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Impact of unplanned excision on prognosis of patients with soft tissue sarcoma in adults: A comparative study at Regional Cancer Centre

Oncology

KEYWORDS: Soft tissue sarcoma; unplanned excision; re-excision; recurrence

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ABSTRACT

Introduction: Soft tissue sarcoma is a heterogeneous group of malignant mesenchymal tumours, and accounts for approximately 1% of all malignancies. The preoperative evaluation of the disease with specific radiological and histopathological examination has a pivotal role in the management. The unplanned excision of these tumours has a significant role in terms of oncological outcome in about 24% to 60% of all patients. Aim of this study was to compare the outcomes of planned excision, with those of re-excision after unplanned surgery in terms of local recurrence and distant metastasis.

Material and methods: A retrospective analysis of the recorded data was done for patients, who presented with soft tissue sarcoma from 2005 to 2014 at our institute. All patients were classified in to two groups, "planned excision" and "re-excision after unplanned excision". Patients with a median follow up of 25 months, with existing complete records were analysed.

Results: After exclusion, a total of 320 patients were enrolled in our study. 253 patients underwent "planned excision" after an optimum pre-operative assessment, and 67 patients underwent "re-excision" for either residual or recurrent disease after a previous unplanned excision. The rate of local recurrence was higher in "re-excision" group, but statistically insignificant (17.9% vs 12.6%; p=0.1). Distant recurrences were more with "re-excision", but statistically insignificant (7.5% vs 4.3%; p=0.2).

Conclusion: Unplanned excision of STS has higher local recurrence and distant metastasis rates even after favourable baseline features. Soft tissue mass over any part of body of unknown identity should be appropriately imaged, biopsied and managed by the Oncologist at a specialized centre. Re-excision following unplanned excision has higher frequency of positive surgical margin leading to local recurrence as well as distant metastasis.

Introduction

Soft tissue sarcomas (STSs) are rare primary malignant neoplasms having a diverse and complex behaviour, and arising from undifferentiated mesenchymal stem cells which may reside anywhere in the whole body. These account for approximately 1% of all cancers in adults.[1,2] The worldwide annual incidence of STSs, as per World Health Organization (WHO), is 30 cases per million population.[3] These have an aggressive clinical behaviour, with a reported case fatality rate of 40% to 50%.[1,3] A well-defined aetiology of STSs is still unknown, and majority cases are sporadic in presentation. Several risk indicators and predisposing factors have been pronounced, including genetic mutations in mesenchymal cells (eg. APC, NF1, Li-Fraumeni, etc.), lymphedema, radiation, trauma, and chemical carcinogens.[2,3 Lower extremity is the most common site of occurrence of STSs, in approximately one third cases. Although, the primary and secondary prevention including screening and early detection have no role, the accurate assessment of the disease by clinical examination and imaging has an added value for local control in 95% of cases.[4,5] The establishment and implication of prompt diagnostic and therapeutic measures with planned excision followed by adjuvant therapy has a pivotal role in reducing the burden of unplanned excision with an increase in the 5-year survival rates from 62% to 84%.[6-9] The benign tumours are much more common compared to malignant STSs (ratio 100:1), and rarity of STSs coupled with a low index of suspicion of malignancy often leads to an inadvertent and inappropriate excision, or even an enucleation without a histopathological diagnosis.[3]

The term, "unplanned total excision", was defined by Giuliano and Eilber, as the macroscopic removal of STSs without consideration of preoperative images or the surgical margins of the normal tissue around the tumour.[10] This may be associated with the in-experience of the surgeons at non-oncological centres, resulting into a complicated residual disease in 24% to 60% of patients with STSs.[1,5,8,10-12] The negative impact of this unplanned management on precise oncological treatment and outcome is controversial, and this factor is still not considered as negative prognostic indicator for STSs. Furthermore, in addition to factors associated with local control of the disease, as surgical margin and adjuvant radiotherapy, tumour-related factors as clinical stage, histological subtype and grade, size, depth, location, and metastasis at diagnosis, unplanned excision also has a significant role in prognosis. Currently, limb salvage surgery (LSS) is the emerging modality of treatment in extremity STSs, with concerns to the advances in imaging modalities with better tissue resolution, surgical technique, and well-precised adjuvant radiotherapy. The tissue violation done by unplanned excision is supposed to be associated with higher chances of margin positive resection that influence local recurrence and preclude subsequent LSS.

Aim of this study was to compare the outcome of patients who underwent a single planned excision with those who underwent re-excision after an unplanned surgery, in terms of local recurrence and distant metastasis. We also wanted to see the factors more prevalent in patients with residual or recurrent disease after unplanned excision, and their association with prognosis.

Material and methods

We conducted a retrospective study based on the prospectively maintained medical records of patients with soft tissue sarcomas, except intraabdominal and intrathoracic location, from January 2005 to December 2014. The data was collected in accordance with the local guidelines for research ethics with a minimum follow-up of 12 months after the institutional review board approved the study design. The inclusion criteria were as following: (1) STS patients aged between 18 and 70 years; (2) Patients who underwent standard preoperative assessment followed by primary oncological resection with or without adjuvant radiotherapy based on histopathology results were included in group "Planned excision"; (3) Patients who presented to our institute with a history of previous excision without preoperative planning, with residual or recurrent disease and underwent "re-excision", were included in the other group. The exclusion criteria were as following: (1) Patients with poor performance (ECOG>2), with metastatic disease, incomplete follow-up, unwilling for surgical treatment; (2) In "re-excision" group, patients who underwent brachytherapy.

Patient characteristics

We enrolled 394 patients with STSs, who presented to our institute over the period of ten years without previous therapeutic or diagnostic excision. Among these, 45 patients did not come after the diagnosis, 18 patients had evidence of metastatic disease at the time of diagnosis, 15 had poor performance status (ECOG>2), and 19 were not willing for the surgical treatment; and were excluded. Two-ninety-seven patients underwent surgical excision after complete preoperative planning. During the follow-up period, 25 patients were lost to follow, 10 patients expired, and in 9 patients the performance status deteriorated and they were also excluded. At the end of the study, 253 patients were eligible for the analysis.[Fig 1] In the other group, 126 patients presented to our institute with a history of previous excision biopsy or therapeutic excision. Eighty-five out of 126 underwent a re-excision after adequate imaging and planning for an evidence of residual or recurrent disease, detected either clinically or on imaging. At the end, 67 patients were eligible in this group for analysis, after exclusion of patients who had metastatic disease (n=22), underwent brachytherapy (n=8), were lost to follow-up (n=8), had poor performance status (n=11), died within 12 months of surgery (n=6), or were unwilling for surgical treatment (n=4).[Fig 1] The annual incidence of unplanned resected cases presenting to our institute was surveyed previously by our department and showed a constant rate over the last decade.[13]

Pre-operative assessment

All patients in the group with primary presentation were diagnosed with sarcoma on percutaneous core needle biopsy, and/or definitive cross sectional imaging. Further treatment plan was decided after discussion in the multidisciplinary meeting. Among the patients with previous history of intervention, the stained slide and/or paraffin blocks were reviewed by the onco-pathologists, and MRI was performed in all patients at our institute. Tumours were graded as per FNCLCC (French Federation Nationale des Centres de Lutte Contre le Cancer) system. Grade 1 was defined as low grade, and Grade 2 and 3 were considered as high grade tumours for analysis. Stage of the tumour was defined according the recommendations of the American Joint Committee on Cancer (AJCC) 7th edition. Patients with metastatic disease and locally advanced tumors not amenable to optimal resection were referred to medical oncologist for chemotherapy. For all patients in both groups, demographic and tumour characteristics were recorded from the medical records including site (upper or lower extremity, trunk), size, depth (superficial or deep to the fascia of the underlying muscle), and histologic grade (low, intermediate, or high).

Surgical treatment

Patients in the "planned excision" group, underwent definitive standard surgical excision with adequate surrounding normal tissue of 1 to 2 cm as per guidelines.[1,9,10/D] According to the size and proximity to the vital structures, this involved wide resections or functional/ total compartmentectomies, and marginal resections with macroscopic clearance specially for large well-differentiated low grade STSs abutting crucial neurovascular structures with preservation of adjacent muscles and neurovascular structures. In the third dimension, the fascial layer deep to lesion was removed, and periosteum and perineurium removed in the lesions abutting the adjacent bone and nerves. In context of function-preserving resection, cases with suspicious close margin were marked with titanium clips in all dimensions to guide adjuvant radiotherapy.

For patients who had undergone an unplanned operation elsewhere and presented with residual or recurrent disease on postoperative MRI, the initial treatment was re-excision of the surgical bed after ruling out systemic metastasis. This involved re-excision of the previous scar with as wide margins as would be compatible with primary closure without recourse to cutaneous/ myocutaneous reconstruction. The extent of the deep resection was wide enough to encompass the whole seroma cavity and drain-exit points, but with preservation of crucial anatomical structures. On occasions, where wide resection of the surgical bed and seroma cavity was possible but primary closure was not possible, synchronous cutaneous/ myocutaneous reconstruction was undertaken. In certain cases, the multidisciplinary opinion was that no re-excision could be performed in a meaningful oncological sense, because of the anatomical location of the tumour or the nature of the previous surgery.

Histopathology

The surgical specimens in the "planned excision" group were examined thoroughly for the confirmation of the diagnosis, histologic type, grade (as per FNCLCC), resection margins, and response to preoperative treatment. Size of tumour was assessed in the specimen using the largest diameter as a reference and categorized into two groups, smaller than 5 cm and larger. Negative surgical margin was defined as the absence of tumour within 10 mm of the inked surface, and further classified into the following categories: negative margin ≥10mm and negative margin 1-9mm, which was defined as "close margin". positive margin was defined as the microscopic presence of tumour within 1 mm of the inked surface. In the other group, with patients who had history of previous unplanned excision, assessment of surgical specimen was done similarly.

Adjuvant treatment

Patients with high grade, large tumour (>5 cm), and close margins received radiation therapy to the entire surgical bed with a 3 to 5 cm margin beyond the surgical scar and/or beyond postoperative seroma or areas of ecchymoses as per institutional protocol. The dose delivered was 50Gy in 25 fractions, using computed tomography based three-dimensional conformal treatment planning. The field size was then reduced to the primary surgical bed plus a 2 cm margin for a further dose of 10Gy in 5 fractions. If the margin was microscopically positive, a further 6Gy in 3 fractions was delivered to that area. Among the high-grade cases, patients with chemotherapy sensitive STSs were subjected to Adriamycin plus ifosfamide based postoperative systemic chemotherapy based on the Japan Clinical Oncology Group's 0304 regimen.

Outcome

The oncological and functional outcome were analysed in both the groups, and the impact of unplanned excision was highlighted. Local recurrence was verified after definitive surgery using clinical examinations and MRI during the follow-up exams, and confirmed on fine needle aspiration cytology. Distant metastases were identified using computed tomography examinations, and/ or bone scintigraphy. The endpoints in this study for oncological outcomes were local recurrence-free survival, metastasis-free survival, and overall survival. Disease free survival was measured from the date of admission to occurrence of recurrence. The overall survival time was measured from the date of patient admission to patient death. Patients who left prior to the end of minimum 3-year follow-up were punctually censored on survival curves.

Statistical analysis

Categorical variables were analyzed using frequency tables, and quantitative variables were analyzed using descriptive measures (e.g., the mean, and standard deviation). Chi-squared association tests (e.g., Fisher's exact test and Pearson's Chi-square test) were used for bivariate analyses. An analysis of survival was performed using Kaplan-Meier curves. A value of $p<0.05$ was considered to be statistically significant.

Results

Study patients

A total of 320 patients underwent surgical treatment for STSs at our institute over the period of ten years. Out of them, 253 patients (79%) comprised group "A" as the control group, who underwent a single definitive oncological operation as their primary procedure, after a preoperative core-needle biopsy and/or diagnostic imaging had established the diagnosis of STS. The group "B" comprised of 67 patients (21%) who were referred to our institution after an unplanned operation and later underwent surgical resection for evidence of residual or recurrent disease. The age at the time of presentation, gender, and tumour-site distribution between both groups were comparable.[Table 1]

Tumour characteristics- diagnosis, treatment, and resection margin

Group A: Planned resection: Mean age of patients in this group was 39.2±14.2 years; younger than that patients in the other group but statistically insignificant (p=0.92). Males were more common in this group with a ratio of 1.5:1, compared to 0.8:1 in Group B (p=0.72). Majority of the tumours were located in the extremities, and accounted for 79% of cases in this group. The ratio of depth-wise distribution, superficial or deep seated lesions, was reverse in both the groups as 0.6:1 versus 1.3:1 (p=0.3). The size of the lesion on clinical examination was larger than 5cm in the majority of patients (75%), and most of the tumours were high grade (73%).[Table 1] Based on resection margin status, 10 patients (3.9%) had positive margins, 78 patients (30.8%) close margins, and 165 patients (65.3%) had negative margins. Postoperatively, according to size, grade, and resection margin, 52 patients (20.5%) were given external beam radiotherapy, and 29 patients (11.5%) chemotherapy, as per institutional protocol in patients with high risk features for recurrence.

Group B: unplanned excision: A total of 67 out of 126 patients with a diagnosis of STSs and history of previous surgical excision underwent planned re-excision at our institute. Mean age was 43.3±16.9 years. Gender distribution showed slight female preponderance, with a ratio of 1:0.8. All patients had the diagnosis of residual or recurrent disease confirmed with a core needle biopsy and MRI for assessment of local extent. Most of the tumours were located in extremities (74%), small in size <5cm (61%), superficial lesions (57%), and high grade (64%). In contrast to group A, the significant clinical characteristics in the group B were low grade (36% versus 27%; $P<0.05$), and small tumor volume (61% versus 25%; $P<0.01$). On histopathology examination, 4 patients (6%) showed positive margins, 21 patients (31%) had close margins, and 42 patients (63%) had negative margins. Re-excision is an important prognostic factor for local recurrence; therefore adjuvant radiation therapy was administered in 27 patients (40%) and chemotherapy in 14 patients (21%). Postoperative complications were significantly more common in this group, 21% versus 9.5% (p=0.01).[Table 1]

Oncological outcome: local recurrence

The average follow-up of patients in both groups was 25.5±9.7 months. The overall isolated local recurrence (LR) in all the patients was 13.8%, with a median interval of 21 months (9-78 months). Local recurrence was more common in Group B compared to Group A, at 17.9% versus 12.6% (p=0.1), but statistically insignificant. The factors affecting local recurrence were correlated with recurrence separately in both the groups. The proportion of patients with low grade tumour developing LR in group B was twice that in the group A, 42% versus 22% (p=0.001). The influence of the size of tumour and the depth of extent on LR was observed to a lesser extent in group B. One third (4/12) of patients in group B with LR had size of the lesion smaller than 5 cm (p=0.01), and 40% (5/12) patients with LR had superficial lesions(p=0.01). The positive resection margin was more common in group A (18% vs 8%; p=0.6). The administration rate of adjuvant treatment radiotherapy and chemotherapy was similar in both groups.[Table 2]

Oncological outcome: distant recurrence

The overall distant recurrence (DR), isolated or with LR, was 5% with a median interval of 26 months (range 13-45). There was a significant difference between the rates of DR in both the groups as 7.5% versus 4.3% in groups A and B, respectively (p=0.02). Factors affecting distant recurrence were not analysed due to the small number of patients.

Oncological outcome: cancer specific survival, disease free survival

The total number of deaths noted in group A was 22 (8.7%), and in the group B, was 5 (7.4%). Median time to death from disease was 28 and 25 months, respectively. The cancer-specific survival was not analysed due to the unavailability of the cause of death in all patients. Two-, three, and five-year recurrence free survival rates were compared between the two groups. Two-year local recurrence free survival was significantly better with planned resection (98.4% versus 92.4 %; p= 0.03). Three- and five-year local recurrence free survival was better in group A but statistically insignificant.[Table 3; Fig 2]

Discussion

As we know, surgery is the principal modality for the management of STSs. We determined and presented the actual incidence of unplanned resection presenting at tertiary cancer care centre over the last decade, which was consistently a major burden of patients (30%) with either residual disease or recurrent disease potentially leading to the poor outcomes.[13] Unplanned resection of STSs is a universal problem due to the rarity of the disease and performance of these procedures by the surgeons working outside cancer centres. We observed that 22.3% of the patients, who underwent surgical treatment at our centre, had previous unplanned excision, within the range reported in the literature as 18% to 64.6%.[1,6,14-18]

The various factors responsible for this detrimental outcome include undetermined malignant potential, incorrectly placed incisions, excessive postoperative hematoma, violation of the tissue compartments, wrong drain tube and suture placement.[19] We analysed earlier that the prevalence of tumour related unfavourable prognostic factors in patients with unplanned excision was less compared to the favourable counterparts.[13] In this study, we analysed the outcome of surgical treatment at a single institute between these two groups of patients as described in the earlier section.

In this study the rate of local recurrence was estimated 13.8% among all patients who had received treatment at our institute, similar to the 13% reported by Lewis et al.[20] The variables influencing local recurrence in published literature including surgical margin and introduction of adjuvant radiotherapy, were not associated in our study.[12,14,15,21-23] In contrast to the earlier reports by various authors regarding rate of distant metastases, as 32% by Novais et al, 18% by Lewis et al, and 22% by Pisters et la, lower rate was observed in the present study as 5%, which may be explained by the different exclusion criteria in the present study.[20] Exclusion of the patients with short follow up, patients with advanced disease less amenable to cure or chances of potential incomplete resection, and censoring of the patients who had local recurrence, influenced the rate of systemic metastasis rate in our study.

The proportion of low grade tumour in the resected specimen was

higher in Group B (36%) than in Group A (27%), more significant trends were observed in the analysis of association with local recurrence 42% versus 22% (p=0.001), respectively. The superficial lesions had higher frequency of undergoing unplanned excision. Peabody et al revealed that 94% of superficial lesions had surgery prior to referral to a Cancer centre, whereas only 52% of deep lesions underwent the same[24] In the present study, the ratio was revealed same, with 28% of the patients with superficial lesion having undergone previous excision, compared to only 15%, almost half, of the deep lesions, an unplanned excision. In contrast, no significant difference was shown by Umer et al.[25] Convincingly, superficial STSs seems to be less challenging than deep lesions for surgical excision at non-oncology centres, but the results are contradictory.
Other than the depth of the lesion, size of lesion is also an important factor predicting aggressiveness of STSs, in that the larger lesions are more often high grade, and need more aggressive multimodality treatment than smaller lesions. In our study, 40% of all patients with small STSs (<5 cm) underwent resection after a previous unplanned surgery, while this proportion was much lower in larger lesions, only 12%. Qureshi et al revealed the same result with a higher significance as 80% versus 23%, respectively, but it was not observed by Hanasilo et al.[26]

The significant impact of unplanned excision on prospective surgery is seen in the form of challenge to achieve a wide negative margin of normal tissue, which is a strong prognostic factor for local recurrence as well as survival outcome. The identification of residual or recurrent cancer separate from the scarring tissue is very difficult due to violation of tissues, inadequate haemostasis, and more proximity to vital structures. A significantly higher margin positive resection rate after re-excision for unplanned excision was observed by Hanasilo et al, as 17.4%; five times higher than in patients who underwent a planned excision, 3.4% (p=0.034).[26] We also found a higher margin positive resection as 6.0% versus 3.9%, statistically not significant, but at a lower rate than reported in the literature (p=0.1). This difference of significance may be due to exclusion of the patients with incomplete follow-up from analysis in our study. On the contrary, Fiore et al showed a higher margin positive resection rate with the primary planned excision.[16] This was explained by the tumour location adjacent to neurovascular bundle or bone, which precluded the resection with an adequate negative margin. It is well proved that the previous excision is a major cause of positive margin resection, resulting in poor oncological outcome.

The presence of residual disease in the resected specimen after planned re-excision signifies an inadequate previous treatment. This is often under-detected on physical examination and imaging, reported with a range from 35% to 59%, compared to the reported rates of presence of viable disease in the specimen after re-excision with a range from 23.6% to 91%.[1,6,8,15,16,18,27] Same rate was noted in our study, with 92% (79 out of 86) patients having residual disease in group B.[Fig 1] Taking it into consideration with margin negative resection, this rate supports notion of an incomplete treatment in the non-oncology centres, and also the need of re-excision in these cases at the centres with expertise.

Local recurrence rates in both groups in our study were noted within the range of rates in previous reports. We noted overall local recurrence in our study in 13.8% cases, which was lower in group A, compared to group B, 12.6% and 17.9%, respectively. Potter et al observed a significant difference in the rates of LR between the two groups, 34% versus 6% in unplanned excision and planned excision group, respectively. They concluded that the influence of unplanned excision of STSs on LR could not be overcome by further extensive resection and additional adjuvant radiation therapy.[15] In contrast, the difference was not significant, as noted by other several authors, which is similar to our results.[14,16,18,28,29] We noted the trends towards better local control of the disease with initial planned surgery in STSs, but it was statistically not significant (p=0.1). Therefore, the poor oncological outcome can be improved with the planned re-excision and adjuvant radiotherapy in patients who had undergone an initial unplanned surgical treatment. The insignificant difference in LR rate between the two groups in our study can be due to STSs with low malignant potential being proportionately higher in number in the group B, and also due to re-excision leading to amplified margins resulting in improved local control results. The first recurrence after unplanned excision was only due to inadequate resection, not because of the aggressive malignant potential of tumour.

Several theories regarding different recurrence have been postulated, that low recurrence rates may be due to 1) wide margin re-excision; 2) unplanned excision promotes immunity activation of dendritic cells, which recognize antigens in the residual disease, resulting in an immune response with a long-term memory and protecting patients from local recurrence as well as distant failure; 3) complete excision in planned treatment results in loss of inhibition of microscopic satellite deposits leading to recurrence. All theories are inconclusive due to variable results in different studies.

The rate of distant recurrence can be increased with unplanned excision, but the results are not convincing.[16,29,30] In our study, there was no difference in distant recurrence rates between the groups, 7.5% in group B versus 4.3% in group A (p=0.2). We analysed the patients with recurrence in both groups regarding all factors and observed that local recurrence was more with small size, superficial lesions, and low grade tumours compared to recurrent lesions in patients who underwent an initial planned excision. It seems that the effect of initial unplanned surgery in STSs remains throughout of the course of disease.

Conclusion
Unplanned excision is a poor prognostic factor for local recurrence in STSs. Although, the poor outcomes can be improved with a planned re-excision, but consequent outcome of STSs is persistently affected by the initial unplanned excision.

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Author's contribution
SNP, KD, AP and SK contributed in acquisition of data, design of study, analysis and drafting of manuscript. KD, JG and SK searched literature and drafted manuscript. All authors read final manuscript and have given agreement for the publication.

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Figure 1 Study schema

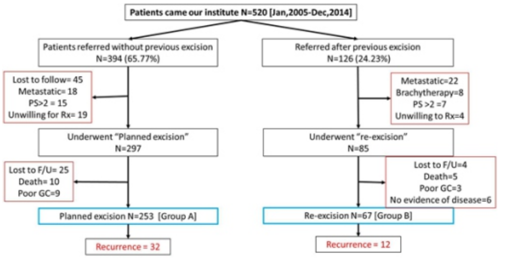
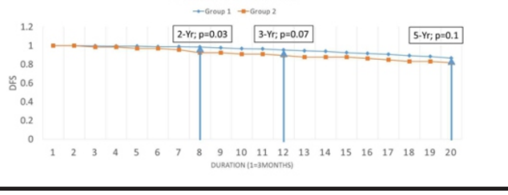


Figure 2 Disease free survivals



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Tables

Table 1:

Table 1: Characteristics of patients					
Characteristics		**Total no 320**	**Group A (planned resection= 253)**	**Group B (Re-resection =67)**	**p value**
Gender	Male	174(54.4%)	152 (60.0)	30(44.8%)	0.72
	Female	146(45.6%)	109 (40.0%)	37 (55.2%)	
Mean Age (Years)		40.8±11.2	39.2±14.2	43.3±16.9	0.92
Mean Follow up (months)		25.5±9.7	25.5±9.7	25.5±9.7	
Site	Etremety	252(78.8%)	202 (79.8%)	50 (74.6%)	0.8
	Trunk	68 (21.2%)	51 (20.2%)	17 (25.4%)	
Histoloigical Grade	Low	92 (28.8%)	68 (26.9%)	24 (35.8%)	0.05
	High	228(71.2%)	185 (73.1%)	43 (64.2%)	
Size	<5cm	103(32.2%)	62 (24.5%)	41 (61.2%)	0.01
	≥5cm	217(67.8%)	191 (75.5%)	26 (38.8%)	
Depth	Superficial	134(41.9%)	96 (37.9%)	38 (56.7%)	0.3
	Deep	186(58.1%)	157 (62.1%)	29 (43.3%)	
Surgical margins	Positive	14 (4.8%)	10 (3.9%)	4 (6.0%)	0.1
	Negativ (<10mm)	99 (30.9%)	78 (30.8%)	21 (31.3%)	
	Negative (≥10mm)	207(64.3%)	165 (65.3%)	42 (62.7%)	
Radiotherapy		79 (24.7%)	52 (20.5%)	27 (40.2%)	0.4
Chemotherapy		42 (13.1%)	29 (11.5%)	14 (20.8%)	0.01
Post operative complications		38 (11.9%)	24 (9.5%)	14 (20.8%)	0.01
Local recurrence		44 (13.8%)	32 (12.6%)	12 (17.9%)	0.1
Distant metastasis		16 (5.0%)	11 (4.3%)	5 (7.5%)	0.02

Table 2:

Table 2: Characteristics of patients with recurrence					
Variables		**Total ecurrence (N=44)**	**Recurrence in group A (n=32)**	**Recurrence in group B (n=12)**	**p value**
Gender	Male	23 (52.3%)	17 (53.1%)	6 (50%)	0.85
	Female	21 (47.7%)	15 (46.9%)	6 (50%)	
Site	Extremety	34 (77.3%)	24 (75%)	10 (83.3%)	0.9
	Trunk	10 (22.7%)	8 (25%)	2 (16.7%)	
Histoloigical Grade	Low	12 (27.3%)	7 (21.9%)	5 (41.7%)	0.001
	High	32 (72.7%)	25 (78.1%)	7 (58.3%)	
Size	<5cm	9 (20.5%)	5 (15.6%)	4 (33.3%)	0.01
	≥5cm	35 (79.5%)	27 (84.4%)	8 (66.7%)	
Depth	Superficial	11 (25%)	6 (18.7%)	5 (41.7%)	0.01
	Deep	33 (75%)	26 (81.3%)	7 (58.3%)	
Surgical margins	Positive	7 (15.9%)	6 (18.7%)	1 (8.3%)	0.6
	Negativ (<10mm)	21 (47.7%)	15 (46.9%)	6 (50%)	
	Negative(≥10mm)	16 (66.4%)	11 (34.4%)	5 (41.7%)	
Radiotherapy		13 (16.5%)	9 (28.1%)	4 (33%)	0.4
Chemotherapy		9 (21.4%)	6 (18.7%)	3 (25%)	0.6

Table 3

Table 3: Disease free survival			
DFS	**Group 1**	**Group 2**	**p value**
2-Year	98.40%	92.40%	0.03
3-Year	95.10%	89.30%	0.07
5-Year	86.60%	81.40%	0.1

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