoma among children and adolescents by a striking majority, while Malignant Fibrous Histiocytoma (MFH) is the most common in adults. The tumours were classified according to the 2005 WHO classification and graded using the French Federation Nationale des Centres de Lutte Contre le Cancers (FNCLCC) grading system, which is based on tumour differentiation, mitotic index and tumour necrosis. Our aim is to also provide a descriptive analysis of different grades of sarcomas, prognostic information and clinical usefulness. In history of metastatic disease, our aim is to determine the common sites involved in metastasis. Tumour grade would also be of interest if its determination were easy and were consequently reproducible from one pathologist to another because the precise diagnosis of tumour type and subtype of a given lesion may lead to high discordance rate. In this grading system, tumour grade depends on determination of three criteria, which is mainly quantitative for two (mitosis count and tumour necrosis) and more subjective for one (tumour differentiation) [8,9]. It was assumed that the latter may constitute the predominant problem for reproducing tumour grade [10-12].

Material and Methods

This was a retrospective and prospective study conducted in department of pathology M.G.M. Medical College Indore. A total of 112 cases which were diagnosed as soft tissue sarcoma were included during a period of 5 years and grading done by French Federation of Cancer Centres (FNCLCC) .The Data were retrived from the records maintained in the department including age, Gender, site, residence, clinical diagnosis, histopathological findings. The different tumor types, as diagnosed by different pathologists conducting the study (panel group), were: Rhabdomyosarcoma, liposarcoma, fibrosarcoma, liposarcoma, angiosarcoma, solitary fibrous tumor and others type of soft tissue sarcoma. The study group was asked to review the tumour slides individually and the findings were collected. For each case, the pathologist was asked to determine the tumor type, the tumor differentiation, the mitosis count, the pattern of tumor necrosis and finally the consequent histological grade.

The French Federation of Cancer Centres (FNCLCC)

Tumor differentiation

Score 1: Sarcomas which closely resemble normal adult mesenchymal tissue. (eg. Well differenciated liposarcoma)

Score 2: Sarcomas for which the histological typing is certain.(eg. Myxoid liposarcoma)

Score 3: Embryonal sarcomas and undifferentiated sarcomas and all the sarcomas of doubtful type. (eg. Synovial sarcoma,osteosarcoma,PNET).

Mitosis count

Most mitotic areas where mitoses were studied were sought at g X 250. The count was made at g X 400 in ten successive fields (a high-power field measured 0.1734 mm2). This count was taken to establish the score.

Score 1: 0 to 9 mitoses per 10 fields.

Score 2: 10 to 19 mitoses per 10 fields.

Score 3: More than 20 mitoses per 10 fields.

Tumor Necrosis

Score 0: No necrosis on any examined slides.

Score 1: Less than 50% tumour necrosis for all the ex-

Score 2: Tumour necrosis on more than half of the examined tumour surface.

A three-grade system was set up as follows:

Grade I was defined as a total of 2 or 3 when summing the scores obtained for each of the three histological criteria; Grade II represents a total of 4 or 5; Grade III represents a total of 6, 7 or 8.

Statistical analysis

The results were analyzed in different ways. The kappa values and P values were used to assess agreement between various pathologist by using, SPSS 20.0 software.

The P statistic or overall proportion in agreement, can be considered as an estimate of the probability with which two randomly selected pathologists will agree on the assignment of a randomly selected case. The kappa (K) statistic can be considered as the rate of non-chance agreement. K can vary from 1 (maximal agreement rate) to 0 and can become negative when observers tend to disagree.

Finally, a two-way analysis of variance was used to check the homogeneity of the answers for tumours and observers for the histological typing and the grading.

Results

Total 112 patients were studied, out of which 54 were males and 46 were females. The most common age group was 41 yrs-50 yrs. The most common site was lower limb. The most common type was Rhabdomyosarcoma, liposarcoma, fibrosarcoma, leiomyosarcoma, angiosarcoma, solitary fibrous tumour and others type of soft tissue sarcoma (Figures 1-3 and Tables 1-3).

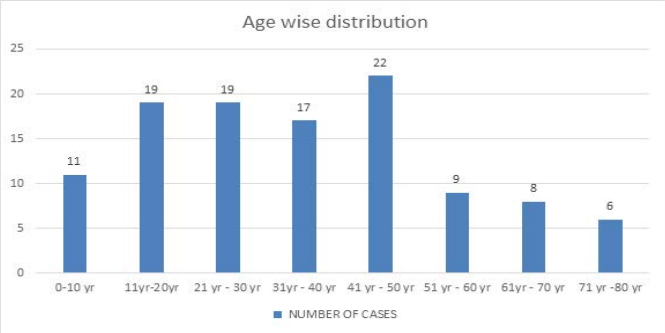

Figure 1. Histological age wise distribution.

Table 1. Gender wise distribution of cases.

Gender	Number of cases
Male	60 (54%)
Female	52 (46%)

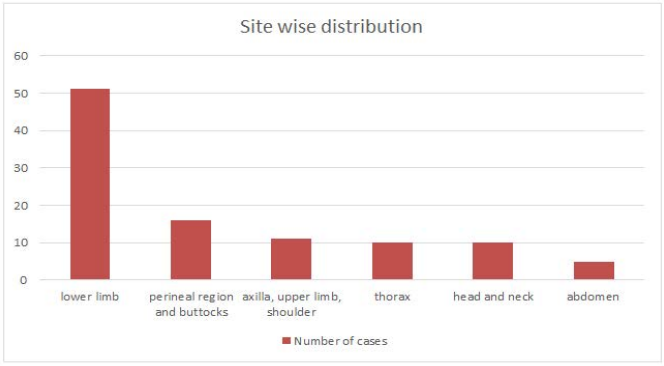

Figure 2. Histological site wise distribution.

Table 2. Site wise distribution of cases.

Site	Number of cases
Lower Limb	51
Perineal Region And Buttocks	16
Axilla, Upperlimband Shoulder	11
Thorax	10
Head And Neck	10
Abdomen	5

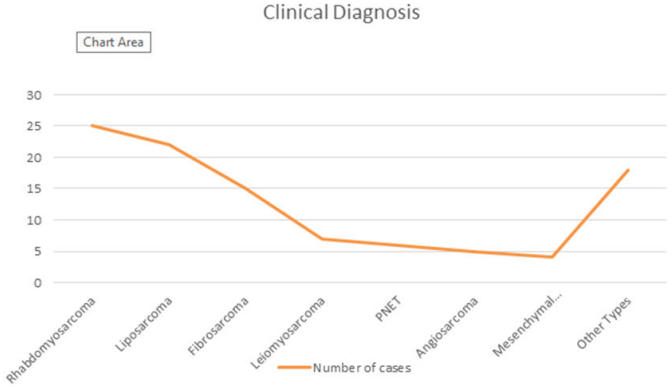

Figure 3. Histological clinical diagnosis.

Table 3. Clinical diagnosis of study group.

Clinical diagnosis	Number of cases
Rhabdomyosarcoma	25
Liposarcoma	22
Fibrosarcoma	15
Leiomyosarcoma	7
PNET	6
Angiosarcoma	5
Mesenchymalsarcoma	4
Others Type	18

The crude proportion in agreement between different pathologists was 86% for tumour differentiation, 85% for mitosis count, 90% for tumour necrosis, 81% for grade and 63% for the diagnosis of histologic type (Figures 4-5 and Tables 4-10).

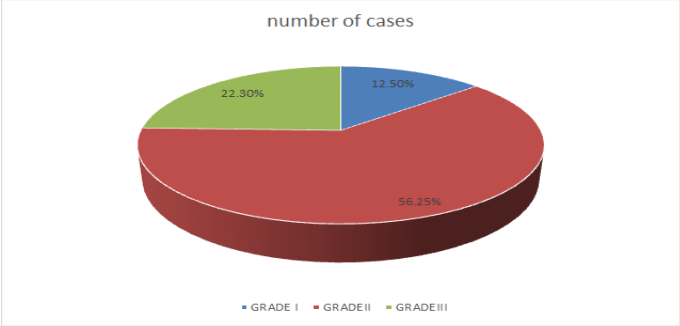

Figure 4. Histological number of cases.

Table 4. Grade wise distribution of cases.

Grade	Number of cases with percentage
GRADE I	14 (12.5%)
GRADE II	63 (56.25%)
GRADE III	25 (22.3%)

Table 5. The statistic or overall proportion in agreement.

Statistics					
Descriptive Statistics	N	Minimum	Maximum	Mean	Std. Deviation
AGE	113	1	79	36.9	20.342
Valid N (listwise)	113				

Table 6. Nonparametric correlations.

Correlations			AGE	grade
Spearman's rho	AGE	Correlation Coefficient	1	-0.07
		Sig. (2-tailed)		0.464
		N	113	113
	grade	Correlation Coefficient	-0.07	1
		Sig. (2-tailed)	0.464	
		N	113	113

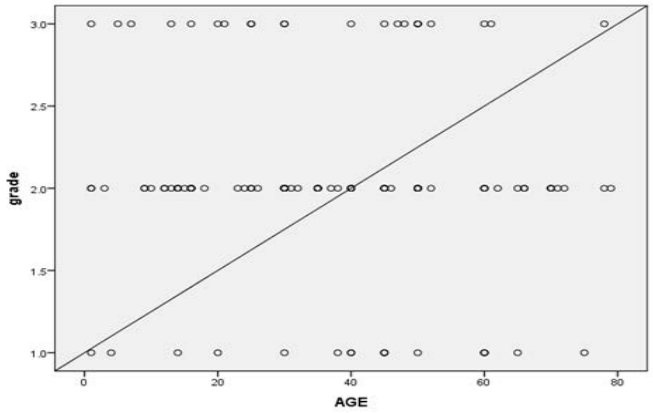

Figure 5. Number of cases with grade and age of factors.

The proportion in agreement between the two groups concerning the attribution of a tumor grade was significantly better than that in the diagnosis of histologic type, which was 81% (P<0.05). Moreover, the proportion in agreement among the pathologists of the study group for the diagnosis of histologic type was 63%.

Table 7. The diagnosis of histologic type.

S.No.		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	17	15	15	15
	2	74	65.5	65.5	80.5
	3	22	19.5	19.5	100
	Total	113	100	100	

Table 8. The best proportion in agreement was in the evaluation of tumor necrosis.

Type * Gender Cross tabulation				
Count				
		Gender	Total	
		1		2
type	1	13	10	23
	2	10	11	21
	3	10	5	15
	4	5	2	7
	5	2	4	6
	6	3	2	5
	7	2	1	3
	8	16	17	33
Total		61	52	113

Table 9. The diagnosis of histologic type, which was 81% (P<0.05).

Chi-Square Tests			
Value	df	Asymp. Sig. (2-sided)	
Pearson Chi-square	3.930a	7	0.788
Likelihood ratio	4.001	7	0.78
Linear-by-Linear association	0.272	1	0.602
N of valid cases	113		

Table 10. The best proportion in agreement was in the evaluation of tumor necrosis (90%; kappa statistic: +0.90).

Case					
Valid		Missing	Total		
N	Percent	N	Percent	N	Percent
113	1	0	0	113	1

Kappa statistics take into account any eventual agreement which is due to chance only. The proportions in agreement for grading between different pathologists of the study group. The proportions in agreement for the three histologic criteria. The best proportion in agreement was in the evaluation of tumor necrosis (90%; kappa statistic: +0.90) (Tables 11 and 12).

Table 11. The study group were mainly due to discordant appreciations of tumor.

Gender * grade crosstabulation					
Count					
		grade	Total		
		1		2	3
Gender	1	8	39	14	61
	2	9	35	8	52
Total		17	74	22	113

Table 12. The pathologic diagnosis of soft tissue sarcoma thus increases.

Chi-Square tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	1.202a	2	0.548
Likelihood Ratio	1.215	2	0.545
Linear-by-Linear Association	1.121	1	0.29
N of Valid Cases	113		

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 7.82.

A significant proportion in agreement was not attained for score 1 of tumour differentiation; this may be due in part to the low number of cases of this category of tumour in this study. The discrepancy in tumour grade was mainly due to the differences in determining mitosis count and tumour differentiation factor.

Discussion

Evaluation of tumor grade by different observers is significantly more reproducible than diagnosis of histological type. In their study proportion of agreement i.e., Tumor differentiation 74% (86% in my study), mitotic count 73% (85% in my study), tumor necrosis 81% (90% in my study), histological grade 75% (81% in my study) i.e., kappa value show strong agreement and histological type 61% (63 % in my study) i.e., kappa value show moderate agreement.

Observe that tumor grading provides reliable prognostic information and clinical usefulness.

Found that inter observer variation was much less in histologic grading compare to histologic typing.

In the current study, the evaluation of tumor grade by different pathologist is shown to be significantly more reproducible than diagnosis of histological type. The proportion of agreement between different pathologist concerning the attribution of tumor grade was significantly better than that in diagnosis of histologic type.

In the current study, the evaluation of tumor grade by different observers is shown to be significantly more reproducible than is the diagnosis of histologic type. This may be considered to be related to the rarity of soft tissue sarcomas, which are also a heterogeneous group of tumors with a wide range of variety of histologic types and subtypes this difficulty of precise histologic typing has also been demonstrated by another study showing the same discrepancies in diagnosis and with a mean of three tumor types given for the same lesion.

This confirms the difficulty of making therapeutic decisions on the basis of this criterion. The reproducibility of grading soft tissue sarcomas is better than that of typing, agreement between different pathologists 81% can also be considered as encouraging, when one considers that none of the participating pathologists was familiar with the grading system used, apart from the information displayed at the beginning of the study.

The differences observed for tumor grading inside the study group were mainly due to discordant appreciations of tumor differentiation and of mitosis count. For tumor differentiation, this may be explained by the subjectivity of the evaluation of this criterion and most disagreement was encountered while attributing scores 2 and 3; this in fact, is due to the difficulty in recognizing the different histologic types.

As regards mitosis count, the subjectivity may lie in the choice of the most mitotic areas where the evaluation had to be made. Moreover, most disagreement about the necrosis factor was encountered in the attribution of scores 0 and 1 (i.e, in the identification of necrosis). This should be eliminated by a more precise definition of tumor necrosis in the instructions of how to grade. Thus, the degree of agreement among different pathologists in the evaluation of the histologic criteria used and in the attribution of tumor grade can certainly be improved.

Adequate training of pathologists should be facilitated by the constitution of a national sarcoma register as has been already set up by the pathologists of the FNCLCC sarcoma group. Tumor grade was demonstrated to be the predominant prognostic factor in soft tissue sarcomas,' and the reproducibility of this grading system, while already appreciable, could be improved. Its usefulness in therapeutical decisions appreciated.

Conclusion

In the current study, the evaluation of tumor grade by different pathologist is shown to be significantly more reproducible than diagnosis of histological type. The proportion in agreement between different pathologist concerning the attribution of tumor grade was significantly better than that in diagnosis of histological type by this grading system we get reliable information about disease, diagnosis and Prognosis, Advent of metastasis, patient survival rate by post chemo and radio therapy monitoring risk of relapse assessment and treatment pattern. The uniformity in the diagnosis is facilitated by routine use of simplified grading system, which in turn facilitate the relationship between pathologists and clinicians and validity of the pathologic diagnosis of soft tissue sarcoma thus increases.

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