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Long Term Outcome of Preoperative Isolated Limb Infusion and External Irradiation in Management of Locally Advanced Extremity Soft Tissue Sarcoma

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Abstract: *Background*: We report our long term results of isolated limb infusion (ILI) in cases of locally advanced soft-tissue sarcoma (ASTS) of the extremities.

Methods: Forty cases of ASTS received ILI with doxorubicin. Preoperative external beam radiotherapy started within 3-7 days after ILI was administered. After 3-7 weeks, surgery was performed aiming at limb preservation. The long term outcome of these cases (Group I) was reported and compared to the outcome of comparable group of patients followed prospectively and treated by neoadjuvant systemic chemotherapy (NACT) and external irradiation (Group II).

Results: The study included 40 cases in Group I, and 46 cases in Group II. Overall response to preoperative treatment was 85% in Group I versus 43% in Group II. Wide local excision was performed for 75% of Group I patients and in 34% of Group II cases. After a median follow up period of 76 months, local recurrence rate was 35% in Group I and 67% in Group II (P= 0.02). The overall survival rate was 60% in Group I and 35% in Group II (p= 0.008). Only initial response to ILI was associated with overall survival in Group I.

Conclusion: The outcome of ILI in management of ASTS is significantly better than systemic NACT in terms of disease free and overall survival.

Keywords: Isolated limb infusion, extremity soft tissue sarcoma, long term survival.

INTRODUCTION

The management of locally advanced extremity soft tissue sarcomas continues to be a challenge. The prognosis of patients with advanced soft-tissue sarcoma (ASTS) remains poor for decades with a median survival of at best 12 months [1]. Current improvement in patients' quality of life and survival in STS have resulted from contribution of many advances in its management. There have been contributions from centralization of service, multidisciplinary management, improved surgical technique, multimodality therapy and the development of limb sparing surgery. However, controversies surround the main pillars of treatment such as the type of surgery (e.g. indications for limb salvage) and the neo-adjuvant and adjuvant treatment modalities, such as radiation therapy or chemotherapy [2].

Neoadjuvant chemotherapy (NACT) in treatment of patients with STS is an area of controversies where small progress has been made over the past years. Sarcomas show variability in response to chemotherapy, which emphasizes the heterogeneity of this tumor entity. It is probably that the lack of distinction of sarcoma subtypes with regard to cytostatic therapies might be responsible for the conflicting data we have when patients are treated in a neoadjuvant setting [3].

Data on prognostic and predictive factors for outcome to neoadjuvant chemotherapy are not available from large series. Identification of such factors is essential for patient management and clinical trial design, in particular for STS given its heterogeneity. While tumor size and grade are well-established risk factors for local or systemic recurrence, other factors (e.g. tumor location, histologic type, margin status) have only been vaguely defined, which complicates the development of evidence-based treatment algorithms [4].

Neoadjuvant isolated regional chemotherapy is an attractive treatment option because it allows much larger doses of chemotherapy to be delivered to the tumor with minimal systemic toxicity. Furthermore, where the tumor responds to the therapy, vital anatomical structures may be able to be preserved at the time of subsequent surgical excision, and previously unresectable tumors may be converted into resectable ones [5]. Isolated limb infusion (ILI) is a minimally invasive technique of delivering regional chemotherapy in ASTS patients. This technique was developed and implemented in the early 1990s by Thompson *et al.*, at Sydney melanoma unit with the objective of obtaining the benefit of conventional isolated limb perfusion (ILP) without incurring its major disadvantages [6].

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1876-5041/11

The authors present their initial results of isolated limb infusion (ILI) in patients with ASTS of the extremities in 2006 [7]. The goal of the present study is to discuss the results of ILI on ASTS cases on the long term (more than 5 years). We compared the survival of ILI cases with a comparable group of patients that received neoadjuvant systemic chemotherapy and external irradiation followed by limb salvage surgery. In addition, analysis for prognostic factors was performed aiming to establish independent predictive factors for best overall response (RR), disease - free survival (DFS) and overall survival (OS).

PATIENTS AND METHODS

Patients

The data of the 40 cases that underwent ILI (Group I) since 2005 was collected and compared to a comparable group of cases that received NACT and external irradiation (Group II). Therefore, we retrospectively reviewed the medical records of 234 extremity STS patients treated at our institutions from 1998 to 2004. Among those cases, 153 cases were locally advanced. After applying the inclusion criteria, excluding patients that lost follow up (n= 23) and matching the patients in both groups regarding age, sex, tumor site, size, type, we got a cohort of 46 patients that could be compared as a control group. Inclusion criteria were the following: 1- high grade sarcoma, 2- large size > 5cm, 3- proximity to a neurovascular bundle and/or the bone, and 4- a minimum of 5 years follow up duration since the initiation of treatment. Patients with the chemosensitive subtypes Ewing sarcoma, rhabdomyosarcoma, and desmoplastic small round cell tumor were excluded from the study.

This study was performed retrospectively from our data base. However, patients treated with ILI since 2005 gave written consents that their follow up data will be used in this research and our IRB approved this.

Treatment Programs

1. Preoperative isolated limb infusion (ILI) and external irradiation: ILI was performed using the same technique as had been described earlier by Thompson *et al.,* [6], and the investigators [7]. In brief, standard radiologic catheters were inserted percutaneously into the axial artery and vein of the disease-bearing limb *via* the contralateral groin. The catheter tips were positioned at the level of the major feeding vessels of the tumor. Then the contrast medium (urovidio) was injected through the catheter to evaluate the vasculature of the tumor region and to obtain angiographic run, determining the feeding vessel of the tumor (Fig. **1**). When it was confirmed that the position of the angiographic catheter was satisfactory, a pneumatic tourniquet was inflated around the root of the limb to be treated and the cytotoxic agent (doxorubicin 0.7 and 1.4 mg/kg for the upper and the lower limbs, respectively) was infused into the isolated limb *via* the arterial catheter. For the duration of the ILI procedures (15-25 min), the infusate was then continually circulated by repeated aspiration from the venous catheter and reinjection into the arterial catheter by using a syringe attached to a three-way tap in the circuit. After 15-25 min the limb was flushed with 1 L of Hartman's solution *via* the arterial catheter. The limb tourniquet was then deflated to restore normal limb circulation and the catheters were removed. External beam radiotherapy (35 Gy in ten fractions) started within 3-7 days after ILI. After 3-7 weeks, limb sparing surgery was performed. Usually this period allowed for enough shrinkage of the tumor and allowed the soft tissues to recover from the inflammatory reaction of radiotherapy.
2. Neoadjuvant systemic chemotherapy (NACT) and external irradiation: The systemic chemotherapy of each cycle consisted of doxorubicin (adriamycin) 50 mg/m2 on day 1, etoposide 125 mg/m2 on days 1 and 4, and ifosfamide 1250 mg/m2 for 60 min on days 1-4. A total of 3-4 neoadjuvant courses were given before assessment of the tumor response. External beam radiotherapy (35 Gy in ten fractions) started within 3-7 days after completion of the chemotherapy cycles. All cases were referred to surgery after finishing their neoadjuvant protocols.

Treatment Evaluation and Statistics

After neoadjuvant protocols, systemic and limb toxicity and tumor response were assessed regularly. Systemic toxicities were graded according to the World Health Organization (WHO) grading scale. The scale proposed by Wieberdink *et al.,* [8] was used to assess limb toxicity. After 3 - 6 weeks, the tumor response was evaluated. Clinical response was classified as follow: complete response (CR: complete disappearance of all measurable or evaluable tumor for a minimum of 4 weeks), partial response (PR, greater than 50% reduction of the tumor volume lasting at least 4 weeks), minor response (MR, reduction of the tumor volume by less than 50% for at least 4 weeks), stable disease (SD, less than 25% increase in the tumor volume for at least 4 weeks), and progressive disease (PD, an increase of greater than or equal to 25% of the tumor volume and/or occurrence of new lesion). In this study, response to chemotherapy was analyzed as a binary variable: responders were those who were reported as having achieved a complete, partial, or minimal radiologic response (according to the WHO criteria); all other patients were classified as non-responders.

By definition, patients were classes as NED (no evidence of disease) at the time of surgery in cases of R0 (negative margins on frozen section examination), R1 (positive margins on frozen section). Patients with R2 (residual disease), were considered non- NED.

Overall survivals (OS) were measured from the start of treatment until death from any cause or last follow up. Disease free survival (DFS) was defined as the time from start of treatment until radiologic documentation of disease recurrence or last follows up. For the patients not followed up in our institutions or missed a follow up visit, the referring surgeon or the patient's family was contacted to determine the patient's long term follow up status.

Survival curves were calculated by the Kaplan Meier method. Comparison of survival curves were performed using the log rank test (Mantel-Cox). Age, sex, histologic type, grade, site of the tumor, type of surgery and margin status were investigated as potential prognostic factors for OS and DFS by means of a univariate log rank analysis. The

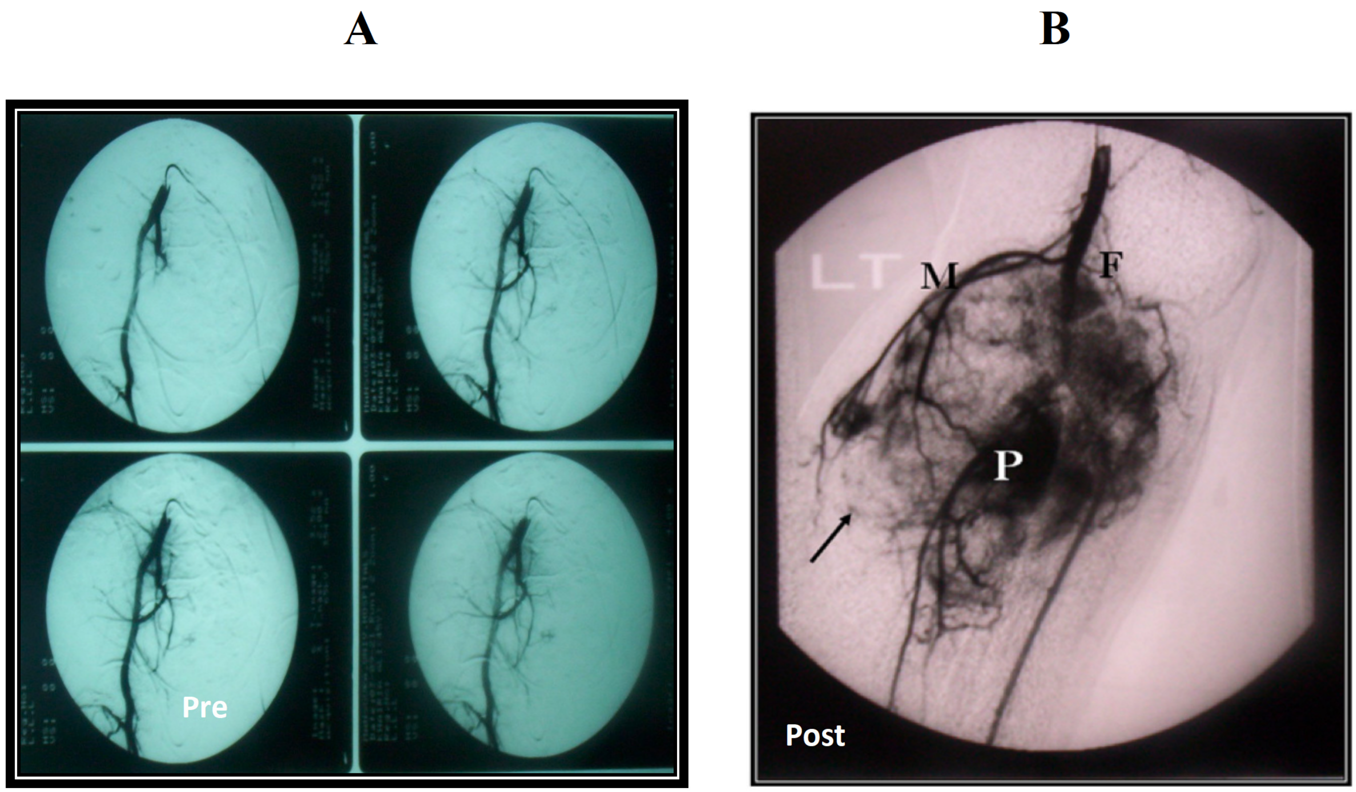

Fig (1). **A**. ILI; the angiographic catheter was introduced over the guide wire for enough distance upward into the aorta till reaching bifurcation of the aorta. **B**. angiogram showing a hypertrophied feeding artery (F), marginal pathologic vessels (M), tumor plush (P), and intratumoral microaneurysms (arrow).

independent significance of variables was assessed in a multivariate Cox regression analysis.

RESULTS

Patients' Characteristics

We retrospectively reviewed the medical records of 234 extremity STS patients treated at our institutions from 1998 to 2004. Among them, 153 cases were locally advanced and 97 cases received NACT and preoperative irradiation. After applying the inclusion criteria and matching the 2 groups regarding age, sex, tumor site, size and type, a total of 46 cases were picked as a control group (Group II). These patients were compared to 40 patients who were treated by preoperative ILI and external irradiation (Group I). The mean ages (± SD) of the two groups at the time of diagnosis were 42 (±13). Men constituted 71 % of the patient population (n=65). The tumor site was upper extremity (at or beyond the shoulder) in 22% of the patients (n=19) and lower extremity (at or beyond the groin in 78% of patients (n=67). Tumor size was defined according to the pathologic report as the maximum diameter of the tumor. Tumors > 5cm were present in 95% of the patients. Of the 86 patients, 42% (n=36) had low grade tumors and 58% (n =50) were high grade (Table **1**).

Response and Surgery Results

In Group I; disease control rate was 85% (n=34 patients). Twelve cases (30%) showed partial response and 22 (55%) showed minimal response. All patients showed an increase

Table 1. Patients Characteristics of the 3 Groups

	Group I ILI (n=40)	Group II Systemic CT (n= 46)	P Value
Age (mean±SD)	42±10.3	41±14	0.95
Sex			
Male	33	38	0.33
Female	7	8	
Tumor Size (cm)			
Median	11.7	11.3	0.24
range	5-14	7-13	
Tumor site			
Lower limb	35	39	0.31
Upper limb	5	7	
Pathology			
MFH	16	13	0.12
Liposarcoma	18	21	
Fibrosarcoma	12	2	
Spindle cell sarcoma	0	2	
Synovial sarcoma	0	3	
Neurogenic sarcoma	4	5	
Tumor Grade			
Low	22	25	0.46
High	18	21	

in the extent of necrosis and extensive cystic degeneration of their tumors as detected in MRI. In Group II, disease control rate of neoadjuvant chemotherapy was 43% (n=20). Radiographic responses consisted of seven patients (15%) with partial response and 13 cases (28%) with minimal response. There was no complete response in either group.

Surgical resection was carried out for 36 cases (34 responders and 2 cases that showed stable disease). Local excision (wide or marginal) was done in 30 cases (75%) and compartmental excision was needed for 6 cases only (15%). Four cases showed progressive disease; amputation was performed in three cases and the fourth case refused amputation and was referred for EBRT (external beam radiotherapy) and/or systemic chemotherapy. For cases who underwent limb salvage surgery (n= 36), R0 resection was achieved in 29 cases (72.5%) and R1 in 7 cases (17.5%). Only one case in this group needed reconstructive surgical procedure (arterial graft).

In Group II, 20 cases showed response and 17 patients showed stable diseases. These 37 cases underwent surgical excision of their primary tumors. Local excision (wide or marginal) was done in 20 cases (43%), compartmental excision in 15 cases (33%), and debulking in 2 case (4%). R0 resection could be performed in 18 cases (39%), R1 resection was achieved in 17 cases (37%), and R2 in the 2 debulking cases (4%). Seven cases in Group II needed reconstructive procedures (3 arterial grafts, 1 nerve graft, and 3 pedicled fascio-cutaneous flaps). Nine cases showed progressive disease on systemic neoadjuvant systemic chemotherapy. Amputation was performed in 6 cases, and the other 3 cases developed systemic metastasis. The surgical outcome of the study groups are summarized in Table **2**.

Table 2. Surgical Outcome of the Study Groups

	Group I ILI (n=40)	Group II Systemic CT (n= 46)	P Value
Surgery performed:			
local excision	30 (78.5%)	20 (43%)	0.025
Compartmental excision	6 (15%)	15 (33%)	
Debulking	0	2 (4%)	
Amputation	3 (7.5%)	6 (13%)	
None	1 (2.5%)	3 (7%)	
Resection status in limb sparing surgeries:			
R0	29 (72.5%)	18 (39%)	0.037
R1	7 (17.5%)	17 (37%)	
R2	0 (0%)	2 (4%)	
Reconstruction			
Yes	1 (2.5%)	7 (15%)	0.014
No	39 (97.5%%)	39 (85%)	

Extensive histopathological examination for response after surgery was performed in all specimens. Histologic response was significantly better (P=0.002) in ILI cases (32 cases, 80 %), than in Group II cases (14 cases, 30%).

In group I, 34 cases completed adjuvant chemotherapy, and 6 cases didn't receive any postoperative treatment. In Group II, 42 cases completed adjuvant treatment.

Treatment Related Toxicity

During neoadjuvant and adjuvant treatment, nonhaematological toxicity was usually mild (WHO grade 1); severe side effects were not seen in our study population. The most frequent side effects were alopecia, which was observed for all patients, and nausea, which was seen in 36% of patients. Hematological toxicity mainly consisted of leucopenia and lesser extent thrombocytiopenia. In Group II cases, 44 patients (96%) experienced leucopenia, commonly WHO grade 3 (n= 26, 57%), and grade 4 (n= 10, 22%). The rate of systemic complications was significantly lower in Group I cases (P=0.002) where only 12 cases (30%) developed leucopenia mainly WHO grade 2.

Local morbidity to ILI developed in 12 patients (30%). These were graded using the scale proposed by Wieberdink *et al.,* [8]. Eight cases experienced grade 2 complications (slight edema and/or erythema) and four cases experienced grade 3 complications with only one case having slight motility impairment. No long term systemic or local toxicity was encountered in the two groups.

Relapse and Survival

After a median follow up period of 76 months (range: 13-114 months), ILI cases showed 35% local recurrence rate with a median time of 29 months (range: 11- 98). This result was significantly better (P=0.02) than Group II cases that showed a local recurrence rate of 67% with a median time of 13 months (range 9- 102). (Fig. **2**)

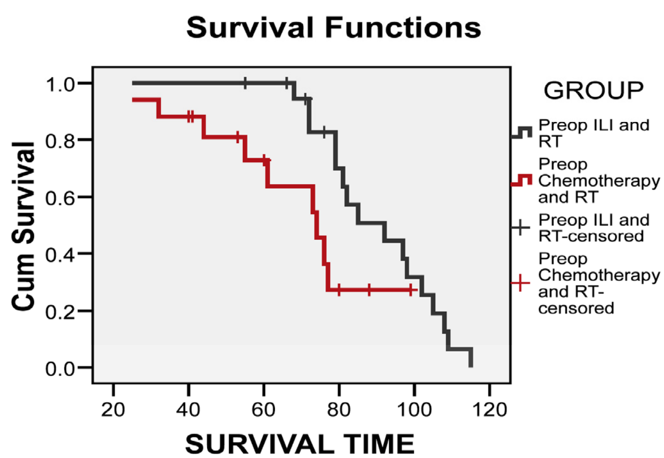

Fig. (2). Kaplan Meir estimate of disease free survival in the studied groups.

Univariate analysis of DFS in the whole cohort of patients revealed significantly better survival with cases treated surgically by wide local excision (P= 0.032), and non metastatic cases (P= 0>002). In each group there was no significant difference in local recurrence rates according to age, sex, site of the tumor, size, stage, histologic type, grade, type of surgery or margin status. Only in group I, local recurrence rate was significantly affected by the tumor size after ILI (P=0.004)

Distant metastasis occurred in 40% of group I cases (median time 48 months, range: 14- 104), and in 63% in group II (median time 42 months, range: 7- 96). The difference just failed to show statistical significance (P=0.07). Margin status only was shown by logistic regression to be a prognostic factor related to metastasis in the whole population of patients (P=0.002). Metastasis was not influenced by any of the study parameters in each group.

At present, 60% of our ILI patients are alive with a median survival of 105 months (range 22-114). This result was significantly better (P=0.03) than Group II cases {35% alive with a median of 82 months (range: 13- 96)} (Fig. **3**). In the whole population of patients, overall survival was significantly correlated with tumor size after treatment (P=0.001), type of surgery performed (WLE versus compartmental; P= 0.003) (Fig. **4**), margin status (P=0.0059), presence of local recurrence (P=0.0007), and presence of metastasis (P=<0.0001). In group I overall survival was correlated with the tumor size after ILI (P=0.0005), and surgical margin (P=0.04). In group II, OS was correlated only with type of surgery (P=0.04). Using a multivariate analysis with logistic regression, parameters (excluding response to chemotherapy) independently correlated to a poor 5-year survival rate were similar to those previously identified as independent prognostic variables for overall survival in the same series: tumor size after treatment (Relative Risk RR: 2.1), presence of local recurrence (RR: 2.3), distant metastases (RR: 4.5) and type of surgery performed (RR: 2.7).

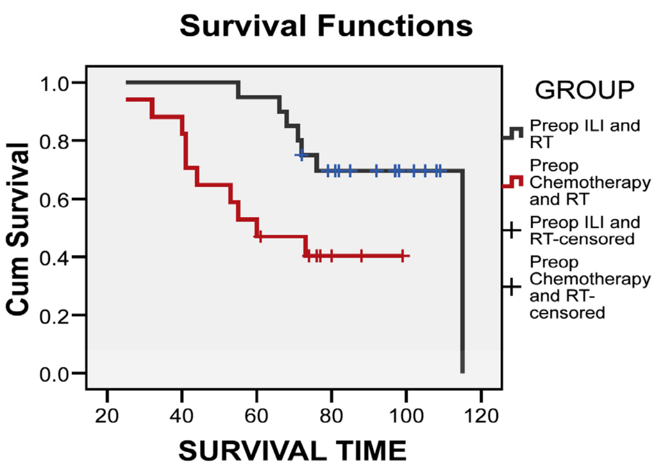

Fig. (3). Kaplan Meir estimate of overall survival in the studied groups.

The disease free and overall survival events in the study groups are summarized in Table **3**.

DISCUSSION

Regional chemotherapy is an attractive treatment option for patients with advanced extremity sarcoma. It has been traditionally carried out using a procedure called isolated limb perfusion (ILP), first developed in New Orleans in the mid-1950s [9]. The technique was based on the proposal that vascular isolation and perfusion of the extremity with chemotherapy would allow regional drug concentrations several orders of magnitude higher than could be attained with systemic administration. ILP is technically complex, however, and associated with significant morbidity and cost. Vascular isolation of the extremity for ILP requires surgical exposure and open cannulation of the artery and vein to the extremity. The extremity is then placed on bypass, requiring the presence of a perfusion team and a cardiopulmonary bypass machine in addition to surgical and anesthesia staff. ILI was developed at the Sydney Melanoma Unit (SMU) by Thompson and colleagues [6] as a simple alternative to ILP. Percutaneously placed catheters replace open surgical cannulation and the chemotherapy is recirculated manually so that no pump oxygenator is needed. Operating room time is approximately 1 h, compared with the 4 or 5 h needed to perform ILP. Most importantly, Thompson and colleagues reported that ILI has an efficacy similar to ILP. They reported significant clinical responses in 135 patients treated with ILI, with 41% CR and 44% PR [10].

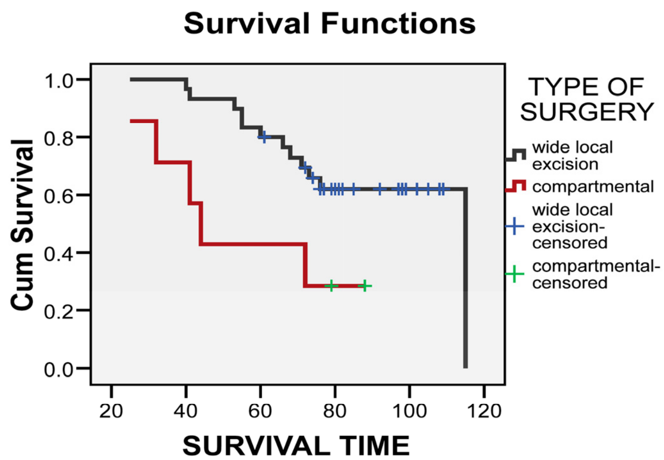

Fig. (4). Correlation between the type of surgery and overall survival in the whole patients' population.

Table 3. Disease Free and Overall Survival Events in the Study Groups

	Group I ILI (n=40)	Group II Systemic CT (n= 46)	P Value
Local recurrence			
Number (%)	14 (35%)	31 (67%)	0.02
Treatment			
Re-excision	6	6	
CRT	4	2	
Metastasis			
Number (%)	16 (40%)	29 (63%)	0.07
Site			
Lung	10	17	
Skeletal	4	7	
Brain	2	5	
Overall survival			
Alive	24 (60%)	16 (35%)	0.03
Dead	16 (40%)	30(65%)	
Median survival (m)	105	82	

The authors report their experience with ILI in a cohort of 40 ASTS patients and showed that they can effectively be treated when a combination of pre-operative ILI and radiotherapy is administered. All patients underwent surgical resection 3-7 weeks after the pre-operative treatment [7]. Survival rates were not mentioned in this study because we were convinced that the follow up period was too short to draw conclusions. After a median follow up of 76 months (range: 13-114 months), local recurrence occurred in 35% of cases with a median time of 29 months (range 11-98 months). Distant metastasis occurred in 40% of patients with a median time of 52 months. At present, 60% of ILI cases are still alive (Fig. **5**) with a median survival of 105 months (range: 22-114 months). In a Sidney Melanoma Unit based study, the effect of ILI on STS was analyzed in 21 patients. Fourteen (67%) patients underwent ILI as neo-adjuvant therapy prior to surgery and seven patients underwent ILI to treat inoperable recurrences or for palliation. 57% of the patients had a CR and limb salvage was achieved in 76%. Local recurrence rate was 42% with a median recurrence free survival of 25 months. The overall disease specific survival was 62%. A lower stage of disease was a significantly associated with longer survival (P=0.008) [11].

A group from Switzerland reported their experience with ILP with TNF and melphalan for non resectable STS. After a mean follow up period of 38.9 months (4-159), 44% of their patients survived more than 5 years. Local recurrence occurred in 37% of cases and they explained this high rate on one hand by a longer follow up time (more than 3 years) allowing the recurrence registration and on the other hand by a higher proportion of high grade and advanced stage sarcomas. Systemic metastasis occurred in 68% of cases [12]. In 2003, Noorda *et al.,* reported 48% 5- years disease free survival, but with 20% grade I and 41% stage I and II tumors [13]. Other series did not mention 5- years survival rates because of a shorter follow up.

In order to document a survival advantage of ILI, we compared our results with a comparable group of ASTS cases that was treated with neoadjuvant systemic chemotherapy.

In the literature, conflicting data have been presented concerning the role of NACT in treatment of high risk extremity sarcomas. Merice *et al.,* [14], reported that only 12% of patients responded to chemotherapy enough to facilitate or simplify their tumor resection. Additionally 9% of patients required a larger surgery because of tumor progression despite of ongoing chemotherapy treatment. Menendez *et al.,* [15], in a retrospective review, determined that there was no statistical significance in recurrence free survival or overall survival in a group of 82 patients who received three to four cycles of neoadjuvant doxorubicin, ifosfamide and cisplatin. In contrast, Eilber *et al*., [16] suggested that although the percentage of patients who respond is low, clinical benefit may be seen in a subset of patients. In the small group of patients (14%) that demonstrated a complete response to chemotherapy (95% necrosis), the 10-year local recurrence rate in that group was 11% as compared to 23%, and the 10-year survival rate was 71% as compared to 55%. The current clinical dilemma is that it is impossible to determine which patients will respond to chemotherapy, and unfortunately the percentage of patients that respond to treatment is near equivalent to the number of patients who progress on therapy and require larger resections [17]. In the only randomized clinical trial evaluating the effect of neoadjuvant chemotherapy upon disease-free and overall survival (EORTC 62874), 134 high-risk patients (with tumors of any grade >8 cm, grade II/III tumors <8 cm, or tumors either recurrent or residual from a prior operation) received three cycles of neoadjuvant AI (doxorubicin: 50 mg/m2/cycle as an intravenous bolus; ifosfamide: 5 g/m2/cycle as a 24-hr infusion) or surgery alone. The 5-year disease-free survival rate in the chemotherapy arm (56%) was slightly higher than in the control arm (52%) but was not powered for statistical significance [18]. In the present study, the results of systemic NACT are compatible with the previous negative reports. Overall response to treatment was present in 43% of cases. Although limb salvage surgery could be performed in most cases (35 cases, 74%), NACT did not facilitate a wider resection; R1 resection rate was similar to R0 resection (47%). Moreover the only R2 resection in the whole series of patients was among this group. Local recurrence rate was 67%, distant metastasis occurred in 53% of cases, and 35% of them are still alive with a median survival of 82 months.

Age, sex, tumor size, grade and localization are declared as prognostic factors on overall survival in the literature [19]. Positive margin, age and localization of recurrences are the prognostic factors for local recurrence [20]. According to this study, the statistically significant prognostic factors influencing the overall survival were: size of tumor after neoadjuvant treatment (reflecting tumor response), type of surgery performed (WLE versus compartmental excision), margin status, presence of local recurrence, and presence of metastasis. Age, sex and tumor location were found to have no impact on overall survival. The factors influencing local recurrence were the type of surgery and presence of metastasis. In Group I cases, the only factor that had a significant impact upon both overall survival and disease free survival was the tumor size after ILI reflecting tumor response. This is consistent with the results of ILP in treating melanoma, where CR was a statistically significant positive prognostic indicator after long term follow up which may reflect a more favorable tumor biology [21]. Moncreiff *et al.,* [11] reported that there was a trend for a CR to be associated with improved OS in their series of ASTS cases treated by ILI, but this just fails to reach statistical difference (P=0.07). Meanwhile radiologic tumor response did not affect local recurrence or overall survival. This is consistent with Issels *et al.,* [22] who treated 59 ASTS patients with neoadjuvant 4 EIA (etoposide, ifosfamide, and doxorubicin) cycles combined with regional hyperthermia to be followed by surgery and adjuvant treatment. The authors stated that responding patients appeared to have survival rates that were similar to those patients who did not respond to preoperative systemic chemotherapy. In the whole cohort of these patients complaining locally advanced STS, cases that underwent wide local excision had better local recurrence and OS rates. This may be attributed to the fact that the need for a more aggressive surgery to obtain a NED status reflects a less favorable response to preoperative treatment and more aggressive tumor biology.

Fig. (5). MRI of Pleomorphic Liposarcoma in the posteromedial aspect of left thigh showed a minimal tumor volume response (18%). Post treatment film show increased extent of necrosis (N) and cystic degeneration (C). Below are photos of the same patient at presentation, 10 months, and 7 years after ILI, External irradiation and surgery.

Limitations of this retrospective study include difficulties for collecting data. Twenty four percent of Group II patients were coming from outside the referring population of our University Hospital. The present study is a retrospective review of ASTS cases treated by ILI and NACT in our center. It is very heterogeneous when regarding different histopathological diagnoses, different TNM and different stages together in the same series. However it is homogeneous and different from other series in that there are almost only large size (>5cm) and high stages (IIa-IV). There is a selection bias and the authors acknowledge this. This is not a randomized trial and comparison between groups could never be that perfect although the differences between both groups were statistically insignificant.

CONCLUSION

In 2006, the authors inaugurated ILI as a simple method that provides a novel therapy in order to obtain local control and avoid amputation in cases of limb threatening soft tissue sarcoma. In this study, assessing the long term outcome of ILI in the treatment of advanced-stage STS, a 12-year experience has been analyzed and presented. ILI cases experienced not only better tumor response rates but also significantly better local recurrence and overall survival rates than a comparable group of cases treated by preoperative systemic chemotherapy. Tumor response to ILI (and not systemic NACT) was associated with a better disease free and overall survival.

ACKNOWLEDGEMENT

We are grateful to our colleagues at the surgery department of Mansoura University Cancer Center. This work was supported by internal fund from Mansoura University Oncology Center.

CONFLICT OF INTEREST

None declared.

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Received: November 30, 2011 Revised: December 12, 2011 Accepted: December 13, 2011