Original Investigation

Results of an internal audit on the survival of patients with uterine sarcoma

Ebner et al. Surgery in uterine sarcoma influences the survival

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Abstract
Objective: In the last 5 years there has been a lot of discussion about the surgical procedure for uterine fibroids and essentially also uterine sarcoma. Still there exist no reliable presurgical diagnostic tool to differentiate between benign fibroids and uterine sarcomas. The aim of this study was to confirm the suspected an association between intraoperative spread of tumor by morcellation and impaired outcome in sarcoma patients.
Material and Methods: After local ethics commission positively reviewed the study protocol the oncological database of our university hospital was retrospectively reviewed for patients with uterine sarcomas over a time period of 13 years (2002-2015). Data was extracted from the medical files and survival information was collected by contacting patient´s general practitioners if last follow-up-status was older than 6 months. For the analysis patients were split into two groups with either intrasurgical morcellation (M+) or no morcellation (M-) regarding information provided by the surgical report.
Results: Data on 57 uterine sarcoma patients was available for further analysis. The median age was 63years with a BMI of 27 kg/m². The sarcoma subtypes were 25 leiomyosarcoma (LMS), 19 carcinosarcoma (KS), 9 endometriod stroma sarcoma (ESS), 3 adenosarcoma (AS) and one case without further differentiation. In the majority, no morcellation was done (44 patients in M- group) and 51 patients received open surgery (3 laparoscopic, 1 vaginal and 2 incomplete surgeries). Median time of follow-up was 31 months. The disease free survival was 50.5 months and the cox regressions analysis showed a hazard ratio of 3.06 (no significant difference between the two subgroups (p=0.079; 95%-KI: 0.9 – 10.6)). The overall survival was found to be 62.2 months and the cox regression analysis showed a hazard ratio of 3.216 with statistical significantdifference between the two subgroups (p=0.013; 95%-KI: 1.3 - 8.1)
Conclusion: Despite the efforts to find a pre-surgical diagnostic tool, the clinical situation remains unsatisfactory. Overall sarcoma prevalence is low during the last 13 years at our university center, but morcellation occurred in a relevant portion of patients (13 out of 57). If a sarcoma is suspected or diagnosed the en-bloc resection of the uterus can prolong the survival. Thus, morcellation of the uterus and not the surgical technique (en-bloc resection) is the prognostic factor and should be avoided in any suspicious case.
Keywords: Sarcoma, uterine, hysterectomy, fibroids, risk factors

Introduction

Uterine sarcomas are a rare malignant entity of the uterus [1,2] and are diagnosed in approx. 0.2-0.5% [2-5] cses of all hysterectomies. The WHO classification differentiates between mesenchymal and mixed (mesenchymal and epithelial) tumors [6]. Pure mesenchymal tumors are further differentiated into leiomyosarcomas (LMS), endometrial stromal sarcomas (ESS) and smooth muscle tumors of uncertain malignant potential (STUMP), while mixed tumors are differentiated into adenosarcomas (AS) and carcinosarcomas (CS). The carcinosarcomas along with Muellerian mixed tumors (MMT), malignant mesodermal mixed tumors and metaplastic carcinoma are considered a subclass of endometrial carcinoma [6]. Generally the prognosis of uterine sarcomas is unfavorable. Whilst FIGO Stage Ia still has a 5 year survival rate of 84.3% this dramatically decreases for stage II (43.6%), III (38.8%) and IV (19.8%) [7]. Clinical symptoms of this heterogenic tumor group might include uterine enlargement, bleeding and pelvic pain and are therefore rather unspecific and also common in many other gynecological diseases (e.g. uterine leiomyomas). Blood parameters (serum-LDH, CEA, CA 125, CA 19-9, and CA 15-3)[3,8], or presurgical imaging (US, MRI, CT) has thus far room for improvement [9,3,10]. Two case series for MRI scans found a positive predictive value of 52% [11] (negative predictive value 100%) and a specifity of 92% [12] to presurgically identify an uterine sarcoma. Even PET-

CT is not capable of differentiating between benign uterine leiomyomas and malign uterine sarcomas [13]. In US elastography case reports on the differential diagnosis of fibroids and sarcoma are being published [14] and report of a 'typical' mosaic pattern in the sarcoma compared to a homogenous pattern in fibroids.
Given the fact that myomas are a common finding in gynecological patients, distinguishing between suspected malignant tumors and benign fibroids has great implications for clinical routine. Due to fertility aspects, hypermenorrhea, urogynecological symptoms etc. surgery in fibroid patients is frequent. Surgical treatment of benign uterine leiomyoma is either focused on the removal of the myoma or the complete uterus. With increasing availability of laparoscopic equipment and surgical training, the number of open abdominal surgery has decreased [15–17] over the last decades in favor of laparoscopic assisted vaginal hysterectomy (LAVH), total laparoscopic hysterectomy (TLH), or laparoscopic supracervical hysterectomy (LASH) are offered to women who do not wish to bear children. A uterus conserving approach is offered if family planning is not complete. Whilst the vaginal approach is limited by patient factors (e.g. BMI, previous vaginal births/surgeries, size of uterus) and surgeons skills, the laparoscopic pathway is possible even with larger uterus size [18,19], increased BMI [20], offers rapid recovery, less blood loss [21] and a low complication rate [22]. Laparoscopic surgery can be considered the standard surgical treatment of uterine leiomyomas, with large specimens often requiring morcellation to be removed through trocar insertion sites. This will increase the numbers of uterine sarcomas accidentally being morcellated. During morcellation, small visible and microscopic parts of the tissue may be dispersed within the abdomen. This might lead to peritoneal dissemination of tumor tissue [23]. Based on the increased numbers of laparoscopic surgeries with subsequent morcellations, also the rate of uterine sarcomas accidentally being morcellated will increase. Given the general poor prognosis of uterine sarcomas [24,3,7] and the lack of sufficiently reliable preoperative diagnostic procedures to identify uterine sarcomas, this article tries to answer if accidental morcellation of uterine sarcomas in abdominal, vaginal or laparoscopic surgery has a negative impact on patients in terms of increased recurrence rates and/or decreased survival.

Material and method

Our university cancer center database has continuously collected data for all oncological patients since 2002. This database was searched for patients with uterine sarcoma or carcinosarcoma including patients up to January 2016. Though the documentation into the database is done by well trained and specialised documentaries rare diseases might have been misclassified and not shown in the results. To maximise the results the search was done by diagnosis or surgical procedure. The result list was then checked for matching the inclusion criteria. All patient files with a hysterectomy as surgical treatment at the certified gynaecological oncology center and 18+ years of age were included in this analysis. Retrospectively, the available date was analysed for tumor stage, histological subtype and route of surgery (open/laparoscopic or vaginal). The route of surgery was noted and patients were classified according to the surgical and pathology reports in uterine morcellation (M+) or en-bloc resection (M-). A morcellation in an intraabdominal bag was not performed. The disease free survival (DFS) and overall survival (OAS) were compared between these two groups. Living status and Follow up was provided by the routine annual cancer center follow up. If this data was not available the patient's general practitioner was contacted. Ethics approval (308/2012) was given by the local ethic committee of the university Ulm.
Parameters for the statistical analysis with SPSS software (IBM® SPSS® Statistics Version) were age at histological confirmation of sarcoma (WHO classification), body mass index, ASA-status, date and status of follow up, primary tumor stage (TNM, FIGO classification 2009), resection status (R0 or R1/2), receptor status (Oestrogen, Progesterone) and location of recurrence as well as further treatments (radiotherapy, chemotherapy etc.). Due to small sample sizes, no analyses were performed based on the influence of morcellation regarding the different histological subtypes. Descriptive statistical analysis was used to determinate average, median, standard deviation, minimum and maximum, likelihood and percentiles. The OAS/DFS was defined in months starting the date of surgery to the last documented vital status/date of recurrence. The survival was analysed with Kaplan Meier, log rank test and cox regression. A probability (p) <0.05 was considered significant. Further multivariate testing for differences was done with Wilcoxon-Mann-Whitney-Test, univariate testing with the exact Fisher Test and Mann-Whitney-U-test.

Results

The database search identified 59 sarcoma patients treated at the University hospital Ulm – department gynaecology and obstetrics between 2002 and 2015. Two patients had to be excluded as no follow up was available. The average age of the remaining 57 patients was 63 years and the average BMI was 27kg/m2. The histological subtypes were 25 leiomyosarcoma, 19 carcinosarcoma, 9 endometrial stroma sarcoma, 3 high grad sarcoma and 1 sarcoma without further classification. 29 patients were not TNM classified and only clinically staged, 15 patients were pT1, 10 pT2 and 5 pT3 after surgery. Detailed information on the two subgroups is shown in table 1. Hormonreceptors were negative or unknown in the majority of specimen. Table 2 provides further patient and histological details. Noteworthy is that our M+ subgroup had significant larger tumors and primary metastasised patients.
The surgical access was in 51 patients abdominal, 3 times laparoscopic and once vaginal. Another two patients were considered incurable once the surgery had started. Three patients were started laparoscopically and converted to an abdominal route due to very large fibromas with adhesions (2x) and once to repair a bladder lesion. 28 patients were considered R0, 5 patients had a microscopic tumor rest and 24 patients could not be classified. Further details regarding the surgery are provided in table 3. Further treatments included radiotherapy (11 patients), chemotherapy (25 patients) and no further therapy at all (10 patients). Cause of death was known in 10 patients (2 due to the sarcoma, 8 other

causes) with further 15 patients deceased. The remaining 32 patients had a documented live status which was used for further analysis. Disease recurrence was found in 20 patients. Recurrence occurred mostly as distant or a combination of distant and local metastases, followed by local and lymph node metastases. 44 surgeries removed the uterus without morcellation (M-) and 13 cases were considered morcellated (M+).
The DFS overall patients was 50.5 months and the cox regressions analysis showed a hazard ratio of 3.06 without any significant difference between the two subgroups (12.3 months (M+) vs 54.9 months (M-); p=0.079; 95%-KI: 0.9 – 10.6). The OAS was found to be 62.2 months. Thereby the cox regression analysis showed a hazard ratio of 3.216 and was statistically significantly different between the two subgroups (19.2 months (M+) vs 69.2 months (M-); p=0.013; 95%-KI: 1.3 - 8.1). DFS and OAS are visualised in figure 1&2.

Discussion

The laparoscopic resection of uterine fibroids has been under scrutiny in recent years due to the missing preoperative diagnostic tool for uterine sarcoma. Reliable data on sarcoma incidence, diagnosis, prognosis and further treatment is still rare. Prognosis for uterine sarcoma patients is generally poor with a 5year survival of 50% [25-30] (M+ vs M-: median OAS 10.8 vs. 39,6months[31] or 5y OAS 46% vs 73%[26]). Differences exist among subtypes and type of resection for the survival. Endometrial stroma sarcoma and complete resection seem to be beneficial for the patient [32–34]. Even in our small retrospective analysis the results are in line with existing data on the recurrence pattern [35] with mostly distant recurrences.

Further data was published showing a decrease in survival if the sarcoma were morcellated [31,36-39]. The morcellation resulted in a tissue spill on various intraabdominal organs (ovaries, liver, omentum …) and it did not matter which surgical technique (vaginal, laparoscopic or open) was used [40]. Seidmann et al. published a reduced OAS in patients with morcellation and leiomyosarcoma but could not show this in the other subtypes of uterine sarcoma [41]. Similar results were published by other authors [42,26,43]. Our data contributes to these conflicting results as the DFS is not significantly different between the two surgical study groups – though there is a statistical trend indicating a disadvantage for the morcellated group. But the M+ subgroup had significant larger tumors and primary metastasised patients. However our analysis shows a significant difference for the OAS. Contrary the data published by Morice [38]. In their analysis 123 patients were closely followed up and no significant difference for the 6 month recurrence rate was found between the two treatment group (M- vs M+). But the database includes various histological subtypes (i.e. leiomyosarcoma, carcinosarcoma and endometrial stroma sarcoma with low and high grade cases). The cases series by Liu indicates due to the peritoneal metastasis in both surgical groups that there might be a very aggressive biological subgroup – yet to be identified [44].

Perri et al. [43] and George et al [31] found a 3-fold increased risk for metastasis if the tumor was morcellated (HR: 2.85; 95%-KI: 1.05 – 7.5 [43]; HR: 2.95; 95%-KI: 1.5 – 6.0 [31]) and a significant shorter disease free survival (p=0.03 respective p=0.002). Similar the results from Park et al [45] who showed a significant reduced overall and disease free survival in 56 stage I&II leiomyosarcoma patients. Here patients with a morcellation had more peritoneal and vaginal cuff metastasis. Most current published data indicates that patient with uterine leiomyosarcoma may have a shorter DFS and OAS. Due to the low numbers in our analysis the DFS difference of 42.6 months was not statistically different but still should be considered clinically relevant.

In early stage low grade endometrial stroma sarcoma Park et al [42] found a significant shorter disease free survival but a longer – non significant – 5 year overall survival for the morcellated subgroup. The authors argue with the more aggressive systemic therapy in case of morcellation and the short follow up.
However, incidence of accidental morcellation of uterine sarcoma seems to be low. In a large German monocentric retrospective study, the overall rate of uterine malignancies was 0.13 %
In more than 10.000 patients with morcellated uteri during laparoscopic assisted supracervical hysterectomy. Thereby, the majority of malignancies were endometrial cancer (0.07 %) with only 0.06 % sarcomas (4 endometrial stromal sarcomas (0.04 %) and 2 leiomyosarcomas (0.02 %)) [46].As with any rare diseases our retrospective database misses information on tumor classifications, follow up and most of all the conclusions drawn from the analysis suffer from the small number of cases. Unfortunately this also applies to most of the current literature regarding uterine sarcoma [47]. Only few authors clearly differ between the subtypes of sarcoma [31,42,43]. Other studies – like ours – include various subtypes in the analysis.
Some tumor variables cannot be provided by the pathologist. For example the sarcoma size cannot be measured on a morcellated uterus. Thereby, this factor is not only a limiting point in study analysis. It is also important for appropriate assessment of tumor stage and further required adjuvant therapy and can impact the ability to identify pathological features for determination of tumor entity. In summary, a retrospective database will always miss certain information on the tumor which might be vital for further analysis. But a prospective randomised trial with a known uterine sarcoma and deliberate morcellation on basis of the current data is unethical. So the only possible and ethical way to increase knowledge on these rare diseases are retrospective studies.
Although this is a small, retrospective analysis, it includes all patients with uterine sarcoma over a time period of 13 years at a university hospital and investigates the impact of intraoperativ morcellation. OAS significantly differed between the intraoperativ morcellation (M+) and whole tumor resection (M-) subgroups. DFS showed also a clear – clinically relevant – trend to impaired survival within the M+ group. But did not show a statistically significant

difference. This is a common statistical issue with such small patient and follow up numbers. Relapse mostly occurred as distant relapse. In contrast to some requests for abandoning morcellation in gynaecological surgery, we recommend careful preoperative review and informed consent of intraoperative morcellation. This approach is in line with the society of gynecologic oncology and the German Society for Gynecology and Obstetrics (DGGG) – as purposeful use of morcellation allows less invasive surgery with reduced patients' morbidity[48-50].
Although the overall numbers of patients treated with uterine sarcomas at our certified oncological university center is low, rate of morcellated sarcomas (13 out of 57) underlies the clinical relevance of that topic. For addressing the clinical demand for improved identification strategies, we are currently performing a prospective liquid biopsy study on all patients with suspected LMS and store the drawn blood sample for further investigation in our biobank. Possible target markers include vascular endothelial growth factor (VEGF) and cell free ribonucleic acid (fRNA) with evaluating their use as prognostic and predictive factors. Further studies are also investigating possible mutations in sarcomas for personalized systemic treatment options [51].
Our data supports resection of the whole uterus if any malignancy including sarcoma is suspected or known. For patients and clinicians, a reliable presurgical test to eliminate the risk of uterine sarcoma is urgently needed.

Conflict of interest
The authors declare that they have no conflict of interest.

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Table 1: patient and tumor details in the subgroups.

			group M-	group M+	total
Tumor size pT	pT1	number, n	12	3	15
		% within the subgroup	52,2%	60,0%	53,6%
	pT2	number, n	10	0	10
		% within the subgroup	43,5%	0,0%	35,7
	pT3	number, n	1	2	3
		% within the subgroup	4,3%	40,0%	10,7%
total		number, n	23	5	28
p=0,029		% within the subgroup	100,0%	100,0%	100,0%
lymphnodes pN	pN0	number, n	12	0	12
		% within the subgroup	80,0%	0,0%	75,0%
	pN1	number, n	3	1	4
		% within the subgroup	20,0%	100,0%	25,0%
total		number, n	15	1	16
p=0,25		% within the subgroup	100,0%	100,0%	100,0%
metastasis M	M0	number, n	17	3	20
		% within the subgroup	89,5%	37,5%	74,1%
	M1	number, n	2	5	7
		% within the subgroup	10,5%	62,5%	25,9%
total		number, n	19	8	27
p=0,011		% within the subgroup	100,0%	100,0%	100,0%
Age		Median in years	65	56	63
P=0,045					
Histology	LMS	number, n	18	7	25
		% within the subgroup	40,9%	53,8%	43,9%
	ESS	number, n	6	3	9
		% within the subgroup	13,6%	23,1%	15,8%
	KS	number, n	17	2	19
		% within the subgroup	38,6%	15,4%	33,3%
	AS	number, n	2	1	3
		% within the subgroup	4,5%	7,7%	5,3%
	other	number, n	1		1
		% within the subgroup	2,3%		1,8%
	Total	number, n	44	13	57
P=0,548		% within the subgroup	100%	100%	100%

abbreviations: TNM= TNM classification with T = tumor size, N = lymph nodes and M = metastasis; subgroup morcellated (M+) and non-morcellated (M-); p-values with exact Fisher test.

Table 2: Patient and sarcoma details

Variable		all sarcomas n=57	LMS n=25	KS n=19	ESS n=9	AS n=3	Other sarkomas n=1
Age, years	Average	61	56	68	63	60	61
	Median	63	51	67	60	67	61
BMI, kg/m²	Average	27	24	28	27	29	29
	Missing	5	3	1	1	0	0
Tumor size pT, n (%)	pT1	15 (26,3%)	4 (16,0%)	8 (42,1%)	2 (22,2%)	1 (33,3%)	0 (0%)
	pT2	10 (17,5%)	1 (4,0%)	9 (47,4%)	0 (0%)	0 (0%)	0 (0%)
	pT3	3 (5,3%)	1 (4,0%)	2 (10,5%)	0 (0%)	0 (0%)	0 (0%)
	Missing	29 (50,9%)	19 (76,0%)	0 (0%)	7 (77,8%)	2 (66,7%)	1 (100,0%)
Lymph node metastasis pN, n (%)	pN0	12 (21,2%)	4 (16,0%)	6 (31,6%)	2 (22,2%)	0 (0%)	0 (0%)
	pN1	4 (7,0%)	0 (0%)	4 (21,1%)	0 (0%)	0 (0%)	0 (0%)
	Missing	41 (71,9%)	21 (84,0%)	9 (47,4%)	7 (77,8%)	3 (100,0%)	1 (100,0%)
Grading G, n (%)	G1	7 (12,3%)	3 (12,0%)	0 (0%)	2 (22,2%)	2 (66,7%)	0 (0%)
	G2	13 (22,8%)	12 (48,0%)	0 (0%)	1 (11,1%)	0 (0%)	0 (0%)
	G3	24 (42,1%)	4 (16,0%)	16 (84,2%)	4 (44,4%)	0 (0%)	0 (0%)
	G4	4 (7,0%)	0 (0%)	2 (10,5%)	1 (11,1%)	0 (0%)	1 (100,0%)
	Missing	9 (15,8%)	6 (24,0%)	1 (5,3%)	1 (11,1%)	1 (33,3%)	0 (0%)
Remaining tumor R, n (%)	R0	28 (49,1%)	8 (32,0%)	13 (68,4%)	4 (44,4%)	2 (66,7%)	1 (100,0%)
	R1	5 (8,8%)	2 (8,0%)	1 (5,3%)	2 (22,2%)	0 (0%)	0 (0%)
	Missing	24 (42,1%)	15 (60,0%)	5 (26,3%)	3 (33,3%)	1 (33,3%)	0 (0%)
Estrogen-rezeptor, n (%)	Negative	19 (33,3%)	3 (12,0%)	9 (47,4%)	5 (55,6%)	2 (66,7%)	0 (0%)
	Positive	9 (15,8%)	3 (12,0%)	2 (10,5%)	2 (22,2%)	1 (33,3%)	1 (100,0%)
	Missing	29 (50,9%)	19 (76,0%)	8 (42,1%)	2 (22,2%)	0 (0%)	0 (0%)
Progesteron-	Negative	17 (29,8%)	3 (12,0%)	8 (42,1%)	5 (55,6%)	0 (0%)	1 (100,0%)

rezeptor, n (%)	**Positive**	**11 (19,3%)**	**3 (12,0%)**	**3 (15,8%)**	**2 (22,2%)**	**3 (100,0%)**	**0 (0%)**
	Missing	**29 (50,9)**	**19 (76,0%)**	**8 (42,1%)**	**2 (22,2%)**	**0 (0%)**	**0 (0%)**

Time interval 2002-2015, database comprehensive cancer center University Ulm

Abbreviations: LMS=Leiomyosarcoma; KS=Karzinosarcoma; ESS=endometrioid Stromasarcoma; AS=Adenosarcoma; other sarcoma.=Sarcoma without further classification/details; pT/pN=pathological classification of the tumor size or lymph node status; M-Status=clinical/diagnostic proven metastasis.

Table 3: surgical management, adjuvant therapy and outcome of patients with uterine sarcoma

Variable		all sarcomas n=57	LMS n=25	KS n=19	ESS n=9	AS n=3	Other sarkomas n=1
Hysterectomie, n (%)	Abdomi-nal	51 (89,5%)	21 (84,0%)	19 (100,0%)	8 (88,9%)	2 (66,7%)	1 (100,0%)
	Laparo-skopic	3 (5,3%)	2 (8,0%)	0 (0%)	0 (0%)	1 (33,3%)	0 (0%)
	Vaginal	1 (1,8%)	1 (4,0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Abortion of the surgery	2 (3,5%)	1 (4,0%)	0 (0%)	1 (11,1%)	0 (0%)	0 (0%)
ASA-Score, n (%)	I	5 (8,8%)	4 (16,0%)	0 (0%)	1 (11,1%)	0 (0%)	0 (0%)
	II	21 (36,8%)	11 (44,0%)	4 (21,1%)	5 (55,6%)	1 (33,3%)	0 (0%)
	III	25 (43,9%)	7 (28,0%)	13 (68,4%)	2 (22,2%)	2 (66,7%)	1 (100,0%)
	Missing	6 (10,5%)	3 (12,0%)	2 (10,5%)	1 (11,1%)	0 (0%)	0 (0%)
radiotherapy postoperativ, n (%)	No	10 (17,5%)	4 (16,0%)	3 (15,8%)	3 (33,3%)	0 (0%)	0 (0%)
	Yes	11 (19,3%)	5 (20,0%)	6 (31,6%)	0 (0%)	0 (0%)	0 (0%)
	Missing	36 (63,2%)	16 (64,0%)	10 (52,6%)	6 (66,7%)	3 (100,0%)	1 (100,0%)
chemotherapy postoperativ, n (%)	No	11 (19,3%)	4 (16,0%)	5 (26,3%)	2 (22,2%)	0 (0%)	0 (0%)
	Yes	25 (43,9%)	14 (56,0%)	9 (47,4%)	0 (0%)	1 (33,3%)	1 (100,0%)
	Missing	21 (36,8%)	7 (28,0%)	5 (26,3%)	7 (77,8%)	2 (66,7%)	0 (0%)
recurrance, n (%)	No	14 (24,6%)	3 (12,0%)	6 (31,6%)	4 (44,4%)	1 (33,3%)	0 (0%)
	Yes	20 (35,1%)	11 (44,0%)	7 (36,8%)	0 (0%)	1 (33,3%)	1 (100,0%)
	Missing	23 (40,4%)	11 (44,0%)	6 (31,6%)	5 (55,6%)	1 (33,3%)	0 (0%)
death, n (%)	No	31 (54,4%)	12 (48,0%)	10 (52,6%)	5 (55,6%)	3 (100,0%)	1 (100,0%)
	Yes	25 (43,9%)	12 (48,0%)	9 (47,4%)	4 (44,4%)	0 (0%)	0 (0%)
	Missing	1 (1,8%)	1 (4,0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Time interval 2002-2015, database comprehensive cancer center University Ulm
Abbreviations: LMS=Leiomyosarcoma; KS=Karzinosarcoma; ESS=endometrioid Stromasarcoma; AS=Adenosarcoma; other sarcoma.=Sarcoma without further classification/details;

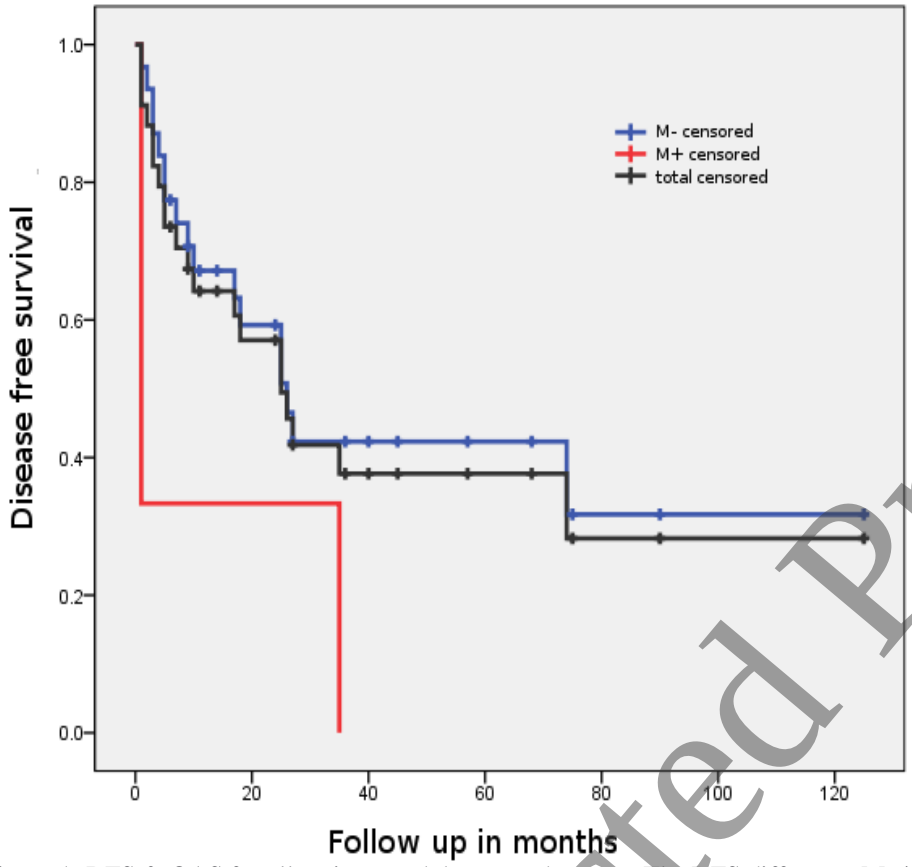

Figure 1: DFS & OAS for all patients and the two subgroups. The DFS difference M+/- is statistically not significant but