

Prognostic value of initial surgical procedure for patients with uterine sarcoma: analysis of 123 patients

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Summary

Background: The aim of this series was to study the clinical impact of initial surgical management, particularly of uterine morcellation, on patients treated for uterine sarcoma (US).

Patients and methods: Clinical data of 157 patients treated for US in our institution were analyzed. Data concerning this initial management was available in 123 patients. We consider as "uterine morcellation" the following procedures: hysterectomy (vaginal or laparoscopic) with uterine "morcellation" described in the surgical report, myomectomy, operative hysteroscopy or simple biopsy of the tumor. The clinical outcome considered as related to the initial surgical procedure was the rate of pelvic recurrence at three months.

Results: Of the 123 patients for whom data concerning initial surgical management was available, uterine morcellation was performed in 34 (28%). One-hundred and sixteen patients had a follow-up ≥ 3 months after surgery. Recurrence was observed in 87 patients. Six had a pelvic recurrence within three months following the end of the treatment. The rates of pelvic recurrence at three months according or not to uterine morcellation were 3/31 (8.82%) and 3/79 (3.66%) respectively ($p = 0.25$). The rates of pelvic recurrences at six months were not different in either group (10% versus 10.4%). Overall and disease-free survival were similar in both groups.

Conclusion: In this preliminary study, the rates of pelvic recurrence at three months was increased in patients who underwent uterine morcellation for US but this difference was not statistically significant. A prospective study should be performed in order to clarify the prognostic value of initial surgery in patients treated for US and to recommend an adequate surgical management for patients in whom the diagnosis of uterine sarcoma is suspected before the surgical procedure.

Keys words: Uterine sarcoma; Hysterectomy; Uterine morcellation; Recurrence; Laparotomy.

Introduction

The prognostic value of the quality of surgery in patients with soft-tissue sarcoma (STS) is well established. Several studies have demonstrated that, in multivariate analysis, a complete surgical excision with free margins is one of the strongest prognostic factors of patients treated for STS [1, 2]. Furthermore, in the series of Dalton *et al.*, peritoneal extension of the disease under the form of "sarcomatosis" is related to transabdominal biopsy [3]. Those results suggest that an adequate surgical procedure in patients with STS is a large resection of the tumor, with free margins and without rupture of the tumor during the surgical procedure. Nevertheless, the prognosis of retroperitoneal STS remains poor with a recurrence rate of 80% at ten years [4].

Uterine sarcoma (US) is a rare class accounting for 3% to 5% of uterine tumors. US has been differentiated in three different histologic subgroups: carcinosarcoma (malignant mixed mullerian tumor), leiomyosarcoma and endometrial stromal sarcoma (divided in high and low grade). The prognosis of US is poor excepted for low grade stromal sarcoma [5]. The rarity of this tumor and its poor prognosis (close to STS) explains why most of

patients with US are included in randomized studies concerning STS. A large number of papers have been published about the prognosis and the medical management of US but surprisingly papers focusing on surgical management are rare.

The aim of this series was to study the impact of initial surgical management, particularly uterine morcellation, on the recurrence rate and survival in patients treated for US.

Material and Methods

Clinical data of 157 patients treated for US in our institution between 1977 and 1997 were analyzed from medical records. All cases were reviewed by the same pathologist (C.G.) with a median of five slides (range, 1-38) for each case. The stage of the tumor was determined retrospectively according to the FIGO classification: Stage I: disease confined to the uterine corpus; Stage II: disease confined to the uterine corpus and the cervix; Stage III: disease with pelvic extension and Stage IV: extrapelvic metastases. Clinical and pathologic prognostic factors of this population were reviewed in a previous publication [5].

The analyses of this study have focused on the initial surgical management, not studied in the previous paper. All data concerning surgical management of the US were reviewed. Most of the patients were initially treated outside our institution. All patients underwent a hysterectomy for the treatment of the US.

Treatment modalities depended on the surgeon, whether the diagnosis of US was proved or not before the surgery, and on the period in which the procedure was performed. In most of the cases the diagnosis of US was fortuitously done after the procedure (pathologic analysis of the surgical specimen). In such cases, a second surgical procedure was sometimes performed in order to complete surgical resection when initial myomectomy or operative hysteroscopy was done or to complete the staging of the initial surgical procedure (adnexectomy, omentectomy, lymphadenectomy or bowel resection). "Uterine morcellation" was considered for the following procedures: hysterectomy whatever the approach was (abdominal, vaginal or laparoscopic) with "morcellation" clearly indicated in the surgical report, myomectomy, operative hysteroscopy with resection or simple biopsy of the uterine tumor.

Patient characteristics were analyzed according to uterine morcellation. Recurrence rates and survival were analyzed. The clinical outcome considered as related to the initial surgical procedure, was the rate of pelvic recurrence at three months.

Results

Of the 157 patients, complete data concerning the surgical management was available in 123 patients. The mean age was 54 years (range, 23-77). Histologic subtypes were: leiomyosarcoma (n = 57, 46%), carcinosarcoma (n = 46, 37%) and endometrial stromal sarcoma in 20 patients (low grade n = 13, 10.5% and high grade n = 7, 5.6%). Stage of the disease according to the 1987 FIGO classification was: Stage I: 62 patients (51%); Stage II: 20 patients (17%); Stage III: 18 patients (15%) and Stage IV: 20 patients (17%). In three patients, disease staging was not possible. Among the 20 Stage IV patients the location of metastasis was: chest (n = 6); liver (n = 4); chest + liver (n = 1), and other sites in nine. Before the initial surgery, 38 patients underwent a dilatation and curettage; 21 patients had hysterosalpingography and five had a diagnostic hysteroscopy.

Surgical procedures: Uterine morcellation was performed in 34 patients (28%): during hysterectomy (n = 24), myomectomy (n = 7), operative hysteroscopy (n = 2) and biopsy (n = 1). Several surgical procedures were associated: omentectomy (n = 10); pelvic lymphadenectomy (n = 20); bowel resection (n = 4); resection of intra-abdominal metastases (n = 3); ovarian transposition (n = 1) and appendectomy (n = 4). Twenty-four patients underwent a total hysterectomy without adnexectomy. Postoperative complications were observed in four cases: pelvic abscess (n = 1); drained lymphocyst (n = 1); bladder fistulae (n = 1) and wound dehiscence (n = 1). The rate of uterine morcellation was higher in patients treated for endometrial stromal sarcoma (7/20; 35%) compared to patients treated for leiomyosarcoma (17/57; 30%) or carcinosarcoma (10/46; 22%).

Among the 34 patients who had a uterine morcellation, 20 patients underwent a second surgery (in order to perform a hysterectomy or complete resection of the tumor). Nineteen of these patients underwent the second

procedure in a median time of two months following the initial surgery. In 14 patients no disease progression was noted and in six progression of the tumor was observed.

Recurrence and survival: The prognostic value of histopathologic factors and details about adjuvant therapy were studied in a previous paper [5]. One-hundred and sixteen patients had a follow-up > 3 months after the surgical treatment. Recurrence was observed in 87 patients. The initial sites of recurrence were: local recurrence (n = 53); chest metastases (n = 37); brain metastases (n = 1) and other sites (n = 25). Six patients had a local recurrence in the pelvic cavity within three months following the treatment. The rates of pelvic recurrence at three months were: 3/31 (8.82%) in patients with uterine morcellation versus 3/79 (3.66%) in patients without uterine morcellation (p = 0.25). Eleven recurrences were observed within six months following the surgical procedure. The rates of pelvic recurrences at six months did not differ in either group (3/30 = 10% vs 8/77 = 10.4%). The number and rates of pelvic recurrences at three and six months according to the histologic subtype in patients with or without uterine morcellation are detailed in Table 1. Survival was similar in both groups. Overall and disease-free survival curves are given in Figures 1 and 2.

Table 1. — Number and rates of local recurrences at 3 and 6 months in patients with or without uterine morcellation during initial surgery.

	Recurrences at 3 months		Recurrences at 6 months	
	Morcellation	No morcellation	Morcellation	No morcellation
Leiomyosarcoma	0/17	0/36	1/15 (7%)	5/36 (14%)
Carcinosarcoma	3/10 (30%)	3/36 (8%)	2/8 (25%)	3/32 (9%)
Stromal sarcoma	0/7	1/10 (10%)	0/7	0/9
Total	3/34 (8.8%)	3/79 (3.6%)	3/30 (10%)	8/77 (10.4%)

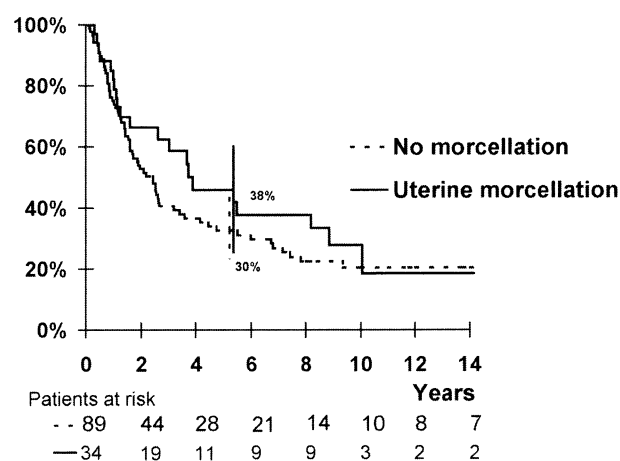


Figure 1. — Overall survival according to the initial surgical procedure.

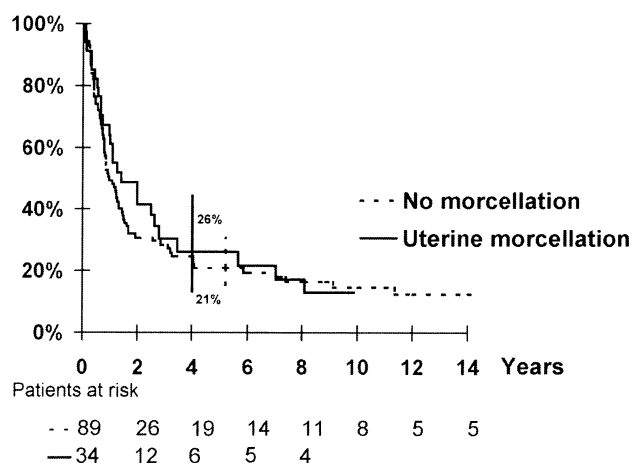


Figure 2. — Event-free survival according to the initial surgical procedure.

Discussion

To our knowledge, this is the first series in the literature studying the prognostic implications of the surgical procedure patients with US. The treatment of reference in these tumors is a total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAHBSO) (with peritoneal cytology) [6-10]. In patients with Stage II disease, some authors recommend radical hysterectomy [6]. A benefit of survival was reported if adnexectomy was performed in order to induce hormonal deprivation in non-menopausal patients [7]. However this point is still controversial [11, 12]. Based on the risk of ovarian metastases from an uterine tumor, salpingo-oophorectomy should be performed at the time of hysterectomy. In patients with carcinosarcoma, the risk of extra-uterine dissemination is important. In the series of Podczaski *et al.*, 39% of patients had extra-uterine spread (Stage III or IV disease) [13]. The most frequent sites of dissemination are lymph nodes (18% to 35%) and peritoneum [14, 15]. Thus, in this subtype of tumor, hysterectomy, omentectomy and pelvic $\pm$ para-aortic lymphadenectomy should be performed. In other histologic subtypes, the risk of nodal metastases is low. In the series of Goff *et al.*, none of the patients with endometrial stromal sarcoma had nodal metastases [16]. In patients with leiomyosarcoma, nodal involvement was associated with intra-peritoneal extension or recurrent disease [16]. Thus, in endometrial stromal sarcoma, routine lymphadenectomy should not be performed. In patients with leiomyosarcoma, if adenomegaly is noticed a lymph node biopsy or dissection may be undertaken.

As in STS, the radicality of surgical resection in US is probably an important, but unstudied, prognostic factor. In the series of Coquard *et al.*, residual disease at the end of surgery is a significant unfavorable prognostic factor with an overall 5-year survival of 62% in patients without residual disease compared to 25% with residual disease ($p = 0.01$) [17]. Thus, surgical resection should be optimal. As in STS, the absence of uterine morcellation probably has a prognostic value. In our experience, we

observed several cases of rapid intra-abdominal dissemination under the form of peritoneal sarcomatosis or vaginal cuff recurrence. These patients were treated for an unrecognized US with uterine morcellation at the time of hysterectomy (abdominal or vaginal) and were sent to our institution a few days or weeks after the initial surgery for adjuvant therapy.

If we want to study the real impact of initial surgery on the prognosis of US, it is very difficult to precise which "end point" should be chosen and evaluated. The prognosis of US, particularly in patients with leiomyosarcoma and carcinosarcoma, is poor and most patients recur within two years following the end of treatment [5]. Due to the natural aggressivity of their tumor several patients had recurrence at six or 12 months. Nearly 50% of relapsing patients had distant metastases without pelvic recurrence [5]. Such distant dissemination is related to the tumor's aggressivity, not to the surgical procedure. Thus the "end point" that we have chosen to study is the rate of local recurrence within the three months following the surgical procedure. Such a rapid recurrence could be perhaps more related to inadequate surgical management than to the natural evolution of the disease.

The rate of local recurrence that we observed in our study was substantially increased in patients who had uterine morcellation (8.8% vs 3.6%) but this difference is not statistically significant low number of patients with local recurrence (6 recurrences at 3 months). Such results are important and seem to suggest that a randomized study should be performed in order evaluate the quality of the initial surgical procedure. However such a study is difficult to perform because US is fortunately a very rare entity. In addition, several questions are still unsolved concerning the indications and results of adjuvant therapy. Meanwhile, we think that the optimal surgical treatment of US should be a "monobloc" hysterectomy and salpingo-oophorectomy without morcellation. In most cases however, the diagnosis was not evoked before the surgery. A small number of patients had suspected US (growing uterine "mass" in postmenopausal women) or proven (uterine curettage for bleeding in patients with carcinosarcoma) before the surgical procedure. In such cases, hysterectomy should be performed by laparotomy in order to avoid the risk of vaginal or peritoneal dissemination. In fact, it should be helpful point is to increase the rate of patients with suspected diagnosis of US before hysterectomy. Magnetic resonance imaging (MRI) could help but the predictive value of this exam is too low to differentiate benign myoma and US. Frozen section analysis of the uterine tumor could be proposed but has a low predictivity (sensitivity of 20% in the series of Schwartz *et al.*) [18]. Recently Kawamura *et al.* recommended performing a transvaginal needle biopsy to differentiate uterine US and leiomyomas [19]. Such invasive management however could also increase the risk of vaginal dissemination of the tumor in patients with US. Perhaps in the near future, biological markers might help detect patients with US and thus help propose the most adequate initial surgical management (hysterectomy with bilateral adnexectomy by laparotomy).

In this preliminary study, the rate of pelvic recurrence at three months is increased in patients undergoing uterine morcellation for US but this difference is not statistically significant. Prospective studies should be performed to clarify the prognostic value of initial surgery in patients treated for US and to recommend adequate surgical management for patients in whom the diagnosis of uterine sarcoma is suspected before the surgical procedure. A multicentric prospective study about adjuvant therapy in uterine sarcoma is now ongoing in France and is being conducted by one of the authors (P.P) in which the characteristics of the initial surgical management will be analyzed. Perhaps after the results of this trial, the real impact of the surgical management will be identified.

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