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Original Research

Survival Outcomes of Minimally Invasive Surgery Versus Open Surgery for Early-Stage Uterine Sarcoma: A Single-Institution Retrospective Study

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Abstract

Background: Uterine sarcoma, frequently diagnosed postoperatively, and often misidentified as benign tumor, is commonly managed through minimally invasive surgery (MIS) and tumor morcellation. This study aims to investigate the survival outcomes of MIS for early-stage uterine sarcoma, and investigate the impact of tumor morcellation on oncologic outcomes. **Methods**: A retrospective study was conducted on 33 patients diagnosed with early-stage uterine sarcoma and were studied from January 2006 to December 2022. Patients were divided into two groups: MIS group and open group. This study assessed the 5-year progression-free survival (PFS) and overall survival (OS) in both groups. Additionally, the study investigated the impact of tumor morcellation on oncology outcomes. **Results**: The 5-year PFS rates in the MIS and open surgery groups were 42% and 65%, respectively ($p = 0.577$); the 5-year OS rates were 77% and 56%, respectively ($p = 0.125$). Sixteen patients had recurrence (48%). The 5-year PFS rates in the morcellated and nonmorcellated groups were 42% and 51%, respectively ($p = 0.732$); the 5-year overall survival rates were 75% and 68%, respectively ($p = 0.584$). **Conclusions**: Although there were not statistically significant differences in survival outcomes between the MIS group and open surgery, intraoperative tumor morcellation may increase peritoneal recurrence risk and negatively affect progression-free survival. Further, a large study is needed to investigate the outcomes of MIS.

Keywords: uterine cancer; morcellation; open surgery; minimally invasive surgery procedures

1. Introduction

Uterine sarcoma is a rare tumor, accounting for 3% to 7% of all uterine malignancies and <1% of all malignancies originating from the female genital organs [1–3]. According to the World Health Organization (WHO), uterine sarcomas are classified into various subtypes because of their rarity and diversity: uterine leiomyosarcoma (LMS)—the most common subtype, endometrial stromal sarcoma (ESS), and undifferentiated uterine sarcoma [4]. Based on WHO classification of soft tissue sarcoma, other extremely rare sarcoma include: adenosarcoma, rhabdomyosarcoma, perivascular epithelioid cell tumor (PEComa), angiosarcoma, neurogenic sarcoma, osteosarcoma, chondrosarcoma, liposarcoma, primitive neuroectodermal tumor, myxofibrosarcoma, alveolar soft-tissue sarcoma and epitheliod sarcoma. Carcinosarcoma [malignant mixed mesodermal tumor or malignant mixed mullerian tumors (MMMTs)] are not classified as uterine sarcoma. This is because its spreading pattern, which resembles a dedifferentiated or metaplastic form of endometrial carcinoma, and it shares similarities in epidemiology, risk factors, and clinical behavior with endometrial carcinoma than uterine sarcoma [5]. However, as its behavior more aggressively than the usual type endometrial carcinoma, it still included in most retrospective studies of uterine sarcoma.

These tumors have a poor prognosis, and preoperative diagnosis is challenging because of the lack of specific symptoms, limited accuracy of preoperative imaging in differentiating between malignant and benign tumors, and risk of false negative results from diagnostic hysteroscopy or dilation and curettage (D&C) [6,7]. Despite these challenges, ultrasound remains the primary diagnostic tool for clinicians assessing preoperative imaging in patients with uterine tumors. Its popularity is attributed to its accessibility, cost-effectiveness, and non-invasiveness. Notably, ultrasound demonstrates moderate diagnostic accuracy in distinguishing between uterine leiomyomas and sarcomas, albeit with lower sensitivity compared to specificity [8]. While magnetic resonance imaging (MRI) has gained popularity for the assessment of uterine malignancies [9], its universal use as a preoperative evaluation method is limited by its high cost. However, an ongoing prospective multicenter study is currently evaluating the potential of transvaginal ultrasound-guided biopsy to differentiate between leiomyoma and sarcoma [10]. This research in the future may pro-

vide a new diagnostic method that could enhance accuracy and broaden the universal applicability of ultrasound. The gold standard treatment for uterine sarcomas is surgical excision with negative margins [11]. Total hysterectomy may be performed; it is preferred for patients with a confirmed malignancy. However, uterine sarcoma is often diagnosed postoperatively, despite initial presumptions of benign disease. These procedures are often performed using the minimally invasive surgery (MIS) technique, which involves tissue fragmentation for extraction. The incorporation of power morcellation into minimally invasive gynecologic surgery in the early 2000s resulted in an increased use of MIS-based procedures for the management of large, bulky leiomyomas.

In 2014, the US Food and Drug Administration (FDA) issued a warning against the use of laparoscopic power morcellation in most female patients undergoing myomectomy and hysterectomy for fibroids [12]. Therefore, most institutions abandoned the use of power morcellation during gynecologic surgery, and most clinicians attempted to modify their surgical approaches [13]. Changes included shifting to open procedures for the removal of bulky tumors during myomectomy or hysterectomy and incorporating the use of laparoscopic bags or scalpel morcellation to facilitate extraction through tissue fragmentation, which attempted to minimize the risk of spreading tumor cells into the peritoneal site [14–17]. However, early-stage uterine sarcomas often present with clinical features similar to those of benign uterine tumors, making them difficult to distinguish pre-operatively [18]. In cases where a pre-operative diagnosis is absent or there is uncertainty regarding uterine sarcoma, patients may undergo laparoscopic surgery with unintended tumor morcellation. Additionally, no consensus has been established regarding the effects of the MIS approach and tumor morcellation on oncologic outcomes in patients with early-stage uterine sarcoma. Therefore, this study aims to evaluate the oncological outcomes of minimally invasive surgery and tumor morcellation in patients with early-stage uterine sarcoma at our institution.

2. Materials and Methods

2.1 Study Design and Participants

This retrospective study was conducted at Taipei Medical University Hospital, Taiwan, and approved by the hospital's ethics committee. Between 2006 and 2022, 9075 patients with suspected benign uterine tumors underwent surgical intervention at our hospital. Among them, we collected data on 110 patients diagnosed with uterine sarcoma who received treatment at our facility, with thirty-three patients presenting with early-stage uterine sarcoma (i.e., stage I or II). Surgery was considered complete if malignancy was identified during primary surgery, and a second surgery should be schedule within 30 days for complete surgery intervention. Only patients who had undergone primary surgery at outside hospital and were referred to our hospital within 3 months after the surgery for further treatment were included in this study. Patients with recurrence or suspected recurrence were excluded from the analysis. We excluded patients with advanced-stage uterine sarcoma (i.e., stage III or IV), those who had undergone incomplete surgery (total hysterectomy) and had no data on margin status, those lacking complete pathologic reports or surgical records, and those were diagnosed carcinosarcoma (Fig. 1).

2.2 Group Allocation

We divided the patients into 2 groups: MIS and open surgery (i.e., laparotomic group). To evaluate the effect of tumor morcellation, we further divided the participants into the morcellated and nonmorcellated groups. The morcellated group comprised patients who had undergone hysterectomy or myomectomy and had records of specimen fragmentation through the vaginal or peritoneal cavity (performed using any surgical method without bag protection). By contrast, the nonmorcellated group comprised patients without any records of specimen fragmentation.

2.3 Data Collection and Study Outcomes

The following clinicopathologic data were collected from each patient: age, medical history, primary surgery type, diagnostic method, body mass index, histologic subtype, tumor size, mitotic index (MI), and lymphovascular invasion status. To evaluate the surgical outcomes and the impact of tumor morcellation on oncologic outcomes, the endpoints included recurrence and overall survival. Progression-free survival (PFS), tumor recurrence or progression, and overall survival (OS), were evaluated during follow-up examinations. PFS, measured from the date of primary surgery to that of disease recurrence or progression, death, or last follow-up, serves as a key indicator of treatment efficacy. Similarly, OS, measured from the date of primary surgery to that of death or last follow-up, provides critical insights into the long-term survival prospects of our cohort. Recurrence or tumor progression was confirmed through secondary surgery (i.e., reoperation), imaging studies, or physical examination.

2.4 Statistical Analysis

Categorical variables were analyzed using the chi-square or Fisher exact test, and continuous variables were analyzed using the Mann–Whitney U test. Survival curves were generated using the Kaplan–Meier method. The groups were compared using a log-rank test with hazard ratios, their corresponding 95% confidence intervals (CIs), and p values. Cox proportional hazards regression was used to construct univariate and multivariate models for PFS and OS to adjust for the effects of potential confounders. Statistical significance was set at $p < 0.05$. All statistical analyses were performed using SPSS (version 26.0.0.2; IBM Corporation, Armonk, NY, USA).

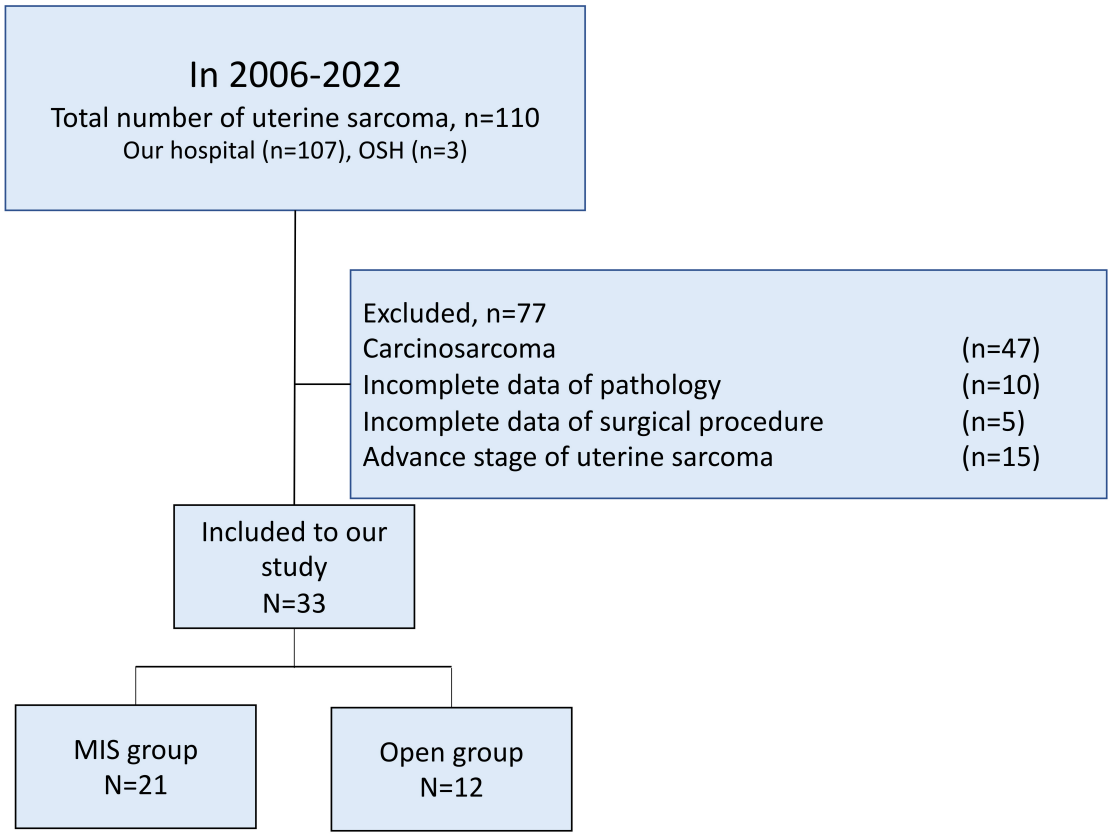

Fig. 1. The flowchart for selecting early-stage uterine sarcoma patients to receive treatment and follow up in our hospital from 2006 to 2022. OSH, outside hospital, referred to our hospital after diagnosis within 3 months; MIS, minimally invasive surgery; Open, open surgery/laparotomic surgery.

3. Results

We enrolled 33 patients who had received a diagnosis of early-stage uterine sarcoma. Among them, 30 (91%) and 3 (9%) patients had undergone primary surgery at our hospital and outside hospital, respectively. The clinicodemographic data of the MIS and open surgery groups were compared (Table 1). The groups did not differ significantly with respect to age, body mass index, tumor size, MI, lymphovascular invasion status, tumor fragmentation, or postoperative chemotherapy. However, adenosarcoma and endometrial stromal sarcoma were more prevalent in the MIS group, whereas uterine leiomyosarcoma was more prevalent in the open surgery group.

Among the 33 patients in our study, 16 (48%) had undergone complete hysterectomy as part of their primary surgery. Seven patients were preoperatively diagnosed with uterine sarcoma through various methods including diagnostic D&C (4/16), hysteroscopic myomectomy (1/16), and cervical biopsy (2/16). Among the remaining nine patients, four were initially suspected to have malignancy based on image findings. Subsequently, they underwent intraoperative frozen section, which confirmed the presence of uterine sarcoma. Another five patients, who underwent preoperative evaluation without detecting malignancy, had discussion with our clinical surgeons, and they decided to proceed with total hysterectomy. Among these 16 patients, their pathology result were 4 cases of adenosarcoma, 7 cases of ESS (4 in MIS group; 3 in open surgery group) and 5 cases of LMS (all open surgery group).

According to surgical records, 13 patients (39%) had undergone tumor morcellation with scalpel during their primary surgery, and tumor was not placed in bag during morcellation. The morcellation procedure was performed in 4 cases of laparoscopic subtotal hysterectomy, 3 cases of abdominal myomectomy and 6 cases of laparoscopic myomectomy in our study. Among these patients, the pathology result showed 7 cases of ESS (4 in laparoscopic subtotal hysterectomy; 3 in laparoscopic myomectomy) and 6 cases of LMS (all abdominal myomectomy). The median follow-up duration was 71 (range: 4 to 147) months, and the median PFS was 84 months (95% CI: 26 to 141). The PFS and OS did not differ significantly between the two groups. The MIS group had a lower 5-year PFS rate than did the open surgery group (42% *vs*. 65%, respectively; $p = 0.577$). However, the MIS group had a higher 5-year OS rate than did the open surgery group, but this difference did not achieve statistical significance (77% *vs*. 56%, respectively; $p = 0.125$; Fig. 2).

Table 1. Description of clinicodemographic variables.

		All	MIS	Open	*p* value
		N = 33	N = 21	N = 12	
Age (years)	Median (IQR)	47 (13)	47 (12.5)	49 (14.25)	0.671
BMI (kg/m^2)	Median (IQR)	23.1 (4.7)	22.4 (4.75)	23.1 (8.45)	0.699
Tumor size	Median (IQR)	6.65 (5.3)	6.0 (4.8)	8.5 (5.9)	0.198
Histology					0.034
Adenosarcoma		4	4	0	
ESS		16	12 (75%)	4 (25%)	
Low-grade ESS		13	11	2	
High-grade ESS		3	1	2	
LMS		13	5 (38%)	8 (61%)	
Diagnosis Method					0.019
D&C/Hysteroscope/Cervical biopsy		7	6	1	
Myomectomy		12	7	5	
Subtotal hysterectomy		5	5	0	
Total hysterectomy		9	3	6	
Primary surgery					0.004
Abd myomectomy		3 (9%)	0 (0%)	3 (25%)	
MIS myomectomy		8 (24%)	7 (33%)	1 (8%)	
ATH ± BSO		8 (24%)	0 (0%)	8 (67%)	
LSCH		4 (12%)	4 (19%)	0 (0%)	
LAVH ± BSO		2 (6%)	2 (10%)	0 (0%)	
RA-SCH		1 (3%)	1 (5%)	0 (0%)	
RA-TH ± BSO		7 (21%)	7 (33%)	0 (0%)	
Morcellation					0.278
Yes		13	10 (77%)	3 (23%)	
Not done		20	11 (55%)	9 (45%)	
FIGO stage					1.000
Stage 1		30	19	11	
Stage 2		3	2	1	
Mitotic index	Median (IQR)	5 (13.5)	4 (6.25)	10 (14)	0.071
LVSI					1.000
Positive		9 (27%)	7 (33%)	2 (17%)	
Negative		14 (42%)	10 (48%)	4 (33%)	
Not done		10 (30%)	4 (19%)	5 (50%)	

Note that *p* value that appear in red are significant.

BMI, body mass index; IQR, interquartile range; ESS, endometrial stromal sarcoma; LMS, leiomyosarcoma; D&C, dilation and curettage; MIS, minimally invasive surgery; Open, open surgery/laparotomic surgery; LVSI, lymphovascular space invasion; Abd, abdominal; ATH, abdominal total hysterectomy; BSO, bilateral salpingo-oophorectomy; LSCH, laparoscopic supracervical hysterectomy; LAVH, laparoscopic-assisted vaginal hysterectomy; RA-SCH, robotic-assisted supracervical hysterectomy; RA-TH, robotic assisted total hysterectomy; FIGO, the International Federation of Gynecology and Obstetrics.

The median survival time was not reached in our study. The univariate and multivariate analyses of PFS revealed that age was independently associated with poor PFS (Table 2.1). The univariate analysis of OS indicated that age, MI, and histologic subtype were independently associated with poor outcomes. However, the multivariate analysis of OS reveals statistically significant associations between age, lymphovascular invasion, and histologic subtype with ESS (Table 2.2).

The analysis of the morcellated versus nonmorcellated groups revealed a lower 5-year PFS rate in the morcellated group than in the nonmorcellated group (42% *vs*. 51%, respectively; $p = 0.732$). However, the 5-year OS rate was higher in the morcellated group than in the nonmorcellated group (75% *vs*. 68%, respectively; $p = 0.584$). Neither group reached the median survival time (see Fig. 3). In our subanalysis of the 5-year OS and PFS rates within the MIS group, we compared outcomes between patients who underwent morcellation (n = 10) and those who did not (n = 11). We found no significant difference in 5-year OS rates between the morcellated and nonmorcellated groups (77% *vs*. 80%, respectively; $p = 0.883$). Similarly, the 5-year PFS rates showed no significant difference (27% *vs*. 55%; $p = 0.162$). Excluding the morcellated cases, our subanalysis of

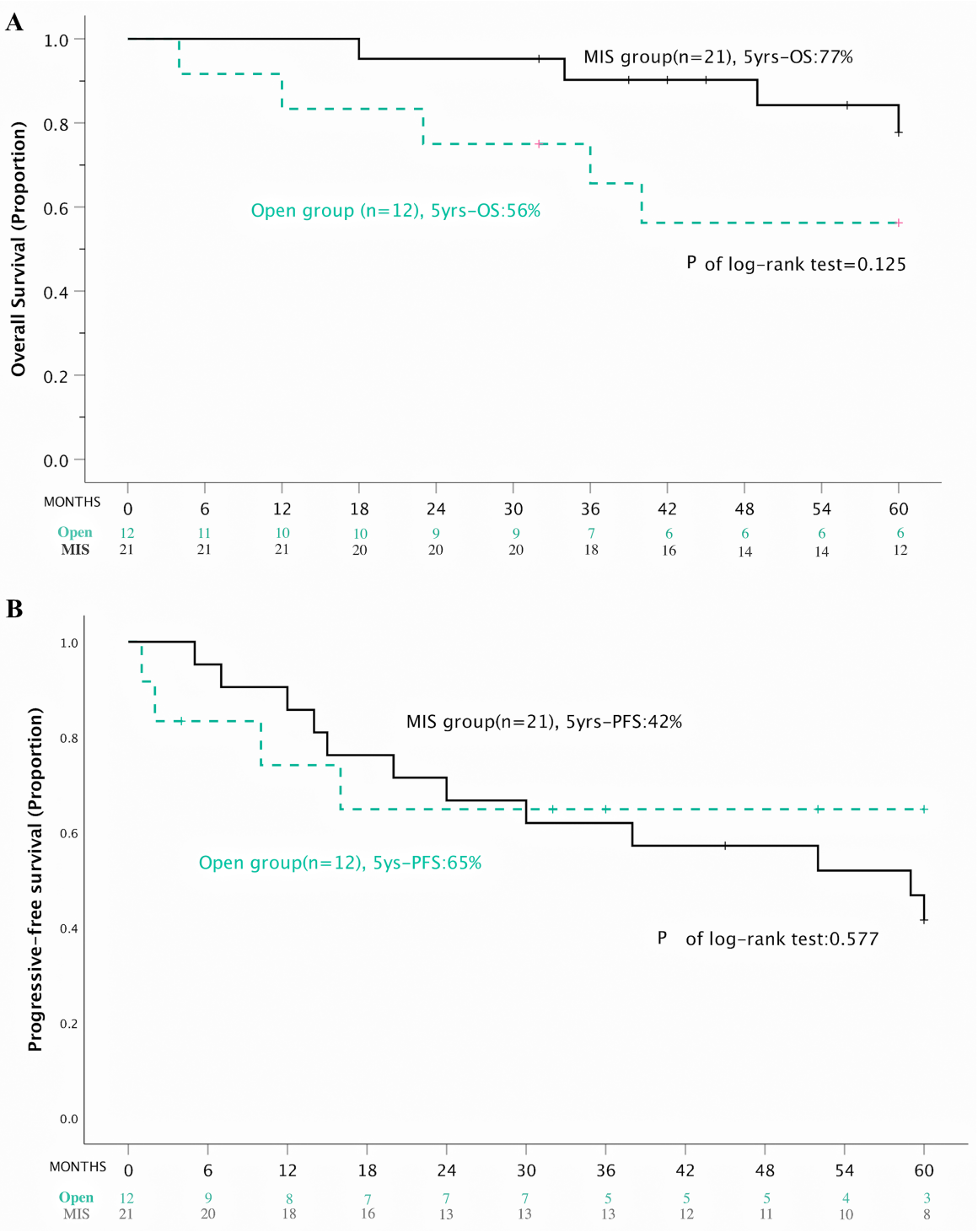

Fig. 2. Five years survival rate and progression-free disease rate in patients of the MIS and open surgery groups, as presented in (A,B), respectively. OS, overall survival; PFS, progression-free survival.

nonmorcellated cases alone for the comparison of surgical outcomes between the MIS (n = 11) and open surgery (n = 9) groups revealed no statistically significant differences in 5-year OS (79% *vs*. 53%; $p = 0.170$) and PFS rates (54% *vs*. 51%; $p = 0.485$).

Furthermore, our analysis includes surgical outcomes and the effects of tumor morcellation for all subtypes of uterine sarcoma in our study. Subanalysis of LMS alone revealed no significant differences in 5-year OS rates (50% *vs*. 24%, respectively; $p = 0.397$) or PFS rates (50% *vs*. 27%, respectively; $p = 0.678$) between the MIS (n = 6) and open group (n = 7). However, the small sample size and uneven distribution of patients among the low-grade (MIS = 11 and open surgery = 2) and high-grade ESS (MIS = 1 and open surgery group = 2) subgroups precluded further subanalysis. The impact of morcellation on surgical out-

Table 2.1. Univariate and multivariate regression analysis of progression-free disease at the end-point.

	Progression-free disease					
	Univariable			Multivariable		
Variable	HR	CI	*p* value	HR	CI	*p* value
Age	1.057	1.015–1.100	0.007	1.085	1.019–1.157	0.012
Approach (Open/MIS)	1.37	0.444–4.279	0.578	1.969	0.533–7.278	0.310
Morcellate	1.189	0.442–3.200	0.732	2.010	0.524–7.710	0.310
MI	1.047	0.980–1.120	0.174	1.045	0.935–1.168	0.436
Histology[1] LMS/ESS	0.556	0.192–1.606	0.278	0.415	0.063–2.753	0.362
LVI	1.309	0.454–3.777	0.618	1.970	0.595–6.530	0.267

Note that *p* value that appear in red are significant.

[1]LMS as the control group: compare the differences between LMS and EMS.

HR, hazard ration; CI, confidence interval; LMS, leiomyosarcoma; ESS, endometrial stromal sarcoma; MI, mitotic index; LVI, lymphovascular invasion; MIS, minimally invasive surgery.

Table 2.2. Univariate and multivariate regression analysis of overall survival at the end-point.

	Overall Survival					
	Univariable			Multivariable		
Variable	HR	CI	*p* value	HR	CI	*p* value
Age	1.108	1.001–1.227	0.047	1.244	1.027–1.508	0.026
Approach (Open/MIS)	0.372	0.100–1.387	0.141	0.680	0.084–5.515	0.718
Morcellate	0.680	0.170–2.727	0.586	0.934	0.087–10.07	0.955
MI	1.096	1.020–1.179	0.013	0.971	0.857–1.101	0.955
Histology[1] LMS/ESS	0.081	0.010–0.665	0.019	0.010	0–0.134	0.005
LVI	1.459	0.364–5.847	0.594	38.266	2.179–672.13	0.013

Note that *p* value that appear in red are significant.

[1]LMS as the control group: compare the differences between LMS and EMS.

HR, hazard ration; CI, confidence interval; LMS, leiomyosarcoma; ESS, endometrial stromal sarcoma; MI, mitotic index; LVI, lymphovascular invasion; MIS, minimally invasive surgery.

comes within these histological subtypes showed no significant differences in 5-year OS and PFS rates for both LMS (Morcellated = 6 *vs*. Nonmorcellated = 7; 5-year OS rates 50% *vs*. 23%, $p = 0.397$) (5-year PFS: 50% *vs*. 53%, $p = 0.585$) and low-grade ESS subgroups (Morcellated = 6 *vs*. Nonmorcellated = 6; 5-year OS rates 100% *vs*. 83%, $p = 0.28$) (5-year PFS rates 38% *vs*. 66%, $p = 0.322$).

In the cohort of 33 patients, 16 (48%) exhibited recurrence at the time of analysis (refer to Fig. 4). Within the MIS group, a total of 12 patients (57%) were diagnosed with tumor recurrence, with 9 undergoing subsequent treatment. In the open group, 4 patients (33%) experienced recurrence, and 3 of them received treatment for the recurrent tumors.

Subsequent to tumor recurrence, fatal outcomes were observed in seven patients during the analysis period. Among them, four underwent combined chemotherapy and radiotherapy, while three opted for hospice care. Within the studied group, the deaths of six individuals were directly linked to tumor progression, resulting in complications such as gastrointestinal bleeding, respiratory failure, acute fulminant hepatitis, and acute kidney injury. Furthermore, one patient passed away due to congestive heart failure, attributed to drug toxicity. In response to the detection of tumor recurrence, four patients chose to give up medical intervention and receive hospice care. This decision was driven by factors including the financial challenges posed by unaffordable medical care, the significant burden of medical expenses, and preference for an enhanced quality of life, prioritizing comfort over potential challenges associated with continued medical interventions.

In the subanalysis of recurrence between the morcellated and nonmorcellated groups (see Table 3), we observed that all recurrences in the morcellated group were confined to peritoneal sites. In the nonmorcellated group, 4 patients (44%) experienced recurrences with a hematogenous pattern, while 5 patients (56%) had recurrences with a peritoneal pattern. However, there was no significant difference between the two groups ($p = 0.728$). The subanalysis of the two groups reveals that tumor morcellation may have an impact and potentially increase the risk of tumor recurrence in peritoneal sites, although the findings did not reach statistical significance.

4. Discussion

We investigated the survival outcomes of MIS in early-stage uterine sarcoma. The results indicated that the survival outcomes of the MIS group were not inferior to those of the open surgery group. Our study revealed that

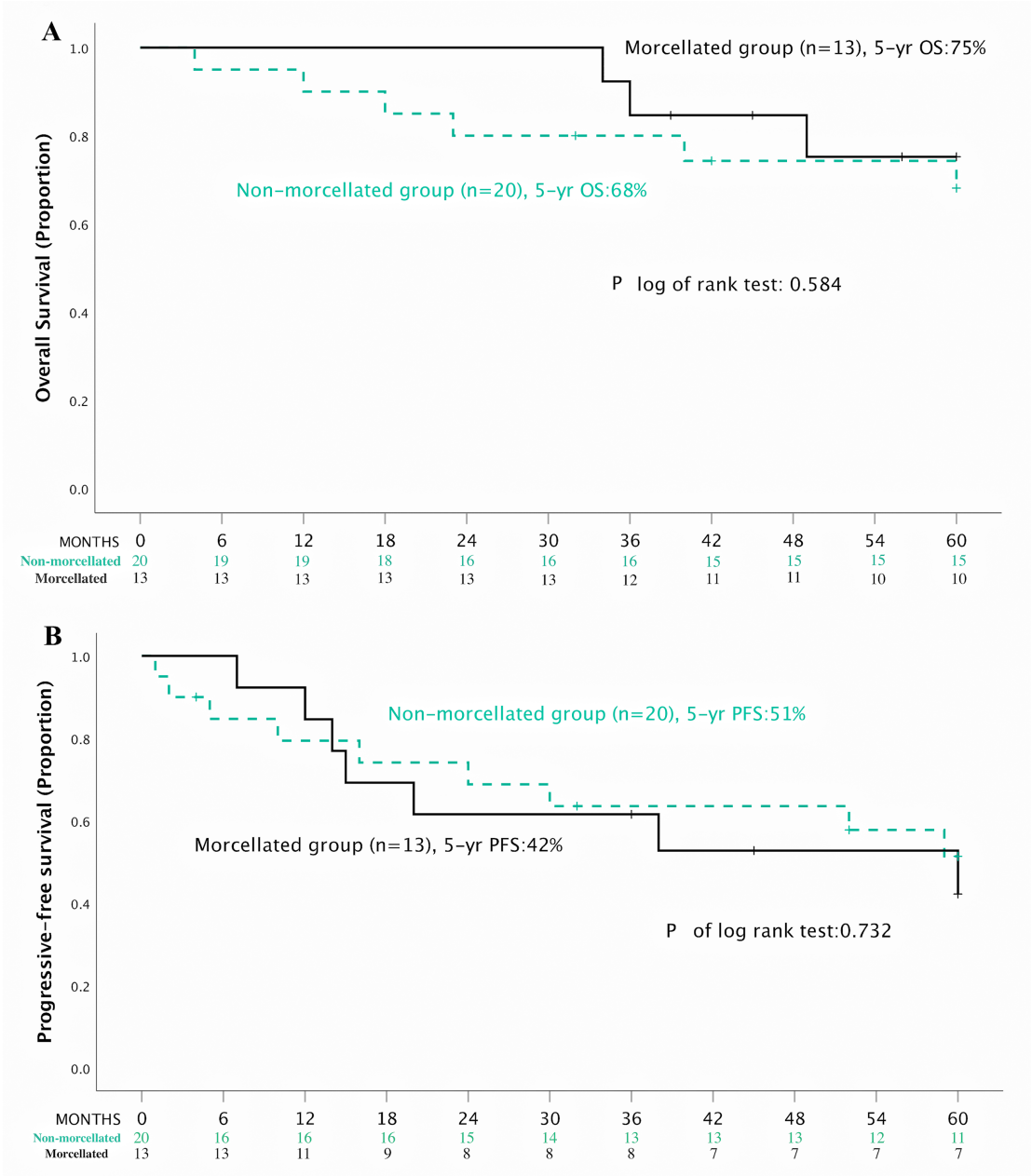

Fig. 3. Five years survival rate and progression-free disease rate in patients who underwent tumor morcellated and nonmorcellated, as presented in (A,B), respectively.

patients who underwent tumor fragmentation had peritoneal recurrence more frequently than did those who did not undergo tumor fragmentation.

Complete tumor resection without tumor fragmentation is the standard surgical management approach for early-stage uterine sarcoma [11,19]. In response to the US Food and Drug Administration's warning against the use of power morcellation, numerous studies have explored the effects of morcellation on survival outcomes in patients with uterine sarcoma [20,21]. However, the diagnosis of uterine sarcoma is often made postoperatively when it is presumed to be benign gynecologic disease. Therefore, our study provides crucial information for clinicians indicating MIS for presumed benign gynecologic disease. Yuk *et al.* [22] reported no difference between laparoscopic and laparotomic approaches in 6-year OS in patients with unexpected uterine malignancy. Another study found that laparoscopic surgery conferred a better OS rate than did laparotomy in patients with unexpected uterine malignancy, excluding endometrial cancer [23].

Similarly, in line with these finding, our study suggest that surgical method approach may not affect the survival outcome of early-stage uterine sarcoma.

In our study, 26 patients presented with malignancies that were undetectable during preoperative evaluation and were initially considered to have benign tumors. The histological subtypes identified included 13 cases of ESS, comprising 3 high-grade ESS and 10 low-grade ESS, as well

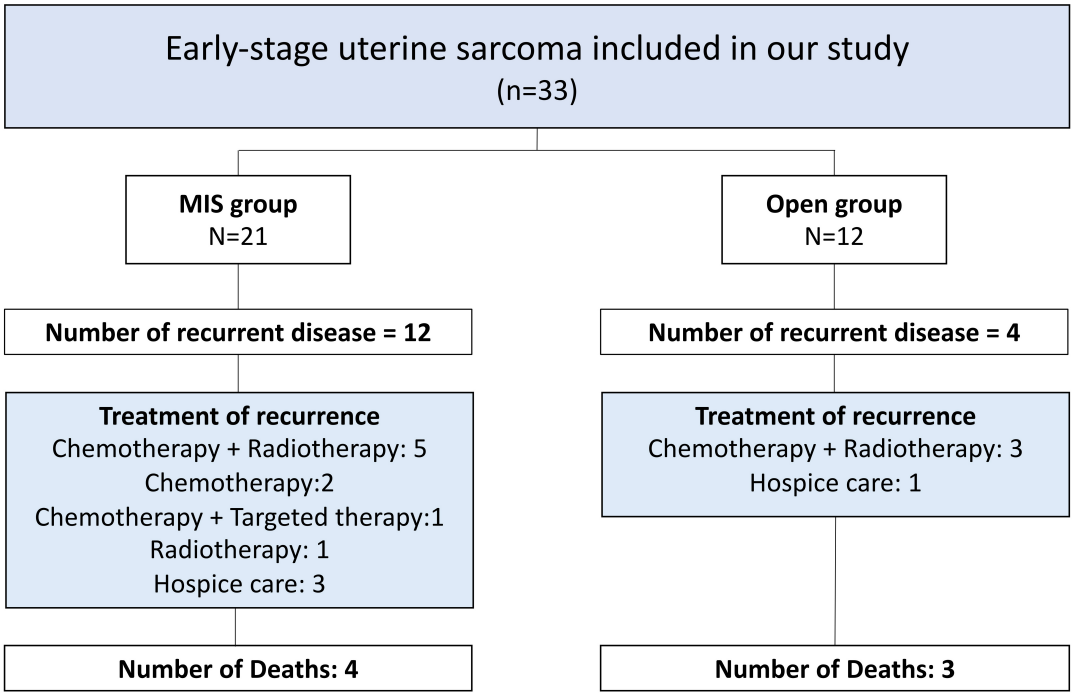

Fig. 4. Flow Chart Illustrating Recurrent Diseases and Outcomes in MIS and Open Groups. This flow chart illustrates the number of recurrent diseases in the MIS and Open groups, respectively. It delineates those who received additional medical treatment and ultimately provides the final count of fatal outcomes in the study.

Table 3. Recurrent patten.

	Total	Morcellated	Non-morcellated	*p* value
	(n = 33)	(n = 13)	(n = 20)	
No recurrence, n (%)	17 (52)	6 (46)	11 (55)	0.728
Recurrence site, n (%)	16 (48)	7 (54)	9 (45)	
Hematogenous	5 (31)	0 (0)	4 (44)	
Bone		0	1	
Lung		0	2	
Lung, Bone and Anxillary lymph node		0	1	
Peritoneal	11 (69)	7 (100)	5 (56)	
Vaginal stump		1	1	
Pelvic, isolated		3	4	
Pelvic and abdomen		1	0	
Abdomen		2	0	
Hematogenous + Peritoneal		0	0	

as 13 cases of LMS. In ESS patients, all preoperative diagnostic biopsies with curettage or hysteroscope biopsy were negative. Although the main tumor mostly occurs intramyometrial, most ESS involves the endometrium and can be diagnosed by endometrial or transvaginal biopsy [24] but it had low sensitivity [25]. However, when lesion is completely within the myometrium, curettage or biopsy may not be helpful; therefore, the definitive diagnosis can only be made by examining the hysterectomy specimen. Preoperative diagnosis of uterine sarcoma is challenging, with several studies addressing the utilization of ultrasound and advanced imaging techniques like MRI to facilitate differentiation between leiomyomas and sarcomas. Borella *et al.* [26] demonstrated that uterine sarcomas can be differentiated from leiomyomas based on specific ultrasound features. These features include the large size of the tumor, the presence of cystic lesions, high percentage of tumor circumference, and intralesional vascularization. Additionally, factors such as age and menopausal status can assist in the preoperative assessment of uterine sarcoma [26]. Ludovisi *et al.* [27] highlighted the clinical and ultrasound characteristics of uterine sarcoma, noting that these tumors typically appear as solid masses with inhomogeneous echogenicity and are most often moderately or highly vascularized. Sun

et al. [28] conducted a comprehensive review and summary of key MRI imaging features that support the diagnosis of LMS as opposed to leiomyoma. Moreover, they have developed and introduced an MRI-based diagnostic algorithm that integrates multiple imaging features to enhance the accuracy of differentiating between leiomyoma and LMS [28].

The effects of tumor morcellation on the survival outcomes of patients with uterine sarcoma remain unclear. Some studies have indicated that tumor morcellation causes cancer cells to spread through the peritoneal site, which increases the rate of recurrence and contributes to poor prognosis [21,29]. By contrast, other studies have contended that tumor morcellation does not adversely affect oncologic prognosis [20,22]. Pedra *et al*. [30] published a study that assessed the impact of tumor morcellation on oncological outcomes in stage I LMS. The study included total of 152 patients, with 45 morcellated cases and 107 nonmorcellated. The median overall survival for the non-morcellated group (82.1 months) higher than in the morcellated group (47.8 months); however, this difference did not reach statistical significance ($p = 0.7$). Conversely, a significant difference was found in median progression-free survival, with the nonmorcellated group (13.8 months) compared to (7.3 months) in the morcellated group ($p = 0.004$). Nonetheless, the study demonstrated that tumor morcellation was associated with a significantly higher risk of recurrence and resulted in a four-fold increase in peritoneal recurrence [30]. Similarly in our study, we observed that tumor morcellation increased the risk of recurrence, particularly in the peritoneal site, although the different was not statistically significant. The tumor fragmentation resulted in lower PFS rate in the morcellated group than in the nonmorcellated group, although the difference was not statistically significant.

Furthermore, analyzing the effect of tumor morcellation on histological subtypes is challenging due to the small sample size, which limits the ability to provide conclusive clinical outcomes. Therefore, a study with a larger sample size is necessary for more definitive results. Additionally, both the univariable and multivariable regression analyses did not show any significant impact or effect on the morcellation factor. Similarly, Pedra *et al*. [30] identified several prognostic biomarkers as significant predictors of oncological outcomes but did not include tumor morcellation in their study Nonetheless, they found it was associated with a higher risk of recurrence. Our results showed that need for caution and thorough discussion with patients regarding the risk of malignancy cell spread when performing morcellation procedure, and tumor should be placed in bag if morcellate is necessary, or this procedure should be avoided. To prevent the spreading of the tumor during morcellation [3], using in-bag morcellation is considered an optimal approach to avoid the dissemination of tissue fragments [13]. However, Salman *et al*. [31] published a case report detailing an unexpected occurrence: a patient with LMS underwent laparoscopic myomectomy and tumor morcellation in a bag, yet experienced tumor recurrence within 5 months. Therefore, the protective effect against tumor spreading when morcellating under a bag container remains debated and requires further investigation through larger studies [32].

Retrospective studies have identified various prognostic factors for uterine sarcoma [33,34]. In our multivariate analysis of overall survival reveal statistically significant associations between age, lymphovascular invasion, and histologic subtype, relevant studies have identified these variables as crucial prognostic biomarkers of uterine sarcoma [30,35,36]. Additionally, the grading of ESS into low or high grades emerged as a critical prognostic factor; notably, high grade ESS was associated with poor survival outcome. In our cohort, high-grade ESS was predominantly observed in open group (n = 2) compared to MIS group (n = 1). This may explain the reason with result: the lower PFS rate but better OS rate in MIS compared to open surgery, as the prominent histological subtype in the MIS group is ESS, while in open surgery, the prominent subtype is LMS. We did not incorporate the histologic subtypes of adenosarcoma in our univariate and multivariate analyses due to their small sample size and potential effect on the results. Therefore, future studies with larger sample sizes are necessary to validate our findings and identify additional potential prognostic factors for uterine sarcoma. This will help enhance the reliability and comprehensiveness of our analyses, providing valuable insights into the management and prognosis of uterine sarcoma across different histological subtypes.

This study has some limitations. First, our study was conducted at a single hospital, which might have limited the generalizability of our findings. Second, histologic subtypes and tumor morcellation status were unevenly distributed between the MIS and open surgery groups, which might have led to a selection bias and confounded the results. Third, the small sample size of our study might have influenced the analysis and interpretation of results, particularly when evaluating prognostic factors such as age, MI, and histologic subtype of adenosarcoma. Because of the rarity of uterine sarcoma, accumulating a large sample size within a single institution is challenging. Therefore, future studies with large sample sizes and multi-institutions collaborations are required to validate our findings and identify additional potential prognostic factors for uterine sarcoma. Fourth, patients' decisions constituted another potential bias that may have affected the study, influenced by factors such as financial burden, personal preferences for extending their lifetime, or prioritizing their quality of life.

5. Conclusions

In conclusion, our study did not identify statistically significant differences in survival outcomes between the MIS group and open surgery. A larger sample study for further investigation of the outcomes of MIS should be performed. However, intraoperative tumor morcellation may

increase peritoneal recurrence risk and negatively affect progression-free survival. Therefore, we suggest surgeon should be avoid performing tumor morcellation. Complete tumor resection without fragmentation appears to be a suitable approach for avoiding intraoperative tumor spread and subsequent recurrence.

Availability of Data and Materials

The data contained in the article cannot be shared due to data protection regulations. According to the ethics committee, only evaluation of anonymized data is allowed for this study.

Author Contributions

Conceptualization: YHC, JTQ, WML and CWC; methodology, HCL and INC; software, HCL and INC; validation, JTQ; formal analysis: YHC, HCL, ITW and INC; interpretation of data: HCL, YHC and ITW; resources: WML and CWC; data curation: HCL and YHC; writing: HCL; original draft preparation: YHC, HCL, ITW, INC CWC and WML; review and editing, YHC, JTQ, CWC and WML; supervision, JTQ and WML. All authors have read and agreed to the published version of the manuscript.

Ethics Approval and Consent to Participate

The study received approval from the responsible ethics committee (Taipei Medical University, reference number: N202306068). Patient consent was waived because of the retrospective feature and de-identified data of this article. Its requirement was also exempted by the institutional review board.

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Conflict of Interest

The authors declare no conflict of interest.

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