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Original Article

Clinical outcome affected by tumor morcellation in unexpected early uterine leiomyosarcoma

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ABSTRACT

Objective: To evaluate the influence of morcellation during surgery on clinical outcome in unexpected early uterine leiomyosarcomas (LMSs) using a tumor-size-matched comparison study.
Materials and methods: We retrospectively reviewed the clinicopathological characteristics, prognostic factors, and treatment outcomes of patients with Stage 1 uterine LMS from April 1993 to April 2014 in a university-based tertiary hospital. Patients who received morcellation via abdomen, vagina, or laparoscopy were compared with tumor-size-matched patients who underwent total hysterectomy without morcellation.
Results: In total, 34 consecutive patients were identified, including 14 patients with morcellation and 20 patients without morcellation. There were no significant difference between the two groups of patients in age, parity, mitotic count, lymph node dissection, and adjuvant therapy. Six (42.9%) patients with morcellation were reoperated at 18.5 days after the initial surgery. Tumor recurrence rates at local and distant sites showed no difference between the two groups of patients. Patients with morcellation had a marginally lower disease-free survival (DFS) and overall survival (OS) rates compared with patients without morcellation. In univariate analysis, morcellation was marginally significantly associated with lower DFS [hazard ratio (HR), 2.62; 95% confidence interval, 0.89–7.71; $p = 0.08$] and OS (HR, 2.70; 95% confidence interval, 0.89–8.20; $p = 0.08$). In multivariate analysis, morcellation was associated with lower OS in marginal significance (HR, 2.94; 95% confidence interval, 0.83–10.39; $p = 0.09$).
Conclusion: Tumor morcellation did not increase the abdominal–pelvic recurrence rate, but may be associated with lower DFS and OS in Stage 1 LMS.

Introduction

Uterine leiomyosarcoma (LMS) is a rare disease with an annual incidence of 0.4–0.64/100,000 women [1,2] and accounts for 1–2% of uterine cancer cases [3]. It is a highly aggressive tumor with a high recurrence rate, and complete surgical resection is the only established curative treatment available [4]. At present, none of the available imaging techniques could differentiate LMS from myoma before surgery [5,6]. Consequently, LMSs are usually underdiagnosed, and treated through myomectomy or minimally invasive surgeries.

The safety of intratumor dissection or using a morcellator during hysteroscopic or laparoscopic myomectomies or hysterectomies has been of great concern [7]. Disruption of unexpected LMS during surgery could cause tumor tissue dissemination, resulting in poor patient survival outcome [8]. However, patient survival in early LMS can be influenced by several factors [9]. Size of LMS is one of the major factors that can affect patient outcome [9,10]. It has previously been reported that tumor size outweighed the risk of morcellation in causing poor patient survival in early LMS [11]. In this study, we included all Stage 1 LMS patients who received hysterectomy during the study period. Clinical outcomes were compared between patients who received morcellation and tumor-size-matched patients who were operated without morcellation.

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We thus aimed to eliminate the influence of tumor size and evaluate the influence of morcellation procedures on clinical outcome in unexpected early stage LMS. Previous studies that evaluated the impact of morcellation on survival outcome in early LMS were also presented for comparison.

Materials and methods

Patients

All constitutive patients with Stage 1 uterine LMS operated in our institute between April 1993 and April 2014 were retrospectively included. Demographic and clinical data were collected from medical records and pathological reports including patient age, parity, operative procedure, size of tumor, mitotic counts, timing, and surgical procedures carried out (operation, reoperation, and postoperative adjuvant therapy). Follow-up data including tumor recurrence, anatomical location of tumor recurrence, and patient outcome were recorded. Pathological slides were reviewed by two experienced pathologists. Patients were divided into the following two groups: those who underwent total hysterectomy without morcellation (nonmorcellation group) and those who underwent surgery including abdominal, vaginal, and laparoscopic morcellation (morcellation group). Only cases in the nonmorcellated group that were matched with tumor size in the morcellated group were included.

This study was conducted with approval from the Institutional Review Board at The National Taiwan University College of Medicine (Taipei, Taiwan).

Statistical analysis

Parametric continuous variables were compared using a *t* test for independent samples. Nonparametric dichotomous variables were compared using Chi-square or Fisher exact tests. Survival time was recorded from the date of operation to the date of death from disease or the date of censor. Kaplan–Meier analysis with a log-ranking test was used to estimate survival probabilities and compare survival distributions stratified by operative procedures with or without morcellation. Univariate and multivariate regression analyses based on a Cox proportional hazard model were used to evaluate the relative importance of variables as predictors of survival time. The statistical analysis was carried out using the Statistical Analysis System (SAS) version 8.0 (SAS Institute, Cary, NC, USA). All *p* values less than 0.05 were considered statistically significant.

Results

A total of 43 patients were included in this study. There were 14 patients in the morcellation group and 29 in the nonmorcellation group. After matching the tumor size, there were 20 patients in the nonmorcellation group; thus, the total number of patients evaluated in this study was 34. Demographic and clinical variables of the two groups of patients are presented in Table 1. Tumor sizes between the two size-matched groups of patients were 8.9 cm in the nonmorcellation group and 7.3 cm in the morcellation group. There were no between-group differences in age, parity, lymph node dissection, ovarian preservation, and mitotic count. In the morcellation group, eight patients underwent laparoscopic-assisted vaginal hysterectomy and six patients received myomectomy: two via abdominal, two via laparoscopic, and two via hysteroscopic approaches. All patients who received myomectomy were reoperated at 7–60 days (median 18.5 ± 20.6 days) after the initial surgery. One patient in the nonmorcellation group received lymph node dissection (staging surgery) at 16 days after the initial surgery.

Surgical and adjuvant managements and patient outcomes are presented in Table 2. Four patients in the morcellation group and five patients in the nonmorcellation group completed the staging procedure. None of the patients was upstaged after the reoperation or staging surgery. Postoperative adjuvant therapies were prescribed in 20 (58.8%) patients. There were no differences in adjuvant therapy, such as radiotherapy and chemotherapy, between the two groups. The median and mean follow-up periods were 24 and 33 (range, 12–99) months for the morcellation group, and 34 and 80 (range, 1–248) months for the nonmorcellation group, respectively. Tumor recurred in eight (57.1%) patients in the morcellation group and in six patients (30%) in the nonmorcellation group. The number and types of morcellation procedures carried out, along with the number of patients who experienced tumor recurrence following the procedure are as follows: eight patients received laparoscopic hysterectomies, with recurrence in six; two patients received myomectomies, with recurrence in one; and two patients received hysteroscopic myomectomies, with recurrence in one. Pelvic recurrence occurred in three (21%) patients in the morcellation group and in two patients (10%) in the nonmorcellation group. In the morcellation group, pelvic recurrence occurred in two patients who initially received laparoscopic hysterectomies and in one patient after myomectomy. There was no cancer recurrence in the two patients who initially received laparoscopic myomectomy. No significant differences were found between the two groups of patients in tumor recurrence rates, location of recurrence, and patient outcomes at the time of analysis.

Figs. 1 and 2 show the disease-free survival (DFS) and overall survival (OS) relative to tumor morcellation in patients with Stage 1 LMS. The 3-year OS rate was 39.0% for patients in the morcellation group and 80.1% for patients in the nonmorcellation group. The 5-year OS rate was 19.5% for patients in the morcellation group and 53.4% for patients in the nonmorcellation group. Results of Cox proportional regression analysis indicated that tumor morcellation was found to be associated with poor survival rate, but had only a

Table 1
Demographic and clinical variables ($n = 34$).

	Morcellation group ($n = 14$)	Nonmorcellation group ($n = 20$)	*p*
Age (y)	49.7 ± 6.2 (42–60)	52.7 ± 11.4 (39–80)	0.38
Parity	1.6 ± 1.3 (0–4)	2.0 ± 1.2 (0–4)	0.37
Tumor size (cm)	7.3 ± 2.9 (3–13)	8.9 ± 3.2 (4.5–14)	0.15
Lymph node dissection	5 (35.7)	5 (25)	0.70
Ovarian preservation	6 (42.9)	5 (25)	0.46
Mitotic count			
Low (<10/10 hpf)	2	5	
High (≥10/10 hpf)	7	12	1.0
Reoperation	6 (42.9)	1 (5)	0.01
Period between initial operation and reoperation (d)	18.5 ± 20.6 (7–60)	16	

Values are presented as mean ± standard deviation (range) or number (percentage).
hpf = high-power field.