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Long-term risk of fibroid recurrence after laparoscopic myomectomy

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ABSTRACT

Objective: The use of laparoscopic myomectomy as a surgical treatment for uterine leiomyoma is associated with low intraoperative morbidity and short hospitalization. Limited data about the long-term outcome of this surgical approach are available. The aims of this study were to estimate the risk of uterine fibroid recurrence after laparoscopic myomectomy and to identify factors contributing to the rate of fibroid relapse.

Study design: Between 1996 and 2003, 331 patients underwent laparoscopic myomectomy to treat uterine leiomyoma in our hospital; 224 of these patients consented to participate in our 2009 follow-up survey. Clinical symptomatic uterine leiomyoma recurrence was defined as relapse. Recurrence rates at 24 and 60 months post-operatively were calculated for the study population. Fisher's exact tests were used to examine the impacts of factors previously linked to an increased risk of fibroid recurrence, including (1) patient age at the time of initial surgery, (2) pre-operative body mass index, (3) number and localization of uterine leiomyoma removed, and (4) pregnancy and (5) delivery after laparoscopic myomectomy on fibroid recurrence in our study cohort.

Results: We observed 75 recurrences in 224 patients. The cumulative risk of recurrence was 4.9% at 24 months and 21.4% at 60 months post-operatively. An age of 30–40 years and the presence of more than one fibroid at the time of initial laparoscopic myomectomy were identified as factors significantly increasing the risk of symptomatic recurrence after laparoscopic myomectomy (31.25% and 38.71%, respectively; both $p < 0.01$).

Conclusion: Patients with multiple uterine leiomyoma and those in the third decade of life should be counselled thoroughly about the risk of recurrence prior to laparoscopic myomectomy. The low observed recurrence rate in peri- and postmenopausal patients in our study may support the use of laparoscopic myomectomy as a uterus-preserving surgical alternative beyond the reproductive period.

Introduction

Uterine leiomyoma (UL), commonly referred to as uterine fibroid, is the most common female pelvic tumor and the most common indication for hysterectomy, with a compound aetiopathology affecting 25% of reproductive-aged women [1–3]. UL frequently causes clinical symptoms and subfertility. The percentage of hysterectomies performed due to UL in women of reproductive age (18–44 years) in the United States decreased from 31.4% in 1997–1998 to 26.9% in 2004–2005 [4].

Hysterectomy and uterus-preserving myomectomy are currently the surgical treatments of choice for non-submucosal UL. The introduction of endoscopic surgery has brought the treatment of symptomatic UL into the current era of fertility- or uterus-preserving therapy, associated with low intraoperative morbidity and short hospitalization [5–7]. Laparoscopic myomectomy (LM) has replaced classical open abdominal myomectomy as the uterus-preserving surgical approach of choice. Despite its widespread use, limited data on the long-term outcome of LM are available.

Non-surgical uterus-preserving approaches, such as embolization and focused ultrasonography, have been associated with high UL recurrence rates; myomectomy is also associated with a considerable risk of fibroid recurrence [8,9]. This risk appears to be associated in particular with the laparoscopic route, for which 5-year cumulative recurrence rates of up to 52.9% have been reported [10]. Some authors have speculated that LM may increase the risk

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of UL recurrence in comparison with open myomectomy [11,12]. However, given the limited availability of data from long-term post-LM follow-up studies and methodological limitations, these comparisons have been received with caution [13,14].

The aim of our retrospective assessment was to evaluate the long-term risk of recurrence after LM in a single-center and to further elucidate the role of parameters, previously found to be associated with fibroid recurrence in the absence of well-established molecular predisposition markers. Factors analyzed included patients' age and body mass index (BMI) at the time of primary surgery, type and number of fibroids present at the time of initial LM, and the post-operative incidence of pregnancies and deliveries.

Patients and methods

Between January 1996 and December 2003 all patients who underwent LM for symptomatic UL in our hospital were identified by searching the hospital's electronic database (ISHMed; SAP, Walldorf, Germany).

For all patients, pre-operative evaluation consisted of gynecological examination, transvaginal ultrasonography, and basic laboratory testing, including the measurement of hemoglobin concentration. Patients received 1.5 g cefuroxim (three times intravenously) and 0.5 g metronidazole (twice a day, intravenously) during the operation and for the first 3 post-operative days. Patients used Foley's catheters until the first post-operative morning. Low-molecular-weight heparin (enoxaparin (40 mg), subcutaneously once a day) was used in all patients as a prophylaxis for thromboembolism. Patients' hemoglobin serum levels were determined on the second post-operative day.

The LM technique used in these patients has been described in detail previously [15]. In brief, LM was performed by placing three 5 mm ports in the lower abdomen. After establishing pneumoperitoneum (12 mmHg, CO_2), the pelvic cavity was explored using a 10 mm laparoscope to localize the fibroid(s). Exploration included anterior, posterior, lateral, and medial sites, as well as the dome, apex, and base of the myometrium. After initial exploration, the uterine serosa and myometrium were incised to expose the fibroid surface(s). A 10 mm port was then inserted to replace the suprasymphysary 5 mm port, and each fibroid was grasped with 10 mm tenaculum forceps. The fibroid was extracted from the surrounding myometrium by blunt dissection. As indicated, interrupted, intracorporeal, single-layer sutures were used to close the uterus. Pedunculated subserous fibroids were dissected sharply using scissors or bipolar coagulation. Fibroids were morcellated using an electric morcellator (Storz, Tuttlingen, Germany) and extracted through the midline trocar, then weighed and photo-documented. After extensive lavage, an intra-abdominal drain (French gauge 18) was placed for post-operative monitoring purposes. UL removal was achieved successfully *via* laparoscopy in all patients. All diagnoses of UL were confirmed by histopathological examination.

All patients were postally contacted during spring and summer 2009, and asked to complete a questionnaire. Herby, information about pregnancies, deliveries and possible recurrences following the initial LM were obtained. Based on the methodological approach by Doridot et al. [11], the main outcome measurement fibroid recurrence, was defined as the reappearance of pre-operative fibroid-related symptoms, reported by patients and the subsequent transvaginal ultrasound diagnosis of a UL. For this purpose, patients were asked to state whether or not they had post-operatively suffered from symptoms, which were pre-operatively linked to the presence of an uterine fibroid, to specifically describe these symptoms and to provide further information on any subsequent diagnostic or therapeutic measures. Questionnaires were double analyzed by two examiners (AW and MPR). In cases of responses, indicating a symptomatic recurrence of an uterine fibroid, patients and their outpatient gynecologist were re-contacted to further inquire about the date of the recurrence, the following sonographic diagnostic work-up and medical or surgical treatment.

For the assessment of patients' baseline characteristics and surgical parameters (body mass index and age at time of surgery, operation time, post-operative hospitalization, numbers of fibroids removed, seize of leading fibroid and intraoperative opening of uterine cavity) patients electronic charts were reviewed and the respective data were retrieved by one examiner from the hospital's electronic database (ISHMed; SAP, Walldorf, Germany) (AW).

For the follow-up analysis, data from all patients who returned the completed questionnaire were included.

Patients were grouped according to age at the time of surgery (0–29, 30–40, and ≥40 years), gestation and delivery after LM (both yes/no), number of UL removed during LM (1 *vs.* ≥2), anatomical localization of the primary leiomyoma removed (types 2–6 *vs.* type 7, according to the Federation of Gynaecology and Obstetrics [16], and pre-operative BMI (≤25 *vs.* >25 kg/m^2). UL recurrence rates at 24 and 60 months post-operatively were calculated for the study cohort.

Recurrence rates at 60 months post-operatively were compared in each of these groups using the two-tailed Fisher's exact test for dichotomous variables and the same test with a Freeman–Halton extension for variables with three categories [17]. A p-value <0.05 was considered to indicate statistical significance. All statistical calculations were performed using the SPSS software (version 18.0; SPSS Inc., Chicago, IL, USA).

Results

From an initial sample of 331 patients, 224 patients (68%), who returned the completed questionnaire, were included in this study cohort. In the remaining 107 patients (lost-to-follow-up rate: 32%), it was either not possible to postally re-contact patients due to address changes (66 women) or the questionnaire was not resend (36 women).

The mean duration of patients included in the follow-up in this study was 108 (range: 74–163) months. Mean patient age at the time of the operation was 37.9 (standard deviation (SD): 8.3) years. The mean pregnancy and delivery indices were 0.8 (SD: 0.6) and 0.5 (SD: 0.4) per patient, respectively. Mean BMI was 23.71 (SD: 4.0) kg/m^2. The indications for LM were menometrorrhagia (56.3%), leiomyoma-related pain (29.0%), and infertility secondary to the presence of UL (14.7%). Of note, 26 patients in this cohort had been treated with gonadotropin-releasing hormone agonists prior to LM.

A total of 443 UL (mean: 2.0 per patient) were removed and the average size of the primary UL removed was 57.9 (SD: 1.7) mm. 155 fibroids were located intramurally, 177 were subserous, and 111 fibroids were pedunculated. Mean operation time per patient was 123.6 (SD: 66.6) min. The uterine cavity was opened in 11 patients. The mean duration of post-operative hospitalization was 3.1 (SD: 0.9) days.

Table 1 provides baseline characteristics and surgical outcome for both, the initially selected study sample (n = 331 patients) and the patients, included in the follow-up, whose data were further analyzed for this study (N = 224). A comparison between both groups showed no significant differences.

80 patients stated in their questionnaire, that they had suffered post-operatively from symptoms, pre-operatively linked to the presence of uterine fibroids. In 75 of these patients these symptoms were linked to the sonographic diagnosis of an uterine fibroid. In the remaining 5 patients, the obtained medical charts indicated the presence of a diverticulosis (n = 3) and a hydrosalpinx (n = 2) as pathophysiological correlates of the initially reported