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Should We Still Be Undertaking Open Myomectomies? A Five-Year Retrospective Case Review

Ioannis Athanasios Dedes[1a]*, Rachel Monique Squires[1b], Eliza Kathleen Thomas[2a], Martin Stuart Mills[1c] and David John Cahill[1,2b]

[1]Reproductive Medicine, Department of Obstetrics and Gynaecology, Division of Women's and Children's, St Michael's Hospital, Southwell Street, Bristol BS2 8EG, UK

[1a]Reproductive Medicine Speciality Doctor MB, DFSRH, MSc

[1b]Specialist Registrar in Obstetrics and Gynaecology MB, MRCOG

[1c]Consultant Obstetrician and Gynaecologist and Medical Director of the Department MB, FRCOG

[2]University of Bristol, Academic Unit of Obstetrics and Gynaecology, Level D, St Michael's Hospital, Southwell Street, Bristol BS2 8EG, UK

[2a]Medical student

[2b]Professor in Medical Education and Reproductive Medicine, University of Bristol MB, FRCPI, FRCOG

***Corresponding Author:** Dr Ioannis Athanasios Dedes, Reproductive Medicine Speciality Doctor, Department of Obstetrics and Gynaecology, Division of Women's and Children's, St Michael's Hospital, Southwell Street, UK.

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Abstract

Introduction: Abdominal myomectomy is a treatment option for symptomatic leiomyomata. We aimed to evaluate the outcomes of open myomectomy using a different surgical technique.

Materials and Methods: 45 women with symptomatic uterine leiomyomas were studied retrospectively during a five-year period. According to protocol, pre-operative GnRH analogues or selective progesterone receptor modulator were administered for 3 months followed by open myomectomy, performed by two Consultants. Intra-operatively, leiomyomas were infiltrated with Vasopressin, excised with a non-touch technique and irrigation with Hartmann's solution. Data analysis included: age, parity, preceding symptoms, peri-operative blood loss, procedure duration, number and size of leiomyomas removed, complications, duration of hospital stay, conception and pregnancy outcomes.

Main outcome measures: Intraoperative blood loss, duration of hospital stay and clinical pregnancy rates.

Results: Women' mean age was 36 years. Most women complained of menorrhagia (60%), voiding difficulties (21%) and abdominal pain (14%). In 51%, infertility was the main indication for myomectomy and 48% had distorted endometrial cavity. Five women received a selective progesterone receptor modulator and thirty-eight were given GnRH analogues. The mean number of leiomyomas removed was 4 and the mean diameter of the largest leiomyomas was 65 mm. Mean values: blood loss 467 mls, pre-operative hemoglobin 130 g/L, post-operative hemoglobin 107 g/L and duration of the operation 161 minutes. 87% had no complications. Postoperatively, 8 live births occurred (mean birthweight 3.2 kg).

Conclusions: Perceptions of myomectomy surgery as being bloody and messy are not confirmed in our cohort. However, these procedures are labour-intensive. Meticulous surgical care can lead to satisfactory outcomes.

Keywords: *Myomectomy; Myomas; Myomata; Leiomyomata; Fibroids*

Abbreviations: Gonadotrophin Releasing Hormone: GnRH; Magnetic Resonance Imaging: MRI; Live Births: LB; Termination of pregnancy: TOP; Miscarriage: MISC; Pregnant: PREG

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Introduction

Uterine leiomyomata (fibroids or myomas/myomata) are benign tumours of smooth muscle cells and fibrous tissue that develop within the wall of the uterus. Uterine leiomyomata are one of the most common gynaecological problems among women in the UK affecting 20-40% of women in childbearing age [1,2]. There is increased prevalence found in black women, who tend to have more and larger leiomyomata when compared to white women [3,4]. Uterine leiomyomata may be asymptomatic and are usually discovered incidentally during a routine pelvic examination or imaging of the pelvis. If asymptomatic, leiomyomata do not require treatment but may require monitoring. However, leiomyomata may cause significant morbidity in women such as menorrhagia, which may lead to iron deficiency anaemia and dysmenorrhoea. They may also cause pelvic pressure or pain and urinary incontinence. They are associated with adverse reproductive health outcomes such as infertility and miscarriage [2,5]. Uterus preserving surgery of symptomatic leiomyomata includes abdominal (open), robotically assisted or routine laparoscopic myomectomy, uterine artery embolisation, magnetic resonance-guided focused ultrasound and myolysis. Radical and uterus non-preserving option includes hysterectomy via any approach. The sub-mucous and some intramural myomata may be managed hysteroscopically and are not included in this review [6]. The decision to proceed with surgical treatment of symptomatic leiomyomata should be patient-centred and would depend on the number, location and dimension of leiomyomata, the women's fertility desire, women's age, presence of other's causes of infertility and whether there is any indication for *in vitro* fertilisation [7].

Advancements in surgical techniques and equipment have afforded women with leiomyomata the option of myomectomy rather than hysterectomy, regardless of their fertility desire [8]. In this paper, we analyse the data from a series of women who underwent open myomectomy and compare these with other published data for open and laparoscopic myomectomy and consider if we should still be undertaking open myomectomies.

Materials and Methods

All patients who underwent open myomectomy (see Table 1) performed jointly by two consultant gynaecologists in a tertiary University Hospital in Southwest England, between November 2010 and December 2015, were identified through the hospital electronic registers. Case notes were reviewed and individually scrutinised. Data were collected on the following characteristics: women's age at the time of surgery, parity, indication for surgical intervention, estimated blood loss post-operatively, pre-operative and post-operative serum haemoglobin, duration of operation, number and size of leiomyomata (the largest leiomyoma diameter by histological measurements), preoperative treatment with selective progesterone receptor modulator or GnRH analogue and duration of treatment, as well as complications, breach of the endometrial cavity, blood transfusion requirement, duration of in-hospital stay, pregnancy rates following myomectomy and pregnancy outcomes (collected from hospital and general practice records). With regard to descriptive statistics, we calculated mean values and standard deviations or median and ranges as appropriate and also expressed frequencies as percentages. Statistical analysis was performed using Minitab 12.23 (Minitab Ltd, Coventry CV3 2TE).

1. Informed written consent obtained
2. Selective pre-operative MRI (to locate the leiomyomata and make a clear plan at the time of the operation)
3. Patient given either pre-operative down-regulation using GnRH analogues or selective progesterone receptor modulator (Ulipristal acetate)
4. Perioperative antibiotics administered
5. Insertion of indwelling catheter preoperatively (until at least first day after procedure)
6. Open myomectomy performed under general anaesthetic
7. Peritoneal cavity opened through a Pfannenstiel or midline incision (depending on the size of the leiomyomata)
8. Infiltration of Vasopressin 10 IU in 20mls Normal Saline (total) to base of leiomyomata (for intraoperative haemostasis)
9. The uterine serosa overlying the leiomyomata opened and the leiomyoma dissected with fine tissue forceps and scissors with a non-touch technique (to minimise trauma to the surrounding tissues) aiming to avoid opening the endometrial cavity.
10. Irrigation of uterine tissue with Hartmann's solution to optimise operator access and to avoid uterine tissues dryness (a potential cause of future adhesions).
11. Selective use of intraoperative intravenous Tranexamic acid 1 gram (after leiomyoma capsule closure)
12. Myometrium repaired in layers with Polyglactin 910 suture
13. Uterine serosa layer repaired with non-absorbable nylon stitch
14. After haemostasis achieved, ilio-inguinal and ilio-hypogastric nerve block performed using long acting local anaesthesia, rectus sheath closure with Polyglactin 910 and skin closure with subcuticular 3/0 monofilament absorbable sutures
15. Thromboprohylaxis administered (dependent on associated venous thromboembolism risk factors and risk of haemorrhage)

Table 1: *Surgical protocol used for open myomectomy.*

Results and Discussion

In a five year period, 45 patients underwent open myomectomies; a total of 182 leiomyomata were removed. The mean age of patients was 36 ± 4.9 years and they were from various ethnic groups with the largest proportion of women being Caucasian (55%) and black African or Caribbean (31%).

The main indications for myomectomy were infertility (n = 23) or other symptoms (n = 22). However, commonly women presented with both (n = 15). The main indication for treatment was considered the presenting complaint. Eight women were operated exclusively for infertility and reported no other symptoms. Of the remaining thirty seven women (with or without infertility), 60% presented with menorrhagia, 2% with irregular menstruation, 14% with lower abdominal pains, 21% with pelvic pressure symptoms with voiding difficulties and 3% with a large pelvic mass. Regarding the infertility patients, 11 had distortion of the endometrial cavity by uterine leiomyomata.

Out of 45 women, 5 received selective progesterone receptor modulator (Ulipristal acetate: Gedeon Richter UK Ltd, London, W9 2EP, UK) for median of 15 weeks (range 7-18 weeks). Two patients had no pre-operative treatment. The remaining 38 patients were down regulated with GnRH analogues for a median of 12 weeks (range 7-24 weeks); with Goserelin implant subcutaneously (n = 1), Triptorelin 3.75 mg injections (n = 11) and Triptorelin 3 mg SR (n = 26) injections intramuscularly.

The mean number of leiomyomata removed was 4 (SD 4.3). The mean diameter of the largest leiomyoma documented by the histological measurements for each patient was 65mm (SD 32 mm). The mean estimated blood loss was 467 mls (SD 602 mls). The mean preoperative haemoglobin was 130 g/L and the mean post-operative haemoglobin was 107 g/L. The difference between mean preoperative and postoperative haemoglobin was greater in the group who underwent myomectomy for symptomatic leiomyomata compared to infertility group (by 23 g/L; $p < 0.001$). The median duration of the operation was 120 minutes (range 60-510 minutes). The mean operation time in our case series was 161 +/- 77.6 minutes. Overall, the number of leiomyomata removed was positively associated with the duration of the operation and the fall in haemoglobin (difference between pre- and post-operative haemoglobin), but not significantly so ($p = 0.65$). The mean hospital stay was 3 days (SD 1.4 days).

Women between 36–40 years of age who required myomectomy were a large proportion of the cohort (n = 24) (see Table 2) with 18 of these women being nulliparous. In this subgroup, the indication for myomectomy was equally divided between infertility (n = 12) and symptomatic uterine leiomyoma (n = 12). Nine women were identified as having an irregular endometrial appearance. The endometrial cavity was breached during myomectomy in 7 cases of which 6 had an irregular endometrium. In this group, 15 attempted pregnancy following myomectomy and 5 women successfully conceived, resulting in 4 live births and one first trimester miscarriage.

Age	No of women	Parity		Indication		Ulipristal	GnRH analogue	Vasopressin Use recorded	Endometrial cavity opened	Inpatient stay days) (mean)	Complications	Subsequently attempted to conceive	Pregnancies	Outcome
		0	1+	Infertility	Other symptoms									
≤ 35	17	14	3	10	7	1	15	13	3	2.6	Intra-operative bleeding	14 2 UNK*	7	4 LB 1 TOP 1MISC 1 PREG
36-40	24	18	6	12	12	2	22	21	7	3	Post-operative bleeding Post-operative adhesions	15 2UNK	5	4 LB 1MISC
≥ 41	4	3	1	1	3	2	1	3	0	3		1	0	0

*Unknown (UNK) if patients tried for pregnancy or conceived after myomectomy, as follow-up was lost.

Table 2: *Characteristics and outcomes of the women who underwent myomectomy according to age groups.*

In the younger age group (≤ 35 years) there were 17 women of which 14 were nulliparous. In this subgroup, 8 women were identified as having an irregular endometrial appearance. There was endometrial cavity breach in 3 cases. Of the 14 women aged ≤ 35 years who tried for pregnancy following myomectomy, 7 conceived with 4 live births, one is currently pregnant in the third trimester, one had termination of pregnancy and one had a first trimester miscarriage.

In the older age group (≥ 41 years) there were 4 women, all of whom were parous. None of the myomectomies in this group had breaches of endometrial cavity. One patient tried for a pregnancy following myomectomy but was unsuccessful.

Overall, most women who had a myomectomy were between 30-45 years of age. Most were nulliparous and infertile (n = 23). At operation, 10 women had their cavity opened, of whom 9 were thought to have had an irregular cavity (and by inference, fibroids protruding into it) on ultrasound scan or MRI. All but 2 women had some form of oestrogen suppression before surgical management of their leiomyomata. Of those 2 patients, one underwent emergency myomectomy due to leiomyoma torsion and the other was postmenopausal (aged 55) with a progestogen containing intrauterine system in-situ. Intra-operative Vasopressin was documented to be given in 37 (82%) of women.

In this series, 39 women who underwent open myomectomy had no complication. In two cases, major complications developed related to the procedure. One woman had a major intraoperative haemorrhage and the other patient had major postoperative haemorrhage and septicaemia.

The first case was a woman who presented with menorrhagia and abdominal pains having an enlarged leiomyoma uterus, extending to her xiphisternum. She had 10 weeks of GnRH analogues for down-regulation. The procedure took 510 min, 28 leiomyomata were removed with the largest diameter being 110 mm (from the histology report). The endometrial cavity was not breached. She bled intraoperatively and was transfused with four units of allogeneic blood products. Total estimated blood loss was 3500 mls. She had postoperative pyrexia which was treated with antibiotics. She stayed in hospital for 6 days and was discharged home with haemoglobin of 103 g/L and oral ferrous sulphate supplementation.

The second woman had previously had a myomectomy and intraoperative haemorrhage. She presented with menorrhagia and lower abdominal pressure symptoms due to her uterine size. She was given GnRH analogues for 10 weeks and intraoperative Vasopressin was administered. A single leiomyoma was removed measuring 105 x 50 x 40 mm (confirmed by histology).Initial procedure time was 150 min. The endometrial cavity was not breached. She was transferred to the ward but subsequently became unstable with a fall in her haemoglobin to 65 g/L. She was then returned to theatre where a haematoma was evacuated from the myomectomy site. The uterine muscle was repaired and the bleeding controlled. She was given six units of blood products and two units of fresh frozen plasma. Total estimated blood loss was 2500 mls. She subsequently developed postoperative septicaemia. Her hospital stay was 7 days. On discharge, her haemoglobin was 104 g/L and she was prescribed oral ferrous sulphate supplementation.

If we exclude these two complex cases from our series analysis, the remaining patients had a mean fall in haemoglobin of only 20 g/L; mean preoperative haemoglobin would be 131 g/L, mean postoperative haemoglobin 111 g/L and mean estimated blood loss 264 mls. None of the remaining patients required blood transfusion and they had a mean post-operative hospital stay of 2.6 days.

Other minor complications that occurred in our case series (n = 4) included cellulitis (n = 1), wound infection (n = 1), post-operative pyrexia treated with antibiotics (n = 1) and adhesions formation (n = 1) confirmed by subsequent laparoscopy due to pelvic pains. The latter patient subsequently conceived and had a live birth by Caesarean section. Of the 45 women, 30 desired pregnancy, 12 conceived and there were 8 live births. The mean birth weight of the live births in this series was 3.2 kg (4 males and 4 females).

Uterine leiomyomata are commonly found in women of reproductive age and may cause infertility, pregnancy loss or pregnancy complications [5]. Larger leiomyomata (> 50 mm) should be managed individually, wherever their location, with the reproductive history being an important consideration [5]. Miscarriage rates are significantly reduced following myomectomy [5]. Abdominal myomectomy is the preferred surgical route for large subserous or intramural leiomyomata, multiple leiomyomata or anticipated entry into the uterine cavity. Each patient should be assessed and counselled individually for the benefits and risks of the surgery, surgical approach and the other available management options. The surgical approach should be considered carefully before offering it [5].

Meta-analyses report that submucosal leiomyomata appear to reduce the chance of pregnancy. Therefore, it is clearly recommended that these should be removed. The common OR (95% CI) for conception and delivery is 0.3 (0.1-0.7) and 0.3 (0.1-0.8), respectively [7]. Subserous leiomyomata do not appear to have any impact on fertility.

With regards to intramural leiomyomata, their effect on fertility remains unclear. There is evidence against myomectomy in women with intramural fibroids (intact endometrium on hysteroscopy) and otherwise unexplained infertility, regardless of their dimensions. If the patient has no other options of becoming pregnant, myomectomy might be considered after careful evaluation of the benefits and the risks and an individualised plan could be discussed [9]. Of note, when assisted conception is attempted, the presence of intramural leiomyomata, even with the absence of cavity distortion, may jeopardise its success. However, it is apparent that further well designed randomised controlled trials are needed to address this issue [10].

The clinical dilemma arises in women with asymptomatic intramural leiomyomata that are not distorting the endometrial cavity and who are experiencing conception difficulty or recurrent miscarriages. Without clinical evidence the risks should be aligned with the benefit based on fertility outcomes alone. Studies are heterogeneous but clinical pregnancy rates in the studies of laparoscopic

myomectomies are 50% higher in women with no other cause for infertility except leiomyomata and miscarriage rates reported as 10-20% [6, 11-15].

One prospective study of 181 women, aged less than 35 years with a single intramural myoma less than 40 mm, compared abdominal myomectomy versus no treatment for women with unexplained infertility. There was no statistical difference in pregnancy rates or miscarriage rates [6,16]. The authors concluded that myomectomies for single intramural leiomyomata do not improve the clinical pregnancy rate compared with that in control subjects [6,17].

In our study the majority of patients had pre-operative down-regulation with GnRH analogue or few patients had selective progesterone receptor modulator to reduce leiomyoma volume, reduce blood supply and reduce intra-operative blood loss. Ullipristal acetate presents a new option for medical management of symptomatic leiomyomata [18]. There is evidence that GnRH analogues for 3-4 months prior to leiomyoma surgery can reduce uterine volume and leiomyoma size. The GnRH analogues provide better control of pre-operative anaemia (due to menorrhagia), reduce intraoperative blood loss and decrease leiomyoma size thus reducing the chance of a midline incision [19].

The mean operation time in our case series was 161 minutes, differing only slightly from that of the laparoscopic approach which was 125 +/- 65.9 minutes reported by Altgassen., *et al.* [8]. The duration of the open myomectomy procedure was dependent on the number of leiomyomata removed. Removal of five or less leiomyomata took 138 minutes on average, whereas six of more took an average of 228 minutes in our series. Operative time varies in randomised controlled studies from no significance difference [6, 20-23] to significantly longer in the laparoscopic myomectomy group [24,25] compared with the abdominal myomectomy in a meta-analysis by 13 minutes (95% CI, 9.38 -17.18; $p < 0.001$) [26].

Major complications occurred in two challenging cases (4%) and minor complications included cellulitis, wound infection, post-operative pyrexia and adhesions formation (overall 8%). Known adhesion formation in our series was only seen in one woman (2%) but the true rate can only be accurately determined by a follow-up procedure to assess adhesion formation, unlikely to be feasible. In comparison with a laparoscopic technique, the intraoperative and postoperative complication rates were 1.4% and 5.7% respectively [8]. The largest case series of 2050 women undergoing laparoscopic myomectomies reported 2% for major complications and 9% for minor complications [6,27].

Laparoscopic myomectomy is a surgical option but there are limitations to its use and intraoperative complications may require the need to convert to open myomectomy or emergency hysterectomy. Only one hysterectomy was reported following 2050 laparoscopic myomectomies, due to haemorrhage [27]. Abdominal myomectomy is associated with emergency hysterectomy in 3-4% of the cases, due to excessive peri-operative haemorrhage [28,29]. The use of a power morcellator during laparoscopic myomectomy has recently come under scrutiny because of concerns about the dissemination of cells in the peritoneal cavity from unexpected malignant myoma [6,30]. There have also been reported cases of ectopic leiomyomata, endometriosis, adenomyosis, and ectopic ovarian tissue as a result of morcellation [31]. In addition, a review of the Manufacturer and user Facility Device Experience (MAUDE) database of the United States Food and Drug Administration reported 55 complications between 1993 and 2013, caused by the morcellator blade that injured intra-peritoneal organs (bowel and vascular injury including vena cava and aorta).

The strength of the open myomectomy technique is the multiple layer stitching and secure closure that reduces the chance of both haematoma and uterine rupture. However, uterine closure after myomectomy has not been examined in randomised controlled studies, and therefore with this lack of evidence the laparotomy approach would be the recommended practice [6]. Some researchers suggest that in laparoscopy the multilayer closure achieves the same degree of wound integrity as with abdominal myomectomy [6,32] and prevention of haematoma can be achieved by placement of full thickness well-spaced sutures to facilitate secure healing [6,33].

In women with infertility secondary to uterine leiomyomata, pregnancy rates following abdominal or laparoscopic myomectomy appear comparable. The laparoscopic approach is associated with quicker recovery, less subjectively reported postoperative pain, less postoperative febrile morbidity and shorter hospital stay when compared to the open approach [9,34]. In selected cases and centres with expertise, laparoscopic approach was associated with decreased length of hospital stay, short length of operating time and hospital resources [35].

The removal of all leiomyomata can never be guaranteed. Recurrence rates have been found to be similar between the laparoscopic and abdominal approaches. Risk factors for recurrence include the number, size and depth of leiomyoma, preoperative uterine size, women's age and use of GnRH analogue [6,26,36, 37].

Conclusion

The small number of patients in our case series does not allow clear conclusions. Further randomised controlled studies are required to address the question as to whether open myomectomy has a valid place in the modern and future surgical management of leiomyomata. For the time being, each surgical approach has relevant indications for each patient. Perceptions of myomectomy surgery as being bloody and messy are not confirmed in our cohort. The procedures are intensive in terms of hours spent in theatre. The mean operative time is almost three hours. Pregnancy rates in our institution were similar to the published averages for this procedure. The abdominal myomectomy approach remains a reasonable treatment option with good outcomes.

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