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Factors of Local Recurrence in Soft Tissue Sarcomas at Yalgado Ouédraogo University Hospital (Burkina Faso)

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Abstract: Soft tissue sarcomas are characterized by their great anatomo-clinical diversity and their high potential for recurrence. Our Objective was to determine recurrence factors in soft tissue sarcomas in the General and Digestive Surgery Unit of Yalgado Ouédraogo University Hospital from 1st January 2010 to 30th August 2015. This is a cohort retrospective study which concerns patients followed-up for soft tissue sarcomas in the General and Digestive Surgery Unit of Yalgado Ouédraogo University Hospital from 1st January 2010 to 30th August 2015. The data were analyzed with Epi-info 7 software. To assess the stability of associations, Pearson's chi square tests or Fisher exact tests were used. A risk α=0.05 was admitted. Fifty-four cases of soft tissue sarcomas were collected and 40 cases included in the study. The frequency of soft tissue sarcomas was 0.03% compared to all cancers in our department. On univariate analysis, recurrences were significantly associated with the tumour resection margin (p=0.014), the operator's qualification (p=0.012), the histologic type (p=0.04) and the recurrence history (p=0.0004). On multivariate analysis, the resection margin remained significantly associated with recurrences (p=0.03). Recurrence factors mostly involved the resection margin, the operator's qualification, the histologic type and the recurrence history. A good mastery of soft tissue sarcomas surgery will significantly reduce recurrence risks.

Keywords: Sarcomas, Soft Tissue, Recurrence, Ouagadougou

1. Introduction

Soft tissue sarcomas are defined as malign tumours that develop at the expense of the common extra-skeletal connective tissue [2, 9]. They are rare tumours representing 0.5 to 1% of malign tumours in adults [11, 19]. Despite therapeutic progress, they still have potential for both local and metastatic evolution. Prognostic factors reported in the literature are mostly age, weakness of the patient's immunity, tumour localization, tumour size, cytological grade, histologic type, the place where first surgery was done, resection margins and absence of adjuvant radiation

therapy [5, 6]. As a developing country, Burkina Faso does not have a Cancer and Radiation Therapy center. Moreover, there is insufficient skilled staff to handle sarcomas and their recurrence seems frequent. Recurrence results from bad prognosis [5, 6]. The only guarantee for better prognosis is the control of local recurrence risk factors. That is the reason why this work was initiated to describe local recurrence factors in soft tissue sarcomas at the General and Digestive Surgery Unit of Yalgado Ouédraogo University Hospital.

2. Methodology

Type and period of study: This is a cohort retrospective study which concerns patients that were followed-up for soft tissue sarcomas in the General and Digestive Surgery Unit of Yalgado Ouédraogo University Hospital between 1st. January 2010 to 30th August 2015.

2.1. Framework of Study

The study took place in Burkina Faso, a country with limited resources located at the heart of west Africa. It is the sixth poorest country according to UNDP 2014 ranking [27]. The data collection was done at the General Surgery Unit of Yalgado Ouédraogo University Hospital (CHUYO) of Ouagadougou. It is the highest level for health referrals in Burkina Faso. The General Surgery Unit with its Oncology Section, represents one of the reference units for the care of soft tissue sarcomas at the national level.

2.2. Population of Study

We were interested in patients admitted for soft tissue mass and we included those meeting the following criteria:

(1) a histologically confirmed sarcoma operated in the General and Digestive Surgery Unit with a resulting local recurrence.
(2) patients operated in other health centres, but followed-up in our department, on condition that enough and reliable information is available.
(3) a minimum follow-up time of at least one month after the surgery.

We excluded from our study the Intra-abdominal, retro and sub-peritoneal sarcomas, because of the specificity of their treatment and their evolution which is related to their localization.

2.3. Size of Sample

For this prognostic study, the population size was calculated with the formula S (size)= Number of prognostic factors × 5. We have eight (8) prognostic factors in our study. The minimum size necessary was therefore equal to 8 × 5 for 40 patients.

2.4. Data Source

Clinical files of patients, admission registers and operating accounts were the sources where we collected our various data.

2.5. Data Management and Strategy of Analysis

The data were typed and analyzed with Epi Info software version 7.1.1.14. A data export was done on SPSS for control and analysis according to the previously defined themes. The construction of figures was done with EXCEL 2013 software.

We first did a univariate analysis establishing links between each risk factor and the occurrence of recurrence, i.e. the relative risk (RR) of tumour recurrence depending on the tumour size, site, histologic type, place of the first surgery (CMA, Hospital, CHU), cytological grade, resection margins and adjuvant radiation therapy done or not done. Then, we did a multivariate analysis to avoid confounding bias. A rate α=0.05 was used for the various calculations. To assess the stability of the association, Pearson's chi square tests and Fisher exact tests according to conditions of application were used.

Ethical aspects: The study was authorized by the Management and the Head of the General Surgery Unit of Yalgado Ouedraogo University Hospital. The data collection was done anonymously and confidentiality was respected for all the patients.

3. Results and Discussion

3.1. Results

Fifty-four (54) cases of soft tissue sarcomas were collected within six (6) years and eight (8) months. Over this period, 1680 cases of malign tumours were registered in the General and Digestive Surgery Unit. Soft tissue sarcomas represent 0.03% of these malign tumours. Forty (40) patients had at least one recurrence. Thirty-three (33) patients were already received for recurrence and seven (7) patients in first consultation. There were 22 male patients and 18 female patients, i.e. a sex ratio of 1.2. The average age was 39.3 ± 16.3 years with extremes of 18 and 70 years. The average deadline for consultation was 20 ±19.2 months with extremes of 2 and 84 months. The average size of tumours was 15.5 ± 6.44 cm with extremes of 5 and 35 cm. Surgery was done outright for 32 patients and resection margins was inferior to 1 cm in 16 cases. We noted an association between resection margin and recurrence (Table 1).

Table 1. *Univariate analysis of STSs recurrence risks.*

Characteristics	Recurrence		Univariate analysis		
	Yes	No	RR	$^{IC}_{95\%}$	P
Histological type					
Fibrosarcoma	6	3	1		
Liposarcoma	4	1	1.2	[0.63-2.26]	0.54
Dermatofibrosarcoma	15	0	1.5	[0.94-2.38]	0.04
Recurrence history					
No	3	4	1	-	-
Yes	33	0	0.43	[0.18-1.008]	0.00038
Size (cm)					
5-10	13	2	1	-	-
>10	20	5	1.08	[0.82-1.43]	0.47

Characteristics	Recurrence		Univariate analysis		
	Yes	No	RR	$^{IC}_{95\%}$	P
Cytological grade					
Grade I	16	4	1	-	-
Grade II	7	0	0.8	[0.64-0.996]	0,27
Grade III	3	1	1.08	[0.58-1.95]	0.63
Resection margin (cm)					
< 1	16	0	3	[0.96-9.30]	0.014
[1-2]	4	1	2.4	[0.71-8.07]	0.17
>2	2	4	1	-	-
Qualification					
Surgeon	12	6	1	-	-
General practitioner	6	1	1.28	[1.08-2]	0.33
Nurse	15	0	1.5	[0.63-2.26]	0.0167

Patients with a resection margin inferior to 1 cm had 200% additional risk compared to those with a resection margin superior to 2 cm (p=0.014). We also noted an association between the qualification of the operator and recurrence (Table 1). Patients operated by a less-skilled staff (nurse) had 50% additional risk of recurrence compared to those operated by a surgeon (p=0.017). An association between histologic type and recurrence was also noted (Table 1). There was 50% additional risk of recurrence in dermatofibrosarcoma than in fibrosarcoma (p=0.04). Recurrence history and recurrence were also associated (Table 1). Patients with a recurrence history had 57% additional risk of recurrence than those not having a recurrence history (p=0.0004). On multivariate analysis, two factors associated were found, resection margin and profession (respectively p=0.03 et 0.02) (Table 2).

Table 2. *Multivariate analysis of STSs recurrence risks.*

Characteristics	Recurrence		Multivariate analysis		
	Yes	No	RR	$^{IC}_{95\%}$	P
Age (year)					
[10-30]	10	1	1		
[30-50]	11	6	1	[0.03-33.32]	
[50-70]	12	0	4.9	-	0.9
Localization					
Limbs	20	5	1	-	-
Chest	12	2	1.3	-	1
Size					
5-10 cm	13	2	1	-	-
>10 cm	20	5	0.4	[0.07-3.20]	0.46
Cytological grade					
Grade I	16	4	1	-	-
Grade II	7	0	55	-	0.97
Grade III	3	1	0.93	[0.07-14.79]	0.99
Resection margin					
< 1	16	0	11	[1.14-106.43]	0.03
[1-2]	4	1	8	[0.50-127.90]	<0.14
>2	2	4	1	-	-
Qualification					
Surgeon	12	6	1	-	-
General practitioner	6	1	3	[0.29-30.92]	0.3
Nurse	15	0	12	-	0.9
Profession					
Others	92.3	7.7	1	-	-
Trader	50	50	0.08	[0.01-0.72]	0.02
Pupils/ students	100	0	13.4		0.99
Employee	50	50	0.08	[0.07-0.95]	0.04

3.2. Discussion

Soft tissue sarcomas have a high potential for local recurrence [5, 6]. This tendency to recurrence depends on the tumour itself, the operator and the means used.

Patients with a tumour size superior to 10 cm had additional 8% recurrence risk of than those with a tumour size between 5 and 10 cm. However, this risk was not statistically significant in our study (p= 0.46). A statistically significant association between tumour size and recurrence was found with Quynh-thux et al [38] in the USA and Atean et al [22] in France, who found p=0.043 and p< 0.001 respectively. This difference may be explained by the small size of our studied population. In fact, tumours' big size occasions invasion of fascia making complete surgical resection difficult. These marginal resections therefore explain the high recurrence in cases of big size tumours [5]. So, early diagnosis could enable reduce recurrence risks.

Compared with grade I tumours, grade III tumours had additional 6% recurrence risk. This risk was not statistically significant in our series (p= 0.63). Authors like Kasse et al [5] in Senegal, Penel et al [10] and Lintz et al [8] in France found a significant association between cytological grade and recurrence with p<0.002, <0.018, <0.006 respectively. The more the tumour is at a high grade, the more its potential for recurrence is high. In most studies relating to the prognosis of soft tissue sarcomas, cytological grade was the most important factor to assess local recurrence risks [8]. This difference between our study and what we have in the literature could be explained by the small size of our population. Moreover, all our patients could not enjoy cytological grading (31 over 40 patients).

Compared to a patient with no recurrence, a patient with a recurrence history had additional 57% risk of new recurrence. This risk was statistically significant in our study. (p=0.0004). Our results support those of Mc Gee et al [40] in the USA and Mandong et al in Nigeria [35], who found a statistically significant association between recurrence and recurrence history with p=0.0013. This could be explained by the fact that the first surgery is always the best [2, 5]. No radiation therapy how pretentious it is and no chemotherapy how ambitious it is can make up for bad surgery. This highlights the interest of redoing surgery in case of R1 or R2 resection.

Patients operated with a margin between 1 and 2 cm had 140% additional risk of recurrence than those with a margin superior to 2 cm (p=0.17). Compared with patients operated with a margin superior to 2 cm, patients with a margin inferior to 1 cm had additional 200% recurrence risk. This risk was statistically significant (p=0.014). Authors like Lintz et al [8], Penel et al [10], Heymanna et al [23] also found a significant association between resection margins and recurrence with p= 0.028; 0.043; 0.0075 respectively. Margins of marginal resection in our study could be explained by the fact that tumours are often operated without histologic diagnosis, so they are treated as benign tumours. The more the resection is wide and takes away at least 2 cm

tissue, as well as the underlying aponeurosis, the more the local recurrence risk is reduced [2]. In our study and in the literature, the tumour resection margin is the main factor for local recurrence.

Compared with patients aged between 10 and 30 years, patients between 30 and 50 years had 29% less recurrence risk (p=0.13). Compared with those aged between 10 and 30 years, patients aged between 50 and 70 years had additional 10% recurrence risk. This association was not statistically significant in our series (p= 0.48). Kasse et al [5], Quynh-thux et al [38] and Takashi et al [39] however found a significant association between age of recurrence with p = 0.016 and 0.009 respectively, making the patient's age an independent factor of recurrence. This difference in results could be explained by the small size of our population. In these studies, as well as in our own, a predominance of recurrence at the extreme ages was found [2, 5].

Patients operated by a less-skilled agent (nurse) had additional 50% recurrence risk than those operated by a skilled agent (surgeon) p=0.0167. In the literature, we did not find a study comparing recurrence and qualification of the operating agent. That is understood, because due to the insufficiency of surgeons, in peripheral areas, nurses specialized in surgery handle the activities of the operating ward. In our study, we have found a significant association between recurrence and the operating agent's qualification. The more the operator was not trained in cancer surgery, the more the recurrence risk was increased. Compared to a patient with fibrosarcoma, the one with dermatofibrosarcoma had additional 50% recurrence risk (p=0.04). Our results support those of Stefanovski et al [17] who found a statistically significant association between the histologic type and recurrence (p=0.02). In the literature, among tumours that can metastasize, histocyto fibrosarcoma remains the one with the highest number of recurrences [5, 6]. In our study, dermatofibrosarcoma was has the highest number of recurrences. This difference could be explained by the fact that histologic types of sarcomas could be confounded with other histologic types as no confirmation by immunohistochemistry was available in our work environment.

On multivariate analysis, resection margin was a factor associated with recurrence. When it was inferior to 1 cm, the patient had 11 times recurrence risk, compared with the one whose margin was superior to 2 cm. These results confirm the data of Gonzalez et al [3], Quynh-thux et al [38] and Heymanna et al [23] with p=0.0001, p< 0.0001 and p=0.0267 respectively. In our study, we found that profession was a factor associated with recurrence risk. In fact, compared with a patient whose profession was ''others'' (housewife and farmer), employees and traders had less recurrence risk. Even though profession as a factor associated with recurrence was not found in the literature, we can explain this by the fact that employees and traders live mostly in towns, therefore, they have access to health centres where there is a at least a surgeon. As farmers and housewives are in rural areas, they are followed-up by a less-skilled staff. This geographic predisposition is supposed to be the reason for associating profession with recurrence risk.

4. Conclusion

This work reveals that soft tissue sarcomas are rare in everyday practice and have potential for local recurrence in our health centres. Over the eight factors of local recurrence found in the literature, our study could confirm the existence of three recurrence factors. These are the resection margin, the histologic type and the recurrence history. Moreover, the study has enabled find a factor associated with recurrence, i.e. the qualification of the operating agent, but there is no supporting data.

A training of enough number of surgeons with acceptable knowledge in cancer surgery and the creation of a Radiation Therapy Centre could help consequently reduce the recurrence risk in soft tissue sarcomas in our work environment. Also, a study with a bigger number of patients could specify better, recurrence risks in our Burkinabe context.

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