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# Differential sensitivity of liposarcoma subtypes to chemotherapy

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**Abstract**

Liposarcoma is one of the most common soft tissue sarcomas and has a number of different subtypes: well-differentiated; dedifferentiated; myxoid/round cell; and pleomorphic. However, the response of these subgroups to chemotherapy is not well documented. In this study, we have conducted a retrospective analysis of a prospectively maintained database of soft tissue sarcoma patients treated at the Royal Marsden Hospital. Eighty-eight liposarcoma patients who received chemotherapy between August 1989 and June 2004 were identified. The response rates to chemotherapy of the different histological subtypes and overall and progression free survival were investigated. Survival according to histological grade was also assessed. A statistically significant higher response rate to first-line chemotherapy was observed in patients with myxoid liposarcoma compared to de- and well-differentiated tumours, 48% (95%CI; 28–69) and 11% (95%CI; 2–29), $P = 0.005$. Similarly, those with myxoid liposarcoma had a significantly higher response rate compared to all other liposarcoma patients, 48% (95%CI; 28–69) and 18% (95%CI; 8–31). Patients with lower grade tumours had better overall survival. This retrospective analysis suggests that myxoid liposarcoma is relatively chemosensitive in comparison to a combination of other liposarcomas, and in particular de- and well-differentiated tumours. Further confirmation of these results should be sought by similar analyses of other databases.


*Keywords:* Liposarcoma; Histological subtype; Chemotherapy; Response rate; Differential sensitivity; Myxoid liposarcoma

## 1. Introduction

Soft tissue sarcomas are a group of mesodermal malignancies that encompass a wide spectrum of different histological entities. One of the most common is liposarcoma, which has a peak incidence between 50 and 65 years of age [1]. Several subtypes exist: well-differentiated, dedifferentiated, myxoid/round cell and pleomorphic. Myxoid and well-differentiated liposarcoma are generally regarded as low-grade malignancies [2]. Myxoid is the most common subtype, accounting for 40–50% of all liposarcomas [1], and tends to metastasise to soft tissue locations such as the retroperitoneum, axilla and chest wall [2–4]. Round cell liposarcoma is considered a poorly differentiated form of myxoid liposarcoma, as round cell and myxoid regions are not infrequently found within the same tumour [5]. Supporting this hypothesis are cytogenetic data demonstrating a consistent, balanced chromosomal translocation, t(12;16)(q13;p11) in both round cell and myxoid variants [2,5,6]. Despite complete gross excision, late local recurrences are common for well-differentiated and dedifferentiated liposarcomas [7,8]. However, the development of dedifferentiation is an ominous feature associated with a greater potential to metastasise [7]. Pleomorphic liposarcoma is the least common variant, accounting for approximately 5% of all liposarcomas [9,10].

Anecdotally, these tumours are chemo- and radio-resistant, although there have been reports of responses in myxoid liposarcoma patients treated with chemotherapy

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[11,3]. The initial treatment modality of choice remains surgical resection. The aim of this study was to ascertain the efficacy of chemotherapy as first-line treatment for metastatic and inoperable disease, with specific attention to the different histological subgroups of liposarcoma.

## 2. Patients and methods

### 2.1. Patients

Full local ethics and research committee approval was obtained prior to commencing the study. A retrospective analysis of a prospectively maintained database of all soft tissue sarcoma patients treated at our institution was performed. Patients with a histological diagnosis of liposarcoma who had also received chemotherapy were identified. Eighty-eight liposarcoma patients received chemotherapy between September 1979 and June 2004. One patient received adjuvant chemotherapy at another institution in 1979, but all subsequent treatment (including further chemotherapy) was administered at the Royal Marsden. All other patients received chemotherapy between August 1989 and June 2004, and data available until 30th November 2004 were used in the analysis. Clinical and demographic data were obtained from the database and survival information, where necessary, was acquired by contacting the general practitioner.

All patients underwent a baseline computed tomography (CT) scan prior to commencing chemotherapy, and subsequent restaging scans were performed after every 2–3 cycles for those not receiving adjuvant treatment. Radiological investigations performed at other institutions were reviewed. Those receiving anthracycline-based treatment had Multi Gated Acquisition (MUGA) scans to assess cardiac function, after every 2 cycles of therapy. In order to monitor renal function, the glomerular filtration rate was performed after every second cycle for patients treated with ifosfamide.

In certain cases, patients were treated within the context of phase I, II and also randomised phase III trials. Toxicity was graded according to the National Cancer Institute Common Toxicity Criteria grading system and recorded at each clinic visit. Following completion of chemotherapy patients were followed up every 3 months, unless otherwise indicated.

Those achieving a complete or partial response were classified as responders and those with a marginal response, stable or progressive disease as non-responders. In most cases, response was evaluated using Response Evaluation Criteria In Solid Tumours (RECIST), but some of the earlier reports used World Health Organisation (WHO) criteria for assessing response.

Histology was reviewed by a specialist soft tissue pathologist. Tumours were graded according to the system developed by the French Federation of Cancer Centres Sarcoma Group [12,13]. This system is based on a score generated by evaluation of three parameters; mitotic rate, tumour differentiation and extent of tumour necrosis. Liposarcomas consisting of more than 20% round cell component were classified as round cell liposarcoma [13]. For tumours that progressed, the histology prior to administration of the first cycle of chemotherapy was documented as the pathological subgroup for that particular line of treatment.

### 2.2. Statistical methods

Lifetables curves were calculated using the Kaplan–Meier method and compared with the logrank test, a test for trend was employed for ordered categories [14]. Analysis of the effect of potential prognostic factors was undertaken using Cox's regression [15]. A test for trend was used for ordered categories or continuous variables otherwise a test for heterogeneity was employed. Tabulated data were analysed using the $\chi^2$ test unless one of the parameters was ordinal, in which case the Mann–Whitney test or Spearman rank correlation was employed. Fisher's exact test was used for $2 \times 2$ tables.

### 2.3. Analysis plan

Our first aim was to compare the response rate to first-line chemotherapy of purely myxoid tumours to the other histological subtypes. The response rate of myxoid liposarcoma was compared to a combination group of de-, well-differentiated and pleomorphic liposarcoma. Further analyses compared the response rate of de-, well-differentiated and pleomorphic liposarcoma separately to myxoid liposarcoma. The second aim was to perform exactly the same analyses, but to include in the myxoid cohort, tumours that had progressed to round cell liposarcoma, and compare the response rates of the different sub-types. Third, we analysed the response rates between those with limb primary sites and patients with all other primary sites. Fourth, we wished to document the response rates and number of patients treated with further lines of chemotherapy. Statistical analyses were not performed for second, third and fourth-line chemotherapy as the numbers of patients treated were deemed too few.

Further aims included: analyses of tumour grade with regard to overall survival and response to first-line chemotherapy (based on the grade of the primary tumour); and comparison of overall and progression-free survival (PFS) from initiation of first-line chemotherapy for the different histological groups.

Adjuvant chemotherapy was not considered as first-line chemotherapy and these patients were only included in the analyses if they subsequently received chemotherapy for recurrent or metastatic disease. Further statistical evaluation was not feasible on patients treated with adjuvant therapy alone, as there were very few cases in this subgroup.

## 3. Results

### 3.1. Patient characteristics

Between August 1989 and June 2004, 88 patients were treated with chemotherapy for liposarcoma. At the time of analysis, 12 (14%) patients remained alive and 68 (77%) had died (apart from one) secondary to liposarcoma. Follow-up information was not available on 8 (9%) people as they returned to their country of origin following their last visit at the Royal Marsden Hospital. The median follow-up was 89 months from diagnosis and 18 months from first-line chemotherapy.

The patient characteristics are illustrated in Table 1, there were 54 (61%) men and 34 (39%) women. The number of patients with each pathological subtype is also displayed in Table 1. In 9 (10%) cases, the histology was not reviewed at the Royal Marsden, and in 1 (1%) of these the histological subtype was not reported. Eight patients with well-differentiated tumours progressed to dedifferentiated liposarcoma and 2 with myxoid tumours progressed to round cell liposarcoma. The retroperitoneum ($n = 38$, 43%) and lower limb ($n = 28$, 32%) were the commonest primary sites. Forty-seven (53%) patients developed local recurrences and 54 (61%) suffered with metastatic disease.

### 3.2. Treatment

Table 2 displays the treatment administered. Adjuvant chemotherapy was given to 12 (14%) patients, 7 of these subsequently received first-line chemotherapy on the development of recurrent or metastatic disease. Eighty-three (94%) were treated with first-line chemotherapy for metastatic disease or local recurrence (in 8 cases administered as neoadjuvant treatment and one as second adjuvant therapy following surgery). Eighty-seven (99%) patients had one surgical procedure, 54 (61%) were treated surgically on 2 occasions and 12 (14%) patients had four or more operations. In 32 (36%) cases, adjuvant radiotherapy was administered and 20 (23%) were treated with palliative radiotherapy.

### 3.3. First-line chemotherapy

Doxorubicin was administered as first-line chemotherapy to 25 (30%), ifosfamide to 14 (17%), doxorubicin in combination with ifosfamide to 28 (34%) and other regimens to 16 (19%) patients.

Table 1
Patient characteristics and pathological data

| Characteristic | Number |
|---|---|
| *Gender* | |
| Male | 54 (61%) |
| Female | 34 (39%) |
| Age mean (range) | 48 (24–73) |
| *Primary tumour site* | |
| Lower limb | 28 (32%) |
| Buttock | 7 (8%) |
| Retroperitoneal/abdominal cavity | 38 (43%) |
| Other site | 15 (17%) |
| *Local recurrence* | |
| Yes | 47 (53%) |
| No | 41 (47%) |
| *Metastases* | |
| Yes | 54 (61%) |
| No | 34 (39%) |
| Myxoid | 27 (31%) |
| Round cell | 13 (15%) |
| Well-differentiated | 16 (18%) |
| Dedifferentiated | 16 (18%) |
| Pleomorphic | 15 (17%) |
| Unspecified liposarcoma | 1 (1%) |

Table 2
Treatment profile of patients

| Treatment | Number of patients (%) |
|---|---|
| *Adjuvant chemotherapy* | |
| Yes | 12 (14%) |
| No | 76 (86%) |
| *Metastatic disease* | |
| First-line chemotherapy | 83 (94%) |
| Second-line | 46 (52%) |
| Third-line | 18 (21%) |
| Fourth-line | 6 (7%) |
| Treated with neoadjuvant chemotherapy as first-line on recurrence/development of metastases | 8 (9%) |
| *Surgery* | |
| One procedure | 87 (99%) |
| Two procedures | 54 (61%) |
| Three procedures | 31 (35%) |
| Four or more | 12 (14%) |
| *Adjuvant radiotherapy* | |
| Yes | 32 (36%) |
| No | 56 (64%) |
| *Palliative radiotherapy* | |
| Yes | 20 (23%) |
| No | 68 (77%) |

Forty-eight percent of patients with myxoid liposarcoma achieved a partial response with first-line chemotherapy, compared to an 18% response rate in a combination group of all other liposarcomas (Table 3). The response rate was statistically significantly higher in patients with myxoid liposarcoma compared to all other liposarcomas, 48% (95%CI; 28–69) and 18% (95%CI; 8–31), $P = 0.012$ (Mann–Whitney). There was a statistically significant higher response rate in the myxoid compared to the well-differentiated subgroup, 48% (95%CI; 28–69) *vs.* 0% (95%CI; 0–23), $P = 0.00259$. Likewise, the response rate in patients with myxoid liposarcoma was statistically significantly higher than the 11% (95%CI; 2–29) response rate in the combination of de- and well-differentiated patients, $P = 0.005$. However, there was no significant difference in the response rate in those with myxoid liposarcoma compared to the pleomorphic group, 48% (95%CI; 28–69) and 33% (95%CI; 10–65), respectively, $P = 0.491$, but the numbers of the latter were small.

The response rate of patients with myxoid liposarcoma in combination with tumours that had progressed to round cell liposarcoma was 38% (95%CI; 23–55) compared with 18% (95%CI; 8–34) in a combination of the other histological subtypes, $P = 0.073$. The 38% response rate of myxoid liposarcoma patients including those that had progressed to round cell liposarcoma was significantly better than the 11% (95%CI; 2–29) response rate achieved by de- and well-differentiated tumours combined, $P = 0.022$. However, there was no statistically significant difference between the 33% (95%CI; 10–65) response rate achieved in pleomorphic tumours and 38% (95%CI; 23–55) in patients with myxoid liposarcoma and those that had progressed to round cell liposarcoma. There was no significant difference in response between the pleomorphic and a combination of the de- and well-differentiated subgroups, 33% (95%CI; 10–65) and 11% (95%CI; 2–29), respectively, $P = 0.185$.

There were too few patients to compare the response between myxoid liposarcoma and those that had progressed to round cell liposarcoma.

Table 3
Response rate (RR) to first-line chemotherapy by pathology + original primary site

| | CR | PR | MR | SD | PD | RR % (95%CI) |
|---|---|---|---|---|---|---|
| *Histology* | | | | | | |
| Myxoid | 0 | 12 | 1 | 4 | 8 | 48 (28–69) |
| Round cell | 0 | 2 | 2 | 5 | 3 | 17 (2–48) |
| Well-differentiated | 0 | 0 | 3 | 7 | 6 | 0 (0–22) |
| Dedifferentiated | 0 | 3 | 0 | 0 | 9 | 25 (5–54) |
| Pleomorphic | 1 | 3 | 2 | 2 | 4 | 33 (10–65) |
| *Primary site* | | | | | | |
| Lower limb | 0 | 10 | 3 | 6 | 9 | 36 (19–56) |
| Upper limb | 1 | 2 | 1 | 0 | 0 | 75 (19–99) |
| Other sites | 0 | 8 | 4 | 11 | 22 | 18 (8–32) |

CR, complete response; PR, partial response; MR, marginal response; SD, stable disease; PD, progressive disease.

Table 4
Response to first-line chemotherapy according to pathology and regimen

| Histology | Chemo | CR | PR | MR | SD | PD | Toxicity and unknown/unspecified response |
|---|---|---|---|---|---|---|---|
| Myxoid | Dox | – | 5 (20%) | – | – | 2 (8%) | – |
| | Ifos | – | – | – | 3 (12%) | 2 (8%) | 1 (Toxicity) |
| | Dox/ifos | – | 7 (28%) | – | 1 (4%) | 3 (12%) | – |
| | Other | – | – | 1 (4%) | – | 1 (4%) | – |
| Round cell | Dox | – | 1 (8%) | 1 (8%) | 2 (15%) | – | – |
| | Ifos | – | – | – | 1 (8%) | 1 (8%) | 1 (Response unknown) |
| | Dox/ifos | – | 1 (8%) | 1 (8%) | 2 (15%) | – | – |
| | Other | – | – | – | – | 2 (15%) | – |
| Well-differentiated | Dox | – | – | – | 3 (20%) | 1 (7%) | – |
| | Ifos | – | – | 1 (7%) | – | 1 (7%) | – |
| | Dox/ifos | – | – | 1 (7%) | 3 (20%) | – | – |
| | Other | – | – | – | 1 (7%) | 4 (27%) | 1 (Second adjuvant chemotherapy treatment) |
| Dedifferentiated | Dox | – | 1 (8%) | – | – | 3 (25%) | 1 (Toxicity) |
| | Ifos | – | – | – | – | 2 (17%) | – |
| | Dox/ifos | – | 2 (17%) | – | – | 2 (17%) | – |
| | Other | – | – | – | – | 2 (17%) | – |
| Pleomorphic | Dox | – | 2 (17%) | 1 (8%) | 1 (8%) | 2 (17%) | – |
| | Ifos | – | – | – | 1 (8%) | – | – |
| | Dox/ifos | 1 (8%) | 1 (8%) | | – | 1 (8%) | 1 (Response unknown) |
| | Other | – | – | 1 (8%) | – | 1 (8%) | – |
| Unspecified | Dox/ifos | – | – | 1 | – | – | – |

Dox, doxorubicin; Ifos, ifosfamide; CR, complete response; PR, partial response; MR, marginal response; SD, stable disease; PD, progressive disease.

In one patient with round cell liposarcoma, treated with ifosfamide, it was not possible to confirm the recorded response to first-line chemotherapy. A further patient with pleomorphic liposarcoma was reported as having a response, but it was not possible to clarify whether this was a partial or marginal response. Table 4 illustrates response to first-line chemotherapy according to histology and chemotherapy regimen.

Comparing response rates between patients with limb and all other primary sites, those with a limb primary had a higher response rate than the others; 75% for upper limb, 36 % for lower limb and 18% for other sites (Table 3).

### 3.4. Second, third and fourth-line chemotherapy

Forty-six (52%) people were treated with second-line chemotherapy. Ten (22%) of these 46 patients had partial response (PR), 7 (15%) had myxoid liposarcoma and 3 (7%) who had progressed to round cell liposarcoma. In addition, there were 4 (8%) who achieved a marginal response (MR), 2 (4%) with round cell liposarcoma and one each with well-differentiated and pleomorphic histology. Nine (20%) patients had stable disease (SD) at the end of treatment, consisting of 4 (8%) with well-differentiated histology, 2 (4%) myxoid liposarcoma, and 1 (2%) each with dedifferentiated, pleomorphic and round cell liposarcoma. Twenty-one (46%) progressed on therapy, comprising of 8 (17%) with myxoid liposarcoma. The others consisted of 5 (11%) with pleomorphic liposarcoma, 1 (2%) with well-differentiated and 2 (4%) each with round cell liposarcoma and 4 (8%) with dedifferentiated and one (2%) with unspecified liposarcoma. One patient did not complete second-line chemotherapy due to toxicity and another died of disease.

Eighteen (21%) patients received third-line chemotherapy. Only 3 (17%) of these 18 patients achieved a PR, 2 (11%) with myxoid liposarcoma and one (6%) who had progressed to round cell liposarcoma. One (6%) patient with myxoid liposarcoma had a MR. One patient each with well-differentiated and dedifferentiated liposarcoma had disease stabilisation. Six (33%) patients with myxoid and 3 (17%) each with round cell and pleomorphic liposarcoma progressed on third-line systemic therapy.

Six (7%) patients were treated with fourth-line chemotherapy, none responded and only one with myxoid liposarcoma had disease stabilisation. Four of the other 5 had myxoid histology and 1 had round cell liposarcoma.

Chemotherapy was generally well tolerated, with only three patients not completing the full course of therapy due to toxicity (two on first-line treatment and one on second-line, respectively). Renal impairment developed in one patient treated with ifosfamide.

### 3.5. Tumour grade

Data on tumour grade were available in 78 (89%) cases. Low-grade tumours had significantly better overall survival from diagnosis compared to intermediate and high-grade tumours, $P = 0.002$. Hazard ratios were low-grade 1.0, intermediate 2.8 (95%CI; 1.4–5.8) and high-grade 3.2 (95%CI; 1.6–6.5). Low-grade tumours also had statistically significant better survival following first-line chemotherapy ($P = 0.031$), hazard ratios being 1 for low-grade, 1.6 (95%CI; 0.8–3.2) for intermediate and 2.4 (95%CI; 1.3–4.7) for high-grade. However, no significant difference in response rate to first-line chemotherapy between high, intermediate and low-grade tumours was observed.

In nine (38%) of 24 patients with low-grade tumours; and 15 (71%) out of 21 patients with intermediate-grade tumours, went on to develop metastatic disease. In 21 (64%) of 33 patients with high-grade tumours also developed distant metastases.

### 3.6. Overall and progression-free survival

Myxoid liposarcoma patients had statistically significant longer overall survival compared to patients with well-differentiated tumours, 119 months (95%CI; 0–326) and 59 months (95%CI; 47–70), respectively, $P = 0.006$. Overall survival is illustrated in Fig. 1. Median survival was 60 months (95%CI 60–76 months). No significant difference in overall survival from first-line chemotherapy was observed between the subgroups.

The median progression-free survival (PFS) was 4 months for myxoid, 16 months for round cell liposarcoma, 11 months for well-differentiated, 2 months for dedifferentiated and 8 months for pleomorphic sarcoma $P = 0.084$ (logrank test) (Table 5 and Fig. 2). The $P$ value for a trend across categories from good to poor prognosis was 0.043.

## 4. Discussion

This retrospective study demonstrates that in liposarcoma patients receiving first-line chemotherapy for palliation of advanced disease, there was a statistically significant higher response rate for patients with myxoid liposarcoma compared to a combination of all other liposarcomas, and in particular to de- and well-differentiated liposarcoma.

Liposarcoma was identified as a favourable prognostic factor for response to chemotherapy in an analysis of 2185 soft tissue sarcoma patients treated with anthracycline-based chemotherapy within 7 clinical trials [16]. The multivariate model for response demonstrated absence of liver lesions, young age, high histopathologic grade and liposarcoma as the only independent

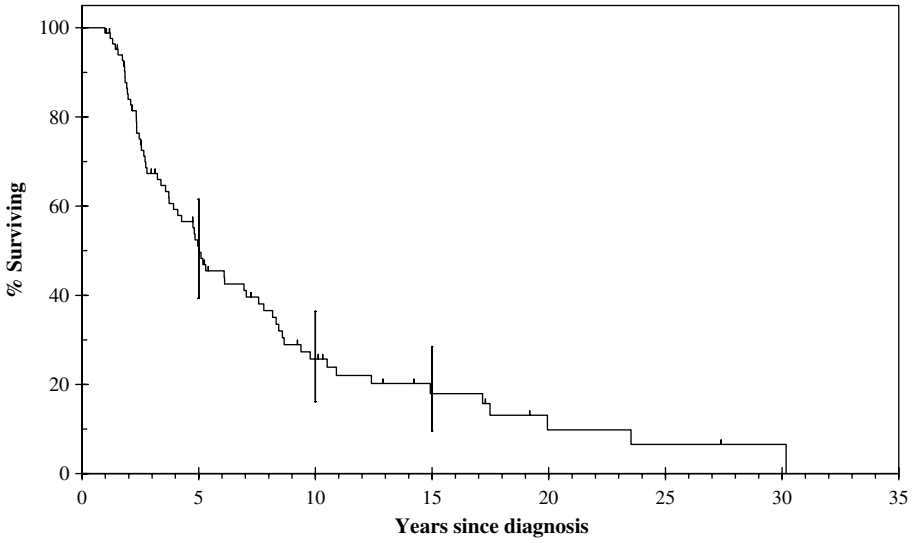


Fig. 1. Overall survival.

Table 5
Progression-free survival (in months)

| Pathology | Median (95%CI) |
|---|---|
| Myxoid | 4 (0–8) |
| Round cell | 16 (7–25) |
| Well-differentiated | 11 (0–22) |
| Dedifferentiated | 2 (0–3) |
| Pleomorphic | 8 (4–12) |
| Overall | 7 (3–11) |

favourable prognostic factors for response. However, multivariate analysis of overall survival revealed good performance status, absence of liver metastases, low histopathologic grade, long disease-free interval and young age as the only independent favourable prognostic factors of survival. Liposarcoma dropped out of the multivariate models when tumour grade was included. The number of liposarcoma patients with grade 1, grade 2 and grade 3 tumours was 39%, 34% and 28%, respectively.

There have been two retrospective studies directly addressing the response of liposarcoma to chemotherapy. The first was a review of 20 myxoid liposarcoma patients treated with doxorubicin and dacarbazine based-chemotherapy. A response rate of 44% (one complete response and seven partial responses) was reported and additionally four patients achieved a minimal response [11]. Thirteen of these had recurrent or metastatic disease and seven had large primary tumours, thus receiving chemotherapy in the neoadjuvant setting. All responding patients, who underwent surgical resection of all macroscopic disease, subsequently received adju-

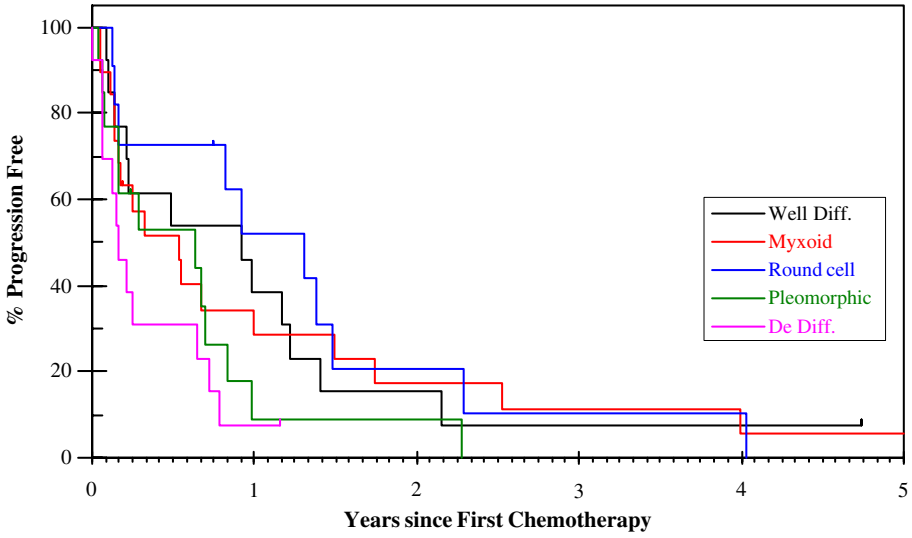


Fig. 2. Progression-free survival of liposarcoma subtypes.

vant chemotherapy. At a median follow-up of 51 months (range 6–199 months) 10 patients were alive with no evidence of disease, 3 were alive with disease and 5 had died.

Recently, Eilber et al. [17] investigated the impact of chemotherapy on survival in patients with high-grade extremity liposarcoma. The authors performed a retrospective analysis of two prospectively maintained databases of patients who had undergone complete surgical resection or amputation of their primary tumour. Patients in this analysis received adjuvant/neoadjuvant doxorubicin or ifosfamide based chemotherapy. Well-differentiated and pure myxoid liposarcoma were excluded from the analysis, as they were considered low-grade lesions. The 5-year disease specific survival of the ifosfamide treated patients was 92% (84–100%) compared with 65% (51–79%) for a contemporary cohort of patients not treated with chemotherapy, (logrank $P = 0.0003$). However, the 5-year disease specific survival for the doxorubicin treated group was 64% (53–74%) compared with 56% (51–79%) for the contemporary cohort who received no chemotherapy.

There have been a number of retrospective studies assessing the clinical and pathological behaviour of the different subtypes of liposarcoma. Smith and colleagues retrospectively evaluated 29 patients with extremity myxoid liposarcoma to assess the amount of round cell component required to adversely affect prognosis [5]. Of 7 patients with a round cell component >5% in their initial tumour, 5 (71%) suffered an adverse outcome. Of the other 22 with <5% round cell component only 7 (32%) suffered an adverse outcome. Thus, those with >5% round cell component had a statistically significant higher incidence of metastasis or death from disease than those with <5% component ($P = 0.05$).

A case series of 58 patients with well-differentiated liposarcoma reported by Lucas et al. [7] demonstrated a high recurrence rate of 53%. Many of these underwent multiple operations over a number of years for local recurrences. Analysis of this series also suggested that dedifferentiation represented tumour progression with the transformation of a locally aggressive tumour into one with metastatic potential. In this series, 37 (64%) patients were alive with no evidence of disease, 7 (12%) were alive with disease and 8 had died of disease (all retroperitoneal or scrotal). Six patients (10%) had died of other causes. Mean follow-up was 9.3 years (range 5 months to 35 years) and of the 10 in this series with dedifferentiation, 5 (50%) were alive with no evidence of disease. Three of these patients had resections and demonstrated no evidence of dedifferentiation in subsequent recurrences. One patient had chemotherapy for metastatic dedifferentiated liposarcoma in this series.

The rarest subtype of liposarcoma is the pleomorphic variant [9], and a series of 63 cases has shown that age over 60, truncal tumour location, deep position, tumour greater than 5 cm in size, vascular invasion and incomplete tumour excision as adverse prognostic factors [18]. After a median follow-up of 38 months for 48 patients (range 7–276 months), 21 (45%) developed a local recurrence. Twenty (42.5%) developed at least one distant metastasis, with the most common sites being lung (12 events) and pleura (4 events). The cumulative 5-year overall survival rate was 57%. Five patients received neoadjuvant chemotherapy and/or radiotherapy, and 31 were treated with adjuvant chemotherapy and/or radiation treatment.

A further series of 24 patients with pleomorphic liposarcoma revealed a 5-year overall survival rate of 40%, with a median survival of 48 months [19]. Univariate analysis demonstrated that patients with tumours located in the upper extremities ($P = 0.021$) and greater than 10 cm ($P = 0.47$) had decreased overall survival.

Five-year local recurrence-free, metastasis-free and overall survival rates of 73%, 45% and 35%, respectively were reported for 18 patients with localised pleomorphic liposarcoma of the extremities [4]. In this series of 120 patients with extremity myxoid and pleomorphic subtypes, 17 were treated with surgery alone, 88 with pre- or post-operative chemotherapy and/or radiation treatment. Twelve were treated with various non-surgical combinations and 3 received no anti-cancer treatment. A multi-modality approach (surgery, radio- and chemotherapy) was the most commonly adopted treatment for those with pleomorphic tumours, in 10 of these 18 patients. Ten developed metastatic disease, with the lungs being the most common site of disease. Three patients developed extrapulmonary metastases. The distant recurrence free survival rate was significantly better for those with myxoid tumours compared to patients with pleomorphic tumours ($P < 0.01$).

A study by Henricks and colleagues of 155 patients with dedifferentiated liposarcoma revealed that 41% of 130 patients with follow-up information had local recurrences, and 17% developed metastatic disease [8]. Interestingly, tumours in accessible soft tissue had significantly better survival than those in the retroperitoneum.

This study supports anecdotal reports of the relative chemosensitivity of myxoid liposarcoma compared to the other liposarcomas. We have demonstrated a statistically significant higher response rate for those patients with myxoid liposarcoma treated with first-line chemotherapy compared to a combination of all other liposarcomas. Patients with myxoid liposarcoma had a significantly better response rate than those with de- and well-differentiated tumours. No significant difference in response rate was observed between myxoid and pleomorphic liposarcoma, although the number of patients with the latter were relatively few. The results are limited by their retrospective nature and the small number of patients, largely as a consequence of the

rarity of the condition. Further analysis of other prospectively maintained databases will be required to verify these results. The chemosensitivity of myxoid liposarcoma would justify prospective trials of alternative chemotherapy approaches such as that that used successfully in leiomyosarcoma [20].

## Conflict of interest statement

The authors declare no conflict of interest.

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