Accepted Manuscript

Laparoscopic myomectomy: A single centre retrospective review of 514 patients

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PII: \$1553-4650(17)30042-0

DOI: 10.1016/j.jmig.2017.01.008

Reference: JMIG 3041

To appear in: The Journal of Minimally Invasive Gynecology

Received Date: 6 December 2016
Revised Date: 6 January 2017
Accepted Date: 7 January 2017

Please cite this article as: Bean EMR, Cutner A, Holland T, Vashisht A, Jurkovic D, Saridogan E, Laparoscopic myomectomy: A single centre retrospective review of 514 patients, *The Journal of Minimally Invasive Gynecology* (2017), doi: 10.1016/j.jmig.2017.01.008.

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1 Laparoscopic myomectomy: A single centre retrospective

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- 10 Disclosure for conflicts of interest:
- AC received honoraria from Johnson and Johnson, Olympus, Karl Storz, hospitality from
- 12 Stryker and consultancy fee from Espiner. ES received honoraria from Johnson and
- Johnson, Olympus and Gedeon Richter and consultancy fee from Gedeon Richter.

15 Precis

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- 16 This is a retrospective review of 514 consecutive cases of laparoscopic
- myomectomy carried out by members of the minimal access surgery team at
- 18 University College London Hospital between January 2004 and December 2015.
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- 25 **Keywords:**
- Leiomyoma, myomectomy, laparoscopy, morcellation, laparoscopic 26
- 27 myomectomy

28 Abstract

- 29 STUDY OBJECTIVE: To review surgical outcomes and histopathological
- findings following laparoscopic myomectomy by a team at a university teaching
- 31 hospital.
- 32 DESIGN: This was a retrospective review of consecutive cases of laparoscopic
- 33 myomectomy carried out by members of our minimal access surgery team
- 34 between January 2004 and December 2015.
- 35 DESIGN CLASSIFICATION: Canadian Task Force Classification II-3
- 36 SETTING: University Teaching Hospital
- 37 PATIENTS: Women undergoing laparoscopic myomectomy
- 38 INTERVENTIONS: Laparoscopic myomectomy
- 39 MEASUREMENTS AND MAIN RESULTS: We collected women's demographic
- 40 data, clinical histories and surgical outcomes, including complication rates and
- 41 the incidence of undiagnosed uterine malignancy. 514 women were booked for
- 42 laparoscopic myomectomy during the study period. 512/514 [99.6% (95% CI
- 43 99.05 100.15)] of procedures were successfully completed. Two cases were
- converted to open surgery: one because of suspected uterine malignancy and
- another due to bowel injury at initial entry. The median number of myomas
- removed at laparoscopy was one (range 1 12, mode of 1). The median size of
- 47 the largest myoma removed at each procedure was 70mm (range 10 200 mm),
- 48 as assessed subjectively by the operating surgeon. The median blood loss was
- 49 73ml (range 5 to 3000ml. The median length of stay in hospital was 2 nights
- (range 0-24 nights). Breach of the uterine cavity occurred in 50/514 [9.7% (95%)
- 51 Cl 7.17 12.29)] of cases. Electro-mechanical morcellation was used in 496/514

52	[96.5% (95% CI 94.9 – 98.1)] of patients. 18/514 [3.5% (95% CI 1.91 – 5.09)]
32	[90.5% (95% C1 94.9 - 90.1)] or patients. 16/514 [5.5% (95% C1 1.91 - 5.09)]
53	women suffered significant complications: blood loss >1000ml (n=15), bowel
54	injury (n=1), bladder injury (n=1), small bowel obstruction secondary to port site
55	hernia (n=1). There were no cases of undiagnosed uterine malignancies
56	following myoma morcellation.
57	CONCLUSION: Laparoscopic myomectomy can be conducted with a low rate of
58	major complications and, in our experience, the chance of discovering occult
59	malignancy is very low.
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Introduction

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63 Uterine myomas are the most common benign tumours of the female genital tract, with a lifetime risk of approximately 70-80% before menopause (1). 64 65 They are clinically apparent in up to 25% of women and can cause significant morbidity, including prolonged or heavy menstrual bleeding, pelvic pressure, 66 pain or subfertility (2). Removal of myomas is frequently performed in 67 68 symptomatic women who wish to retain their uterus via the hysteroscopic or abdominal route. 69 70 Laparoscopic myomectomy was first performed in 1977(3, 4). In comparison to traditional 71 open myomectomy, the laparoscopic approach is associated with less postoperative pain, 72 lower rate of postoperative fever and shorter hospital stay (5). However, this may be at the 73 expense of longer operating times. Other potential advantages of the laparoscopic approach include a quicker recovery time with a more rapid return to work and activities of 74 75 daily living (6). The success of laparoscopic myomectomy is defined as a procedure carried out 76 77 by minimally invasive approach, without need for conversion to open surgery, 78 which results in a complete removal of fibroids selected for surgical excision, 79 without any major complications..Laparoscopic completion of the procedure 80 without serious complications,, depends on the selection criteria which are more 81 strict compared to those for open surgery. Laparoscopic approach is preferable 82 in women with a smaller number of myomas, whilst open surgery remains the 83 operation of choice for women with large multiple myomas. 84 Following the concerns of morcellation of undiagnosed leiomyosarcoma, the 85 need to establish the risk of this occurring and its subsequent effect on life

expectancy has been highlighted (7). Subsequent to the two statements by the

FDA (United States Food and Drug Administration) in April and November 2014,
which discouraged the use of electro-mechanical morcellation in the majority of
women due to the potential risk of spreading occult uterine sarcoma, centres
across the world have been encouraged to publish their surgical outcomes (8,9).

One of the key issues in ensuring successful laparoscopic myomectomy is

One of the key issues in ensuring successful laparoscopic myomectomy is patient selection. There are currently no generally agreed selection criteria to identify women who are suitable for laparoscopic myomectomy. In this report we give an analysis of our experience with laparoscopic myomectomy in our tertiary referral minimally invasive surgical unit.

The primary aim of the study was to assess the success of laparoscopic myomectomy. Secondary aims were to evaluate the complication rates and the risk of undiagnosed uterine malignancy.

Methods

This is a retrospective review of consecutive cases of laparoscopic myomectomy performed by members of our minimal access surgery team in a 12 year period between January 2004 and December 2015.

Cases were identified from the clinical notes, hospital operating theatre records, consultant diaries and histopathology database, and cross-referenced by name and hospital number to avoid duplicate entries. Data were collected on patient demographics (age, parity and menopausal status), presenting symptoms, preoperative imaging findings (number, size and location of myomas), operative details (number and size of myomas removed, complications, intra-operative blood loss, if breach of the endometrial cavity occurred and whether electromechanical morcellation was required for tissue extraction), post-operative

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outcomes (duration of inpatient stay, incidence and nature of complications) and histological diagnosis.

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All women underwent clinical examination and pre-operative imaging by ultrasound or MRI. There were no clearly defined selection criteria but in most cases the procedure was offered to pre-menopausal women with ≤3 intramural/submucous myomas and a dominant myoma measuring 5cm to 12cm in diameter. The selection criteria for subserous myomas were more relaxed both in terms of the number and size of myomas, provided that there was enough room in the abdominal cavity to safely introduce and maneuver laparoscopic instruments. The findings on preoperative ultrasound suggestive of uterine malignancy were: irregularly shaped tumours, blurred margins, signs of necrosis, peritoneal deposits and inability to visualize the endometrial cavity. Seventeen women were referred during the study period to the gynaecological oncology team with possible uterine sarcoma and 12 (70.6%) of these women had this diagnosis confirmed on histological diagnosis following open surgery. Laparoscopic myomectomies were performed using a similar technique under general anaesthesia in all cases. The urinary bladder was catheterised and a simple uterine manipulator was used. Most cases had four abdominal ports including an umbilical port for the telescope, two lateral ports and a suprapubic port, which was later used for morcellation. Patients with very large uteri/myomas had an epigastric port instead of the suprapubic port. The epigastric port was used for the telescope in these cases. 20 international units of synthetic vasopressin diluted in 20 mls of saline was injected into the myometrium as standard practice for all cases. Incisions to remove myomas were planned according to the location and size of myomas. Three different types of energy source

were used to make the incisions. This merely reflects changes in technology and availability. Initially monopolar diathermy was used. We then progressed to use either ultrasound energy(Ethicon Harmonic Scalpel®, Johnson & Johnson) or ultrasound with integrated bipolar energy (Olympus THUNDERBEATTM). A combination of energy device and mechanical instruments were used to enucleate myomas. If the endometrial cavity was opened, it was repaired first using monofilament absorbable sutures, before suturing the myometrium with absorbable traditional or barbed sutures. The serosa was closed separately and a barrier or fluid with anti-adhesion properties was used in selected cases. The myomas were morcellated using a single use electric morcellator (Ethicon Gynecare Morcellex Sigma® Johnson & Johnson, or Kebomed LiNA Xcise™). Skin incisions >10 mm were closed separately, including suturing of the rectus sheath. The amount of blood lost during surgery was determined semi-quantitatively by the operating surgeon. In all women, the material aspirated from the abdominal cavity, which consisted of irrigation fluid, myoma fragments and blood, was collected in suction containers and the volume was measured using a graduated volume scale. The total amount of blood loss was based on this objective measurement. There was no routine postoperative monitoring of haemoglobin or haematocrit and this was left to the lead surgeon's discretion. The urinary catheter was removed on the first or second postoperative day, and patients were allowed home if they felt well and were able to empty their bladder completely.

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Statistical analysis

Data were stored securely on a password protected EXCELTM spreadsheet (Microsoft Corporation, Seattle, USA) with adherence to standards of good clinical practice in research to ensure patient confidentiality. Statistical analysis was performed using SPSS software (SPSS Inc., Chicago, IL, USA). Demographic characteristics of included patients

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164	are expressed as median (range) and proportions are expressed as percentages with 95
165	confidence intervals.
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169	Ethical approval
170	Ethical approval was sought from and approved by the local research ethics committee
171	who deemed that full ethical approval was not required as the project was considered to
172	be solely service evaluation. Such projects do not require ethical review by an NHS or
173	Social Care Research Ethics Committee or management permission through the NHS
174	R&D office. Under these circumstances, there was no need to submit applications to the
175	NHS Research Ethics Committee (REC) or NHS/HSC R&D office (www.hra.nhs.uk).
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177	Results
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178	During the study period, from January 2004 to December 2015, a total of 903
179	women underwent myomectomy. 514 [57.2% (CI 53.97 – 60.43)] of these
180	women were scheduled for laparoscopic myomectomy. At the start of the study,
181	the proportion of myomectomies performed laparoscopically was less than 20%,
182	in the following years the majority of myomectomies were performed
183	laparoscopically with a ratio of approximately 1.5:1 (Figure 1).
184	The median age of women scheduled for laparoscopic myomectomy was 38
185	years (range 17 - 66). 393/514 [76.5% (95% CI 72.8 - 80.2)] were nulliparous
186	and 121/514 [23.5% (95% CI 19.8 - 27.2)] parous. 4/514 [0.8% (95% CI 0.02 -

1.54)] women were post-menopausal. The presenting symptoms are shown in

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Table 1.

189	The procedure was successfully completed laparoscopically in 512/514 [99.6%
190	(CI 99.05 – 100.15)] Two cases were converted to open surgery: one because of
191	suspected malignancy, which proved to be a uterine leiomyosarcoma on
192	histological examination and another due to bowel injury at the initial entry.
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194	Details of the pre-operative findings and intra-operative data are shown in Table 2.
105	The modian time lance between are energive imaging and timing of current, was 112 days
195	The median time lapse between pre-operative imaging and timing of surgery was 113 days
196	(range 0 – 1807).
197	The location of the dominant fibroid removed was posterior in 158/514 [31%
198	(95% CI 26.71 – 34.69)], anterior in 124/514 [24% (95% CI 20.4 – 27.8)], lateral
199	in 96/514 [19%(95% CI 15.3 – 22.1)], fundal in 73/514 [14% (95% CI 11.18 –
200	17.22)] and pedunculated in 57/514 [11% (95% CI 8.38 – 13.82)] women.
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203	Electro-mechanical morcellation was not used during laparoscopic myomectomy for
204	16/514 [3.1% (95% CI 1.61 -4.61)] women, in whom the myoma measured less than two
205	cm in diameter. During some more recent cases, the technique of a surgical containment
206	bag (Morcellation containment system ECOSAC, Espiner Medical Ltd ™) was used for
207	tissue extraction. The purpose of this was to ensure contained morcellation, complete
208	removal of the specimen and reduce the risk of disseminating tissue within the peritoneal
209	cavity.
210	The median length of hospital admission was 2 nights (range $0-24$).

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Overall there were 18 significant complications in the study group of 514 patients, which are displayed in Table 3. This gives an overall complication rate of 3.5% (95% CI 1.91 – 5.09).

Of the 15 women who had blood loss >1000ml, one woman had open surgery because of suspected malignancy, which proved to be a uterine leiomyosarcoma. Of the 14 women who had laparoscopic myomectomy and a blood loss >1000 mls, four [28.6% (95% CI 4.9 – 52.3) required a blood transfusion. The size, number and location of fibroids were similar in the 14 women who had an intraoperative blood loss of >1000 mls and the overall group.

In the woman that developed a port site hernia, this occurred through the 15mm suprapubic port site which was also used for morcellation, despite routine closure of the rectus sheath.

227 Histology

In 511/514 [99.4% (95% CI 98.73 – 100.07)] of the cases, histology confirmed benign leiomyoma. Two patients who had a laparoscopic procedure had a histological diagnosis of smooth muscle tumour of uncertain malignant potential (STUMP). One, who had no desire for future fertility, underwent hysterectomy. The histology revealed adenomyosis and benign leiomyomas, with no evidence of malignancy. The second had a CT and MRI, which were both normal and subsequent in vitro fertilisation and has had one successful birth. The third patient underwent conversion to open myomectomy, without morcellation, as the fibroid looked suspicious at initial inspection. Suspicion was raised on inspection of the mass, due to absence of a clear plane between the fibroid and the surrounding

myometrium, lack of a pseudocapsule, hypervascularity and the soft friable consistency of the tumour. She underwent open excision of the uterine mass, histology revealed a malignant leiomyosarcoma and post-operative imaging revealed distant metastases. One patient re-attended with worsening symptoms of menorrhagia one year after laparoscopic myomectomy. A pelvic ultrasound scan showed a large non-suspicious looking uterine mass. However, there was a clinical suspicion of malignancy due to the rapid growth of the uterine mass. The patient had no desire to retain fertility and underwent an open abdominal hysterectomy. Histology revealed a leiomyosarcoma. The original histology was reviewed and confirmed the initial diagnosis of a benign leiomyomas.

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treated medically with methotrexate.

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One patient, who had a single 10cm posterior intramural myoma removed when aged 37, without breach of the endometrial cavity or use of in-bag morcellation, was re-referred to the gynaecology unit seven years following her laparoscopic myomectomy, due to increasing abdominal pressure symptoms and urinary frequency. An ultrasound revealed 16 uterine myomas, including a 10cm pedunculated right lateral myoma. She chose to undergo a total abdominal hysterectomy. At laparotomy, she was found to have a 15cm parasitic myoma arising from the bladder wall and a 10cm right broad ligament myoma. During resection of the myomas, the bladder was opened and closed by primary repair and the decision was made to abandon the hysterectomy. Histology confirmed leiomyoma. Follow up ultrasound diagnosed four parasitic myomas, which measured five to ten centimetres in largest diameter and were arising from the right lateral port site and other distant peritoneal surfaces. As the patient was relatively asymptomatic, she chose to continue conservative management. One women developed intrauterine adhesions following laparoscopic myomectomy with a breach of uterine cavity and developed an intramural pregnancy which was successfully

Discussion

We report one of the largest single centre series on laparoscopic myomectomy to date
(10). All the cases were performed by experienced surgeons, including consultants and
senior trainees. Procedures were performed by two consultant experts in minimally
invasive surgery (ES and AC), either by themselves, senior trainees or consultants under
their direct supervision during the entire study period. This series appears to have a low
complication rate similar to other published series of laparoscopic myomectomy (Table 4).
The largest multicenter case series reported to date by Sizzi et al showed a major
complication rate of 2.02% [38/2050 (95% CI 1.4 – 2.6)] in their series of 2050
laparoscopic myomectomies, which is similar to 3.5% [18/514 (95% CI 1.91 – 5.09)] in this
series of 514 patients. The number and size of myomas in their report were similar to our
case series. Sizzi et al reported a laparo-conversion rate of 6/2050 cases [0.3% 995% CI
0.06 – 0.54)] and one case of hysterectomy due to excessive bleeding. These outcomes
are similar to our laparo-conversion rate of 2/514 [0.39% (95% CI -0.15 - 0.93)] and no
patients requiring conversion to hysterectomy (11). Dubuisson et al reported a conversion
rate of 16/213 [7.5% (95% CI 3.96 – 11.04)], which was correlated with the size of the
myoma and three times more likely for anterior myomas compared with posterior or fundal
location. Their recommendation was that laparoscopic myomectomy is a reliable technique
but should only be proposed when a myoma is less than 8cm and there are not more than
two myomas to be removed (12). Our series included larger myomas (mean 70mm, range
10 – 200mm) than the cut-off proposed by Dubuisson et al and had a lower laparo-
conversion rate. Over time, advances in laparoscopic imaging, energy sources and suture

technology, especially ultrasound energy sources and barbed sutures in more recent years, have aided the safety and efficacy of laparoscopic surgery. This has enabled a reduction in overall operating time and facilitated development of more complex laparoscopic surgery. This may have resulted in our lower conversion and complication rates than other series.

One of the key issues in ensuring successful laparoscopic myomectomy is patient selection. Our case series shows that myomas of all locations in greater number and size can be successfully and safely removed at laparoscopy with an acceptable complication rate. There are no universally accepted selection criteria published for women in whom laparoscopic myomectomy is planned. As part of patient selection, it is invaluable to have detailed mapping of the fibroids by pre-operative imaging. This will also ensure that the myomas are more effectively localized and removed at laparoscopic surgery, in the absence of tactile examination, and will help avoid persistent myomas.

Table 4 shows data presented from other large case series of laparoscopic myomectomy. It shows the median age of the patients, size and number of myomas safely removed. The median age of patients ranged from 31.7 to 40.33 years, similar to 38 years in this series. The median number of myomas removed at laparoscopic myomectomy ranged from 1.0 to 3.5 and the median size of myomas removed ranged from 4 to 7.8cm. These figures are similar to the median of one myoma excised, with a median size of 70mm in our series. Table 5 shows reported complications associated with laparoscopic myomectomy. The literature is varied in the style and completeness in which complications have been reported. The majority of studies reporting their experience of laparoscopic myomectomy are based on patient data that has been collected retrospectively and are therefore subject to recall bias. Only six studies reported their overall complication rate, which ranged from

312	2.08 to 11.1%, compared to 3.5% (95% CI 1.91 – 5.09) in our series. Twelve studies
313	reported their laparo-conversion rate to open surgery, which ranged from 0.1% to 29% of
314	cases, compared to 0.39% (95% CI -0.15 – 0.93) in our series. Only one death was
315	reported following laparoscopic myomectomy. The median estimated blood loss ranged
316	from 90 to 384ml and median length of stay from 0.58 to 5 days in hospital, which is similar
317	to the 73ml estimated blood loss and two nights median length of stay in our series. Only
318	three studies reported findings of unexpected malignancy, which ranged from 0.1 to 0.4%
319	of cases, similar to the 0.2% of cases in our series. The frequency in which the uterine
320	cavity was opened was reported by six studies and ranged from 0.02 to 11.7% of cases,
321	compared to 9.7% in our series.
322	In a series of 128 patients who underwent myomectomy, Campo et al showed that women
323	were more likely to conceive after laparoscopic treatment of myomas compared with an
324	open procedure (laparoscopy versus laparotomy: OR 14.062, 95% CI: 1.40-141.15) (13).
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326	The FDA discouraged the use of electro-mechanical morcellation in April 2014 (8). The
327	American Association of Gynecologic Laparoscopists (AAGL) and The European Society
328	for Gynaecological Endoscopy (ESGE) released statements advising caution when
329	considering morcellation in the postmenopausal age group. (34,35,36). Four of our
330	patients were post-menopausal and requested myoma removal instead of hysterectomy.
331	Pelvic ultrasound evaluation of the myometrium was reassuring and the maximum myoma
332	size ranged from 30 to 80mm in diameter. Histological examination in these four women
333	showed benign leiomyoma.
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335	The two cases in which histology revealed a STUMP, were both pre-menopausal women
336	aged 37 years and 39 years, who had myomas measuring 60mm in diameter. The woman

who had a suspicious uterine mass that underwent open excision and histology proved to be a leiomyosarcoma, was 32 years old with no risk factors for malignancy and a 100mm myoma on ultrasound.

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Some have suggested pre-operative histological diagnosis prior to laparoscopic myomectomy in women who have risk factors for malignancy before morcellation is considered (37). In order to obtain a tissue sample, without risking dissemination of cells into the peritoneal cavity, a transcervical approach can be considered. This is carried out under ultrasound or CT guidance, to ensure accurate location of the biopsy and to minimise risk to other structures, including the uterine serosa. Although the potential for trans-tubal passage of cells remains, the risk of intra-peritoneal spread is reduced with this method (38).

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Another alternative is to contain the morcellation process to reduce the risk of spreading malignancy with the concept of a contained morcellation bag (39). We utilised a bag for five of our cases. The adoption of such a system is not yet established but may potentially remove the risk of dissemination at morcellation (40, 41). In addition the rare reported complication of iatrogenic peritoneal leiomyomatosis might be avoided (42).

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It is generally considered that thorough lavage and meticulous care in extraction of all myoma fragments should follow laparoscopic myomectomy before completion of surgery. If a myoma appears suspicious at the time of fertility sparing surgery for, it would be reasonable to carry out an open myomectomy rather than to continue laparoscopically, which may reduce the risk of dissemination. In those patients where fertility preservation is not desirable and a uterine mass appears suspicious, a hysterectomy should be considered. In this study, there was one case of parasitic myomas found following

laparoscopic myomectomy. However, the literature suggests that this diagnosis may not
become apparent for several decades following the primary procedure, so longer term
follow up is required to demonstrate the incidence in this study group.
It is important to consider the chance of interval sarcoma in previously assumed benign
myomas. There was one case of interval sarcoma following laparoscopic myomectomy in
this series. Signs that should raise suspicion of interval sarcoma include the onset of
symptoms suspicious of malignancy, irregular or heavy vaginal bleeding, new onset of
pressure symptoms, unexplained fever, weight loss, early satiety or systemic illness.
Conclusion
Our study confirms that laparoscopic myomectomy is an important addition to
gynaecological surgery. Once the practice is established, the number of myomectomies
performed by laparoscopic technique exceeds those done by open surgery.
In experienced hands, laparoscopic myomectomy is safe and effective, with a low
complication rate of less than 10%.
In this series, there were no cases of inadvertent morcellation of uterine sarcoma.
However, morcellation criteria need to be in place to minimize the risk of this potential
complication.

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387	References
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- 1. Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM. High
 cumulative incidence of uterine leiomyoma in black and white women:
 ultrasound evidence. American journal of obstetrics and gynecology. 2003
 Jan 31;188(1):100-7.
- 393 2. Stewart EA. Uterine fibroids. The Lancet. 2001 Jan 27;357(9252):293-8.
- 394 3. Saridogan E, Cutner A. Endoscopic management of uterine fibroids. Human Fertility. 2006 Jan 1;9(4):201-8.
- 4. Saridogan E. Surgical treatment of fibroids in heavy menstrual bleeding. Women's
 Health. 2016 Jan;12(1):53-62.
- 5. Bhave Chittawar P, Franik S, Pouwer AW, Farquhar C. Minimally invasive surgical techniques versus open myomectomy for uterine fibroids. Cochrane Database Syst Rev. 2014;10.
- 6. Tulandi T, Youseff H. Laparoscopy-assisted myomectomy of large uterine myomas. Gynaecological Endoscopy. 1997 Apr 1;6(2):105-8.
- 7. Pritts EA, Vanness DJ, Berek JS, Parker W, Feinberg R, Feinberg J, Olive DL. The prevalence of occult leiomyosarcoma at surgery for presumed uterine fibroids: a meta-analysis. Gynecological surgery. 2015 Aug 1;12(3):165-77.
- 8. US Food and Drug Administration. Laparoscopic uterine power morcellation in hysterectomy and myomectomy: FDA safety communication. Online: http://www. fda. gov/medicaldevices/safety/alertsandnotices/ucm393576. htm. April 17 2014.
- US Food and Drug Administration. Updated laparoscopic uterine power
 morcellation in hysterectomy and myomectomy: FDA safety communication. Online:
 http://www. fda. gov/MedicalDevices/Safety/AlertsandNotices/ucm424443. htm.
 November 24 2014.

	DLAN
413	10. Buckley VA, Nesbitt-Hawes EM, Atkinson P, Won HR, Deans R, Burton A, Lyons
414	SD, Abbott JA. Laparoscopic myomectomy: clinical outcomes and comparative
415	evidence. Journal of minimally invasive gynecology. 2015 Jan 31;22(1):11-25.
416	11. Sizzi O, Rossetti A, Malzoni M, Minelli L, La Grotta F, Soranna L, Panunzi S,
417	Spagnolo R, Imperato F, Landi S, Fiaccamento A. Italian multicenter study on
418	complications of laparoscopic myomectomy. Journal of minimally invasive
419	gynecology. 2007 Jul 31;14(4):453-62.
420	12. Dubuisson JB, Chapron C, Levy L. Difficulties and complications of laparoscopic
421	myomectomy. Journal of gynecologic surgery. 1996;12(3):159-65.
422	13. Campo S, Campo V, Gambadauro P. Reproductive outcome before and after
423	laparoscopic or abdominal myomectomy for subserous or intramural myomas.
424	European Journal of Obstetrics & Gynecology and Reproductive Biology. 2003 Oct
425	10;110(2):215-9.
426	14. Kumakiri J, Takeuchi H, Itoh S, Kitade M, Kikuchi I, Shimanuki H, Kumakiri Y
427	Kuroda K, Takeda S. Prospective evaluation for the feasibility and safety of
428	vaginal birth after laparoscopic myomectomy. Journal of minimally invasive
429	gynecology. 2008 Aug 31;15(4):420-4.
430	15. Paul GP, Naik SA, Madhu KN, Thomas T. Complications of laparoscopic
431	myomectomy: a single surgeon's series of 1001 cases. Australian and New
432	Zealand Journal of Obstetrics and Gynaecology. 2010 Aug 1;50(4):385-90.
433	16. Malzoni M, Sizzi O, Rossetti A, Imperato F. Laparoscopic myomectomy: a
434	report of 982 procedures. Surgical technology international. 2005
	. Sport of ode procedures our great tool holdey international 2000

Dec;15:123-9.

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- 17. Sandberg EM, Cohen SL, Jansen FW, Einarsson JI. Analysis of Risk
 Factors for Intraoperative Conversion of Laparoscopic Myomectomy. Journal
 of minimally invasive gynecology. 2015 Nov 9.
- 18. Koo YJ, Lee JK, Lee YK, Kwak DW, Lee IH, Lim KT, Lee KH, Kim TJ.

 Pregnancy outcomes and risk factors for uterine rupture after laparoscopic myomectomy: a single-center experience and literature review. Journal of minimally invasive gynecology. 2015 Oct 31;22(6):1022-8.

- 19. Seracchioli R, Manuzzi L, Vianello F, Gualerzi B, Savelli L, Paradisi R, Venturoli S. Obstetric and delivery outcome of pregnancies achieved after laparoscopic myomectomy. Fertility and sterility. 2006 Jul 31;86(1):159-65.
- 20. Yoo EH, Lee PI, Huh CY, Kim DH, Lee BS, Lee JK, Kim D. Predictors of leiomyoma recurrence after laparoscopic myomectomy. Journal of minimally invasive gynecology. 2007 Dec 31;14(6):690-7.
- 21. Sinha R, Hegde A, Mahajan C, Dubey N, Sundaram M. Laparoscopic myomectomy: do size, number, and location of the myomas form limiting factors for laparoscopic myomectomy?. Journal of minimally invasive gynecology. 2008 Jun 30;15(3):292-300.
- 22. Radosa MP, Winzer H, Mothes AR, Camara O, Diebolder H, Weisheit A, Runnebaum IB. Laparoscopic myomectomy in peri-and post-menopausal women is safe, efficacious and associated with long-term patient satisfaction. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2012 Jun 30;162(2):192-6.
- 23. Saccardi C, Gizzo S, Noventa M, Ancona E, Borghero A, Litta PS. Limits and complications of laparoscopic myomectomy: which are the best predictors? A

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- large cohort single-center experience. Archives of gynecology and obstetrics.
- 461 2014 Nov 1;290(5):951-6.
- 24. Landi S, Zaccoletti R, Ferrari L, Minelli L. Laparoscopic myomectomy:
- technique, complications, and ultrasound scan evaluations. The Journal of
- the American Association of Gynecologic Laparoscopists. 2001 May
- 465 31;8(2):231-40
- 25. Altgassen C, Kuss S, Berger U, Löning M, Diedrich K, Schneider A.
- 467 Complications in Iaparoscopic myomectomy. Surgical Endoscopy And Other
- 468 Interventional Techniques. 2006 Apr 1;20(4):614-8.
- 26. Rossetti A, Sizzi O, Chiarotti F, Florio G. Developments in techniques for
- 470 laparoscopic myomectomy. JOURNAL-SOCIETY OF
- 471 LAPAROENDOSCOPIC SURGEONS. 2007 Jan 1;11(1):34.
- 27. Chen C. Laparoscopic myomectomy for large myomas. International
- 473 surgery. 2005 Dec;91(5 Suppl):S77-80.
- 28. Tinelli A, Hurst BS, Hudelist G, Tsin DA, Stark M, Mettler L, Guido M,
- 475 Malvasi A. Laparoscopic myomectomy focusing on the myoma
- 476 pseudocapsule: technical and outcome reports. Human reproduction. 2012
- 477 Feb 1;27(2):427-35.
- 478 29. Mettler L, Schollmeyer T, Shelat NR, Jonat W. Update on laparoscopic
- myomectomy. Gynecological Surgery. 2005 Sep 1;2(3):173-7.
- 480 30. Malzoni M, Rotond M, Perone C, Labriola D, Ammaturo F, Izzo A, Panariello
- S, Reich H. Fertility after laparoscopic myomectomy of large uterine myomas:
- operative technique and preliminary results. European journal of
- 483 gynaecological oncology. 2002 Dec;24(1):79-82.

ACCEPTED MANUSCRIPT			TOTAL			NIT	OD.	OD VI	
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31. Marret H, Chevillot M, Giraudeau B, of the French TS, of Gynaecology S. A
retrospective multicentre study comparing myomectomy by laparoscopy and
laparotomy in current surgical practice: What are the best patient selection
criteria?. European Journal of Obstetrics & Gynecology and Reproductive
Biology. 2004 Nov 10;117(1):82-6.

- 32. Nezhat FR, Roemisch M, Nezhat CH, Seidman DS, Nezhat CR. Recurrence rate after laparoscopic myomectomy. The Journal of the American Association of Gynecologic Laparoscopists. 1998 Aug 31;5(3):237-40.
- 33. Dessolle L, Soriano D, Poncelet C, Benifla JL, Madelenat P, Daraï E.

 Determinants of pregnancy rate and obstetric outcome after laparoscopic myomectomy for infertility. Fertility and sterility. 2001 Aug 31;76(2):370-4.
- 34. Worldwide AA. AAGL practice report: morcellation during uterine tissue extraction. J Minim Invasive Gynecol. 2014 Jul;21(4):517-30.
- 35. Bieber EJ, Sanfilippo JS, Horowitz IR, Shafi MI, editors. European Society of Gynaecological Endoscopy (ESGE). Statement on morcellation (of presumed fibroids appearing to be sarcomas). ESGE executive board. 2014. Clinical gynecology. Cambridge University Press; 2015 Apr 23
- 36. Brölmann H, Tanos V, Grimbizis G, Ind T, Philips K, van den Bosch T, Sawalhe S, van den Haak L, Jansen FW, Pijnenborg J, Taran FA. Options on fibroid morcellation: a literature review. Gynecological surgery. 2015 Feb 1;12(1):3-15.
- 37. Tulandi T, Ferenczy A. Biopsy of uterine leiomyomata and frozen sections before laparoscopic morcellation. Journal of minimally invasive gynecology. 2014 Oct 31;21(5):963-6.
- 38. Kawamura N, Ichimura T, Ito F, Shibata S, Takahashi K, Tsujimura A, Ishiko O, Haba T, Wakasa K, Ogita S. Transcervical needle biopsy for the differential

500	diagnosis between utarias sersoms and biomy one Concer 2002 Mar
509	diagnosis between uterine sarcoma and leiomyoma. Cancer. 2002 Mar
510	15;94(6):1713-20.
511	39. Einarsson JI, Cohen SL, Fuchs N, Wang KC. In-bag morcellation. Journal of
512	minimally invasive gynecology. 2014 Oct 31;21(5):951-3.
513	40. Cohen SL, Greenberg JA, Wang KC, Srouji SS, Gargiulo AR, Pozner CN, Hoover
514	N, Einarsson JI. Risk of leakage and tissue dissemination with various contained
515	tissue extraction (CTE) techniques: an in vitro pilot study. Journal of minimally
516	invasive gynecology. 2014 Oct 31;21(5):935-9.
517	41. Cohen SL, Einarsson JI, Wang KC, Brown D, Boruta D, Scheib SA, Fader AN,
518	Shibley T. Contained power morcellation within an insufflated isolation bag.
519	Obstetrics & Gynecology. 2014 Sep 1;124(3):491-7.
520	42. Heller DS, Cracchiolo B. Peritoneal nodules after laparoscopic surgery with uterine
521	morcellation: review of a rare complication. Journal of minimally invasive
522	gynecology. 2014 Jun 30;21(3):384-8.
523	
524	Figure 1 Legend
525	Figure 1. Percentage of myomectomies performed by laparoscopic approach during
526	the study period
527	

Table 1: Indications for surgery (n=514)

Symptom	N (%)
	134 (26.1)
Menorrhagia + Pelvic pain	
Menorrhagia	86 (16.7)
Pelvic pain	84 (16.3)
Infertility	44 (8.6)
Menorrhagia + Pressure symptoms	25 (4.9)
Menorrhagia + Infertility	24 (4.7)
Pelvic pain + Infertility	15 (2.9)
Pressure symptoms	15 (2.9)
Pelvic pain + Pressure symptoms	14 (2.7)
Recurrent miscarriage	2 (0.4)
Infertility + Pelvic pain	2 (0.4)
(Menorrhagia, Infertility, Pelvic pain, Pressure symptoms)	69 (13.4)
Total	514 (100%)

Table 2: Pre-operative ultrasound findings and intra-operative data

Number of uterine myomas on ultrasound	*2 (1 – 13)
Diameter of dominant myoma measured on pre-operative ultrasound (mm)	*70 (10 - 214)
Number of uterine myomas removed at procedure	*1 (1 – 12)
Size of largest myoma removed at procedure as assessed subjectively by the operating surgeon (mm)	*70 (10 – 200)
Blood loss (ml)	*73 (5 – 3000)
Breach of endometrial cavity	**50/514 [9.7% (7.17 – 12.29)]
Power morcellation	**496/514 [96.5% (94.91 – 98.09)]
In bag morcellation	**5/514 [1% (0.12 – 1.82)]

^{*} median (range)

^{**} n [% (95% Confidence interval)]

Table 3: Significant complications

COMPLICATION		n [% (95% CI)]
	Bladder injury	1/514 [0.2% (-0.19 – 0.57)]
Intra-operative complications	Bowel injury	1/514 [0.2% (-0.19 – 0.57)]
	Blood loss >1000ml	15/514 [2.9% (1.46 – 4.38)]
Wound complications	Port site hernia with bowel obstruction	1/514 [0.2% (-0.19 – 0.57)]

Table 4 : Large published case series of laparoscopic myomectomy

	II C	Age, mean ± SD (range) [IQR]	Myomas removed, Median number ± SD (Range)	Size of myoma removed, cm, Median ± SD [iQR] (Range)	Estimated blood loss, ml, Median ± SD (Range)	Length of stay, Nights, Median ± SD (Range)
Sizzi 2007 (11) *M	2050	36.12 ± 5.35	2.26 ± 1.8 (1 - 15)	6.40 ± 2.6 (1-20)	-	1.99 ± 0.9
Kumakiri 2008 (14) *S	1334	33.6 ± 3.4	3.5 ± 3.6 (2.8 - 4.2)	6.61 ± 1.88 (62.6 - 69.2)	115.2 ± 225.1	-
Paul 2010 (15) *S	1001 **	32.62 (19-57)	1.97 (1 - 17)	1 - 20	248 (20 - 1000)	1.5 (1 - 5)
Malzoni 2006 (16) *M	982	-	2.23 (1 - 8)	6.72 ± 2.71 (1 - 20)	-	2.02 ± 0.61
Sandberg 2016 (17) *S	731 ***	40.33 ± 7.28	3.54 ± 4.10		181.54 ± 342.02	0.58 ± 1.00
Koo 2015 (18)	523	31.7 ± 3.5 [31.4, 32.0]	single 64.8% multiple 35.2%	4.9 ± 2.5 [4.7, 5.1] (1 - 15)	162.5 ± 156.2	3.2 ± 1.5
Serracchioli 2006 (19)	514	33.69 +- 3.61	2.55 ± 1.78	5.44 ± 2.46	-	-
Yoo 2007 (20)	512	33.0 (22 - 50)	1.0 (1 - 10)	-	125 (50 - 1000)	4.0 (1 - 11)
Sinha 2008 (21) *S	(21) *S 505 34.36 ± 5.706		1.85 ± 5.706	1.85 ± 5.706 5.86 ± 3.3		24.64 ± 5.45 hours
Radosa 2012 (22)	451***	A: 50.1 ± 7.4; B: 33.6 ± 4.6	A: 1.7 ± 1; B: 1.9 ± 1.6	A: 4.5 ± 1.9; B 4.82 ± 2.2	-	A: 5 ± 1.5; B: 4.4 ± 1
Saccardi 2014 (23)	444	36.7 ± 6.4	-	7.6 ± 2.7	184.1 ± 233.5	2.54 ± 1.1
Landi 2001 (24)	368	-	- () Y	-	384.14 ± 324.8	2.89 ± 1.3
Altgassen 2006 (25)	351	34.5 ± 4.6	1 (1 - 14)	5.3	-	-
Rosetti 2007 (26)	332	35.47 ± 4.8	2.23 ± 1.7 (1 - 8)	6.02 ± 2.71 (1 - 20)	-	2.0 ± 0.57
Chen 2005 (27)	300	-	-	(4 - 20)	300	-
Tinelli 2012 (28)	235	36.5 ± 4.3 (28 - 43)		6.6 ± 3.5 (4 - 10)	118 ± 27.9	****
Dubuisson 1996 (12)	213	-	Y -	-	-	-
Mettler 2005 (29)	178		-	4 (3 - 10)	-	2 ± 0.5
Malzoni 2003 (30)	144	-	1.6	7.8 (5 - 18)	-	2.6 (2 - 5)
Marret 2004 (31)	126	-	-	-	226 ± 320	3.6 ± 1.3
Nezhat 1998 (32)	114	38 (25 - 51)	3	5.9	200 (25 - 1200)	(<24hours - 4 days)
Dessolle 2001 (33)	88	36.1 ± 2.1	1.7 ± 0.6 (1 - 4)	6.2 ± 1.8	-	3.0 ±1(1-10)

^{*}S = single centre; *M = multicentre

^{** 87%} morcellation, 13% mini-laparotomy/colpotomy

^{*** 388} laparoscopic, 342 robotic

^{****} A = peri/postmenopausal; B = premenopausal

^{***** 203 (86.3%)} patients were discharged <48h after surgery (2 - 4 days)

Table 5: Reported complications associated with laparoscopic myomectomy in other published case series

	= c	Unexpected Malignancy, n (%)	Failure to complete surgery, n (%)	Hysterectomy, n (%)	Laparo-conversion rate, n (%)	Breach of uterine cavity, n (%)	Overall Complication Rate, n (%)	Minor Complication, n (%)	Major Complication, n (%)	Intraoperative complication, n (%)	Postoperative complication, n (%)	Haemorrhage, n (%)	Blood Transfusion, n (%)	Haematoma formation, n (%)	Bladder injury, n (%)	Bowel injury, n (%)	Acute Kidney Injury, n (%)	Death, n (%)
Sizzi 2007 (11) *M	2050	2 (0.09)	7 (0.34)	2 (0.10)	6 (0.29)	-	225 (11.1)	187(9.1)	38(2.02)	G	-	14(0.68)	3 (0.15)	10(0.48)	-	1 (0.04)	1 (0.04)	-
Kumakiri 2008 (14) *S	1334	-	-	-	-	13(11.7)	-	-	- /	1-4	-	-	-	-	-	-	-	-
Paul 2010 (15) *S	1001**	1 (0.10)	-	-	1 (0.10)	-	72(7.16)	45(4.54)	26(2.62))-	-	1 (0.1)	10 (1.0)	2 (0.20)	3 (0.30)	0	-	1 (0.10)
Malzoni 2006 (16) *M	982	-	-	-	13(1.29)	-	-	-	3 (0.31)	-	-	-	-	-	-	-	-	-
Sandberg 2016 (17) * S	731***	-	-	1 (0.14)	8 (1.09)	-	-	-	-	-	-	-	3 (0.41)	-	-	1 (0.14)	-	-
Serracchioli 2006 (19)	514	-	-	-	-	10(0.19)	-	-		-	-	-	-	-	-	-	-	-
Yoo 2007 (20)	512	-	-	-	-	8 (1.6)	52(10.2)	-	V- 7	-	-	-	7 (1.4)	-	1 (0.20)	1 (0.20)	-	-
Sinha 2008 (21) *S	505	2 (0.40)	-	1 (0.20)	1 (0.20)	35 (6.9)	-	-	<u> </u>	-	-	-	31(6.14)	1 (0.20)	-	-	-	-
Radosa 2012 (22)	451****	-	-	-	1 (0.22)	1 (0.02)	-	-	3 (0.67)	A: 3(3.5) B: 7(1.9)	-	-	3 (0.67)	1 (0.22)	1 (0.22)	3 (0.67)	-	-
Saccardi 2014 (23)	444	-	-	-	6 (1.35)	-	-	ľ	-	-	-	-	2 (0.45)	-	-	-	-	-
Landi 2001 (24)	368	-	-	-	-	-	- /	-	-	12(3.34)	-	-	10 (2.7)	-	-	-	-	-
Altgassen 2006 (25)	351	-	1 (0.28)	1 (0.28)	1 (0.28)	-	9 (2.6)	7-	-	9 (2.60)	20(5.70)	2 (0.57)	2 (0.57)	2 (0.57)	-	3 (0.85)	-	-
Rosetti 2007 (26)	332	-	-	-	3 (0.90)	-		<i>J</i> -	-	0	2 (0.60)	-	0	-	-	1 (0.30)	1 (0.30)	-
Tinelli 2012 (28)	235	-	-	-	-	-	-	-	-	-	0	-	0	1 (0.40)	-	-	-	-
Dubuisson 1996 (12)	213	-	-	-	16(7.51)	-	8 (3.8)	-	-	-	-	-	-	-	-	-	-	-
Mettler 2005 (29)	178	-	-	-	-	- 4) -	-	-	-	-	-	-	2 (1.1)	-	-	-	-
Malzoni 2003 (30)	144	-	-	-	2 (1.39)	-/\	3 (2.08)	-	-	-	-	-	1 (0.70)	-	-	-	-	-
Marret 2004 (31)	126	-	-	-	37(29.4)	-) -	-	-	-	-	-	0	-	-	-	-	-
Dessolle 2001 (33)	88	-	-	-	-	3 (3.4)	-	-	0	-	-	-	0	-	-	1 (1.14)	-	-

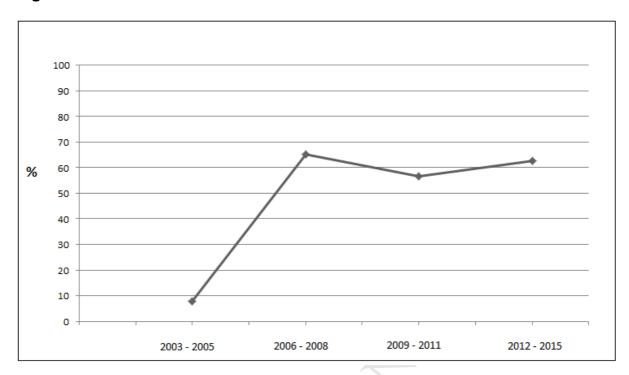
^{*}S = single centre; *M = multicentre

^{** 87%} morcellation, 13% mini-laparotomy/colpotomy

^{*** 388} laparoscopic, 342 robotic

^{****} A = peri/postmenopausal; B = premenopausal

Figure 1:



Precis

This is a retrospective review of 514 consecutive cases of laparoscopic myomectomy carried out by members of the minimal access surgery team at University College London Hospital between January 2004 and December 2015.