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Long-term results of laparoscopic myomectomy: recurrence rate in comparison with abdominal myomectomy

Alfonso Rossetti[1], Ornella Sizzi[1], Liberato Soranna[2], Francesco Cucinelli[2], Salvatore Mancuso[2] and Antonio Lanzone[3,4]

[1]Gynecological Endocrinology Unit, Columbus Hospital of Rome, [2]Department of Obstetrics and Gynecology, UCSC of Rome and [3]Oasi Institute of Research, Troina (EN), Italy

[4]To whom correspondence should be addressed at: Department of Obstetrics and Gynecology, UCSC Lgo Gemelli 8, 00168 Rome, Italy. E-mail: alanzone@rm.unicatt.it

Laparoscopic myomectomy is still a debated procedure and there are conflicting opinions regarding the recurrence rate. Laparoscopic myomectomy may present a higher risk of recurrence compared with abdominal myomectomy. The aim of this investigation was to analyse the recurrence rate of myomas after surgery. From January 1991 to June 1998, 165 myomectomies were performed for symptomatic myomas measuring at least 3 cm in diameter and numbering seven or less per patient. During the first 3 years of this survey, 81 patients were randomized for abdominal or laparoscopic myomectomy. Transvaginal ultrasound examination was performed within 15–30 days of surgery and every 6 months for a post-operative period of 40 months. The two groups had similar pre-operative clinical features and the number and volume of myomas did not differ between the two groups. At the end of the study the group of abdominal myomectomies showed nine recurrences (23%) against 11 (27%) of the laparoscopic group. In order to evaluate the recurrence rate in relation to several risk factors, laparoscopic myomectomies were performed from 1991 in 84 patients who agreed to follow-up (and were not in the randomized group). Of these, 78 patients were evaluated with transvaginal ultrasound for a mean interval of 26 months and 17 (21.78%) recurrences were found. Most recurrences (75%) were seen at ultrasound between 10 and 30 months after surgery. The patient's age, pre- and post-operative gravidity and parity had no influence on recurrence. Neither the number of myomas removed nor the depth of penetration or size were positively associated with the risk of recurrence. However, an associated risk factor was pre-operative gonadotrophin-releasing hormone agonist treatment ($P < 0.02$). None of the women with recurrence required additional surgery. We conclude that laparoscopic myomectomy is a reliable procedure. The recurrence rate is similar to that seen after abdominal myomectomy.

Key words: laparoscopy/myomectomy/recurrence

Introduction

Laparoscopic myomectomy is still a debated procedure: although it is now stated that laparoscopic myomectomy is feasible (Daniell and Guerly, 1991; Nezhat *et al.,* 1991; Dubuisson *et al*., 1991; Hasson *et al.*, 1992; Tulandi and Labarge, 1997), conflicting opinions are still held regarding the supposed higher recurrence rate. It has been suggested that laparoscopic myomectomy may present a higher risk of recurrence (Nezhat *et al.*, 1998) compared with abdominal myomectomy (Butram and Reiter, 1981; Candiani *et al.*, 1991), but prospective or randomized studies are lacking.

Our study shows the long-term results of laparoscopic myomectomy performed from January 1991 to June 1998. The aim of this investigation was to analyse the recurrence rate. All patients were followed and studied by transvaginal ultrasound before and after the procedure. In the first part of the study, a group of patients was selected, randomized for laparoscopic or abdominal myomectomy and followed for 40 months. The results of these procedures have been compared. In addition, over the years, all those patients who underwent laparoscopic myomectomy have been followed in order to evaluate the recurrence rate with associated risk factors and the reintervention rate.

Materials and methods

Patient selection

From January 1991 to June 1998, 165 laparoscopic myomectomies were performed in our department for symptomatic myomas. Indications were infertility, recent and significant uterine enlargement and symptoms (pelvic pain, menometrorrhagia and abnormal bleeding). Inclusion criteria were age $\leq$42 years, the presence of at least one symptomatic myoma $>$3 cm, a number of myomas equal or less than seven and the absence of submucous myomas which could be removed by hysteroscopy. Some authors (Dubuisson and Chapron, 1996;

Donnez *et al.*, 1996) suggested that no more than three or four myomas with diameters <7–8 cm are to be removed; however, others (Hasson *et al.*, 1992; Cittadini, 1998) believe in individual choice based on pathological findings and surgical skill. We chose not to perform laparoscopic myomectomy when more than seven myomas were present because in these cases we believed that the procedure was excessively time-consuming and that the surgeon could miss the smaller myomas after the uterus has been incized and repaired in many places.

Operative technique

Myomectomies were performed with a standard technique using three suprapubic ports. The uterus was always cannulated to allow the correct exposure of myomas. For pedunculated myomas, the pedicle was secured using a pre-tied or extracorporeally-tied loop and coagulated and transected with bipolar forceps and scissors. To reduce vascularization and blood loss, starting in 1997 we injected myomas with diluted (1:100) ornithine vasopressin (POR8; Sandoz, Milan, Italy). For subserous and intramural myomas, we carried out the serosal incision vertically over the convex surface of the myoma using a monopolar hook. After exposure of the myoma pseudocapsule, grasping forceps were positioned to apply traction to the myoma and expose the cleavage plane. Enucleation was carried out by traction on the fibroid and by division with a unipolar hook or mechanical cleavage. Haemostasis during dissection was achieved by bipolar coagulation. Suturing was usually done along one or two layers depending on the depth of incision with interrupted, simple or more frequently cross-stitches tied intracorporeally using 1 or 0 Polyglactin sutures.

Recurrence rate

Randomized subjects for comparison between laparoscopic and abdominal myomectomy

From 1991 to 1994, 81 patients were selected and informed of the aim of the study: those who accepted were randomized for abdominal ($n = 40$) or laparoscopic myomectomy ($n = 41$). All operations were carried out by surgeons with similar clinical experience. Transvaginal ultrasound examination was performed before surgery, within 15 days after surgery (to verify the adequate removal of myomas) and every 6 months for a period of 40 months after the operation. The myoma volume was calculated by the formula of an ellipsoid ($0.5233 \times D1 \times D2 \times D3$). The two groups were compared for pre-operative clinical features (age, gravidity and symptoms requiring surgery) as well as myoma volume and number. Recurrence of myoma was established when a myoma measuring $\geqslant 1$ cm^3 was detected by ultrasound. The two groups were compared for all the parameters and the recurrence rate.

Prospective, not randomized, group for recurrence rate after laparoscopic myomectomy

Patients ($n = 84$) not participating in the randomized group who underwent laparoscopic myomectomy from 1991 to June 1998 were studied for the recurrence rate by means of the same clinical protocol described above. We studied the influence of several factors on the recurrence rate. The risk was studied in relation to age, pre- and post-operative gravidity and parity, myoma size, number and depth of penetration and use of pre-operative gonadotrophin-releasing hormone (GnRH) agonist treatment (at least 3 months of depòt treatment before surgery). The dates used in the analysis were the dates of myomectomy, first diagnosis of recurrence and last follow-up visit.

Statistical analysis

All results are expressed as means ± standard deviation (SD). Patients were randomized by using a computer-assisted random number generator.

Table I. Recurrence rate: comparison between laparoscopic and abdominal myomectomy

	Laparoscopic myomectomy (41 patients)	Abdominal myomectomy (40 patients)
Pre-operative study		
Pelvic pain (%)	29	30
Sterility (%)	34	35
Menorrhagia (%)	31	29
Pelvic mass (%)	6	6
Myomectomy study		
Age (years)[a]	35 ± 5	35 ± 3
Number of myomas	90	94
Volume of myomas (cm^3)[a]	92.5 ± 108.5	152 ± 137
Number of myomas/patient (range)	2.2 (1–7)	2.3 (1–7)
Follow-up study		
Myoma recurrences (%)	11/41 (27)	9/40 (23)

[a]Mean ± SD.

Statistical analysis was performed using the unpaired Student's *t*-test for the comparison of means between two groups. For multiple comparisons, ANOVA was used. The χ^2 test was employed for the comparison of percentages between the groups. The cumulative probability of recurrence was calculated by the product limit methods and the curves were compared by the log-rank test and χ^2 test. The cumulative risk of recurrence was determined by Kaplan–Meier curve and by logistic regression in which the dependent variable was the recurrence of myoma and the co-variates were the number of myomas and the use of GnRH agonists.

A P value $\leqslant 0.05$ was considered to be statistically significant.

Results

A total of 47% of patients had more than one myoma, with a maximum of seven per patient (total myomas: 326; mean myomas removed per patient: 2.1; range 1–7). Myoma size ranged from 1–14 cm (mean 5.42 ± 3.68 cm). Myomas <3 cm were removed during myomectomy for larger ones. We converted to laparotomy in one case for anaesthesiological problems and in another because of the number and size of the myomas. The mean drop in haemoglobin concentration was 1.3 ± 0.9 g/100 ml (range 0.7–2.2). No blood transfusions were required. No major or late complications occurred. The duration of the entire procedure ranged from 40–240 min.

Comparison between laparoscopic and abdominal myomectomy

Eighty-one patients (median age 36 years, range 25–42) were selected and randomized: 40 patients underwent abdominal myomectomy and 41 laparoscopic myomectomy. No patients were lost in the follow-up period of 40 months. The clinical characteristics of the patients and results are shown in Table I.

The two groups were similar for age, parity, pre-operative symptoms as well as myoma number and volume. There were nine (23%) recurrences in the abdominal group against 11 (27%) in the laparoscopic group. The difference was not statistically significant. Most recurrences (84%) were seen at ultrasound within 24 months of surgery.

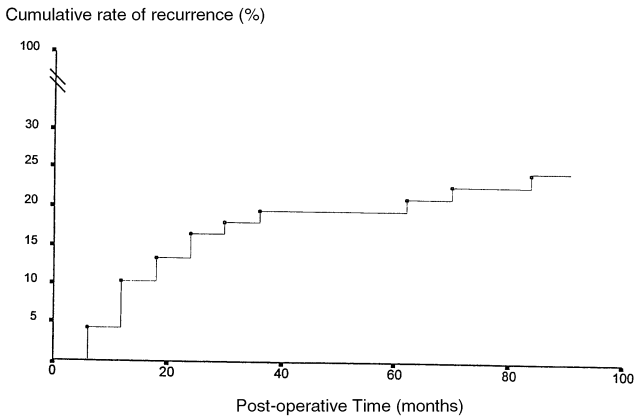

Figure 1. Cumulative rate of recurrence of myoma after laparoscopic myomectomy over 96 month follow-up period (17/78 recurrences: 21.79%).

Recurrence rate in relation to other risks factors

All the other non-randomized 84 patients (median age 36 years, range 25–42) who underwent laparoscopic myomectomy were followed for an average of 36 months (range 10–96). Six patients (7.7%) were lost to follow-up. There were 17 (21.79%) recurrences. Most recurrences (75%) were seen at ultrasound between 10 and 30 months after surgery (median: 26 months), as is shown in Figure 1, featuring the overall 8 year incidence of recurrence after laparoscopic myomectomy. The mean number of myomas diagnosed at recurrence was 1.35 (range 1–5). Fourteen patients had myomas <3 cm, and three patients had myomas >3 cm. Out of 14 patients with smaller myomas, seven (50%) had three or more myomas. Out of 17 recurrences, 14 (82.3%) were in a different site from the first myoma. The distribution of recurrence according to age, reproductive history, pre-operative use of GnRH agonists and the myoma characteristics are shown in Table II. It can be noted that the patient's age, pre- and post-operative gravidity as well as parity had no influence on the recurrence rate. Even if women with two or less myomas tended to experience a lower rate (17.5% versus 36.6% of women with three or more myomas), the difference between rates was not significant. Moreover, differences were not observed in the frequency of recurrence by size or depth of penetration of the myomas at surgery. On the contrary, the only associate risk factor was the pre-operative GnRH agonist treatment ($P < 0.02$). The results were confirmed by logistic regression analysis; in fact the coefficient of correlation between recurrence of myoma and agonist pre-treatment was statistically significant ($P < 0.02$), independently of the number of myomas.

In Figure 2, the 8 year incidence of recurrence after laparoscopic myomectomy according to GnRH agonist pre-treatment is shown: it can be noted that there was a higher and delayed recurrence rate in GnRH agonist-treated patients in comparison with untreated patients. None of the women with recurrence required additional surgery. There was no difference in the number of myomas removed among the two groups, patients pre-treated with agonists (2.2 ± 1.6) versus untreated patients (1.9 ± 1.7).

Table II. Recurrence rate according to risk factors

	Recurrence	
	Yes n = 17/78 (%)	No n = 61/78 (%)
Age (years, %)		
⩽35 (n = 35, 55.1)	6 (17.1)	29 (82.8)
⩾36 (n = 43, 44.9)	11 (25.6)	32 (74.4)
Gravidity		
0 (n = 58, 74.4)	14 (24.1)	44 (75.9)
1 (n = 11, 14.1)	2 (18.2)	9 (81.8)
⩾2 (n = 9, 11.5)	1 (11.1)	8 (88.9)
Parity		
0 (n = 61, 78.2)	15 (24.5)	46 (75.5)
⩾1 (n = 17, 21.8)	2 (11.7)	15 (88.4)
Subsequent gravidity		
0 (n = 51, 66)	9 (17.6)	42 (82.4)
⩾1 (n = 27, 34)	8 (29.6)	19 (70.4)
GnRH agonist treatment		
No (n = 54, 69.2)	8 (14.8)	46 (85.2)[a]
Yes (n = 24, 30.8)	9 (37.5)	15 (62.5)
Myoma size (cm)[b]		
1–4 (n = 48, 28.9)	5 (17.8)	23 (82.2)
>5 (n = 58, 34.9)	12 (24.0)	38 (76.0)
Myomas removed per patient		
1 (n = 43, 55.1)	7 (16.3)	36 (83.7)
2 (n = 16, 20.5)	3 (18.7)	13 (81.3)
>3 (n = 19, 24.4)	7 (36.6)	12 (63.4)
Depth of infiltration		
Pedunculated (n = 14)	1 (7.1)	13 (92.9)
Subserosal (n = 92)	8 (8.6)	84 (91.4)
Intramural (n = 56)	8 (14.3)	48 (85.7)
Intraligamentous (n = 4)	0 (0)	4 (100)

[a]$P < 0.02$: GnRH agonist treated versus non-treated patients.
[b]Myomas <1 cm were not considered of interest for the recurrence rate.

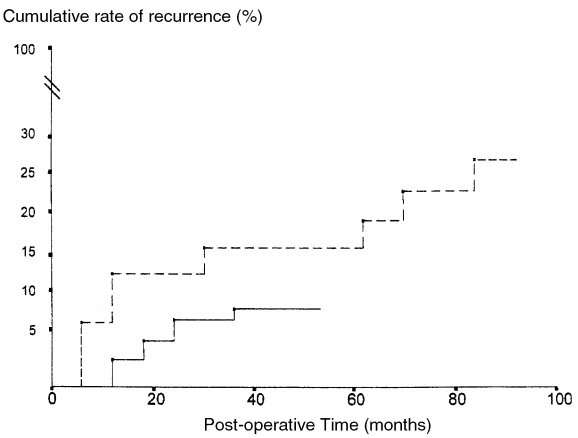

Figure 2. Cumulative 8 year incidence of recurrence after laparoscopic myomectomy according to GnRH agonist pre-treatment: GnRHa-treated (n = 24; nine recurrences), follow-up period 94 months; GnRHa-not treated (n = 54; eight recurrences), follow-up period 55 months.

Discussion

Despite having been performed for 20 years (Semm and Mettler, 1980) the laparoscopic approach to myomectomy is still a debated procedure. Recognized advantages are those related to minimal access surgery (Hasson *et al.*, 1992; Dubuisson *et al.*, 1996; Nezhat *et al.*, 1996) such as fast recovery and reduced post-operative pain (Mais *et al.*, 1996).

Feasibility is now accepted even if attention is still focused on technical difficulties due to myoma location and size and difficulty in reapproximating the incision by laparoscopic suturing that requires perfect mastery of endoscopic suturing. Recurrence of myomas is estimated to range from approximately 4–30%, with a retreatment rate of 10% (Buttram and Reiter, 1981). This wide range may in part be ascribed to different criteria for diagnosis and/or a lack in long-term follow-up. A well-known longitudinal study analysing follow-up of 622 women after abdominal myomectomy reported a 27% recurrence after 10 years (Candiani *et al.*, 1991) but diagnosis was based on bimanual or abdominal ultrasound examination only. More recent reports in which all recurrences have been vaginosonographically examined allowing, therefore, very small myomas (1 cm in diameter) to be detected, had an increased recurrence rate ranging from 46.3–51% (Sudik *et al.*, 1995; Fedele *et al.*, 1995). Little is known about the long-term outcomes of laparoscopic myomectomy. Scanty data on recurrences reported a 4% rate (Hasson *et al.*, 1992; Cittadini, 1998) but the modality of diagnosis and length of follow-up were not specified. The most thorough study so far reported is a retrospective review of 114 laparoscopic myomectomies (Nezhat *et al.*, 1998) whose results suggested that the recurrence of myomas may be higher with the laparoscopic approach, 33.3% after a mean interval of 27 months. Follow-up data were obtained by review of patients' charts, returned questionnaires and telephone interviews. The authors suggest that smaller intramural myomas are hard to visualize and may be overlooked leaving fibroids *in situ*, which may result in higher recurrence rates. Our results do not seem to support this finding. Our recurrence rate of 21.79% is similar to reports after abdominal myomectomy and it better compared with more recent reports based on transvaginal ultrasound. The improved prognosis for laparoscopic myomectomy could be biased by the effect that patients with fewer or smaller myomas are selected for laparoscopic myomectomy. Our data comparing laparoscopic with abdominal myomectomy can overcome this problem, being based on two groups of subjects similar in age, reproductive history and symptoms as well as myoma characteristics. There were no statistically significant differences in the recurrence rate between the two groups (27 against 25% in the abdominal group). In contrast to other authors' results, neither the number of myomas removed (Garcia and Tureck, 1984; Friedman *et al*., 1992) nor the depth of penetration (Nezhat *et al*., 1998) or myoma size were positively associated with risk of recurrence. There was a tendency to a higher risk of recurrence with increasing numbers of myomas removed: from 16.3% in patients with only one myoma to 36.6% in patients with three or more myomas, but the difference was not statistically significant. It could be suggested that the limited number of myomas removed at laparoscopy compared with laparotomy and the small number of patients did not provide the study with appropriate statistical power to draw any definitive conclusions. A few reports (Candiani *et al.*, 1991; Nezhat *et al.*, 1998) stated that the recurrence rate increased progressively with time up to the end of the follow-up. Our results do not confirm this trend: most recurrences are seen between 10 and 36 months after surgery, which is in accord with reports that many of the recurrences are already detectable 6 months after operation (Sudik *et al.*, 1995).

Some authors have counselled the pre-operative use of GnRH agonists to facilitate the surgery and to reduce morbidity after myomectomy. GnRH agonists are able to induce a decrease in the size of uterine myomas with a maximum effect observed after three or four cycles of treatment (Golan *et al.*, 1989; Friedman, 1993). However, there are conflicting data on the advantages of such therapy before laparoscopic myomectomy. Pre-operative GnRH agonist treatment could soften myomas, causing the identification of the cleavage to become more difficult at laparoscopy and hence lengthening the operative time (Campo and Garcea, 1999). Moreover, Fedele *et al.* found that treatment before surgery seems to favour short-term recurrences of small myomas, which can shrink in response to GnRH agonist treatment and are therefore missed at surgery (Fedele *et al*., 1990). On the contrary, other authors (Friedman *et al.*, 1992) reported a similar recurrence rate after combined GnRH agonist plus surgery treatment in comparison with surgery alone and, moreover, that the critical variable for risk of recurrences after myomectomy was the number of myomas at the time of surgery. This finding is confirmed by Sudik *et al.* who did not find a statistically significant difference in the rate of recurrence between patients treated with GnRH agonists (Sudik *et al*., 1995). Yet there is convincing evidence that myoma volume which has decreased after treatment regrows to the initial value 2 years after stopping treatment (Friedman *et al.*, 1994). Therefore the pre-operative use of GnRH agonists has still a controversial clinical interpretation. Data from the present study indicate that the pre-operative use of GnRH agonists is positively associated with a major risk of recurrence ($P < 0.02$). The cumulative risk of recurrence as shown in Figure 2 indicates a more elevated risk with a delay of recurrence in comparison with non-treated patients. It could be postulated that in this case the actual risk is increased by the additional risk of regrowth of myomas missed at surgery.

In conclusion, laparoscopic myomectomy may be a reliable technique and may offer comparable results with those obtained by laparotomy. Moreover, considering the high recurrence rate and consequent risk of repeated surgery, we think that patients should be offered the least invasive surgical approach available.

References

Buttram, V.C. and Reiter, R.C. (1981) Uterine leiomyomata: etiology, symptomatology and management. *Fertil. Steril.*, **36**, 433–445.

Campo, S. and Garcea, N. (1999) Laparoscopic myomectomy in premenopausal women with and without pre-operative treatment using gonadotrophin-releasing hormone analogues. *Hum. Reprod.*, **14**, 44–48.

Candiani, G.B., Fedele, L., Parazzini, F. and Villa, L. (1991) Risk of recurrence after myomectomy. *Br. J. Obstet. Gynecol.*, **98**, 385–389.

Cittadini, E. (1998) Laparoscopic myomectomy: the Italian experience. *J. Am. Assoc. Gynecol. Laparoscop.*, **5**, 7–9.

Daniell, J.B. and Guerly, L.D. (1991) Laparoscopic treatment of clinically significant symptomatic uterine fibroids. *J. Gynecol. Surg.*, **7**, 37–40.

Donnez, J., Mathieu, P.E., Bassil, S. *et al.* (1996) Laparoscopic myomectomy today. Fibroids: management and treatment: the state of the art. *Hum. Reprod.*, **11**, 1837–1840.

Dubuisson, J-B. and Chapron, C. (1996) Uterine fibroids: place and modalities of laparoscopic treatment. *Eur. J. Obstet. Gynecol.*, **65**, 91–94.

Dubuisson, J-B., Lecuru, F., Herve, F. *et al.* (1991) Myomectomy by laparoscopy. *Fertil. Steril.*, **56**, 827–830.

Dubuisson, J-B., Chapron, C., Chavet, X. and Gregorakis, S.S. (1996) Fertility after laparoscopic myomectomy of large intramural myomas: preliminary results. *Hum. Reprod.*, **11**, 518–522.

Fedele, L., Vercellini, P., Bianchi, S. *et al.* (1990) Treatment with GnRH agonists before myomectomy and risk of short-term myoma recurrence. *Br. J. Obstet. Gynecol.*, **97**, 393–396.

Fedele, L., Pazzarini, F., Luchini, L. *et al.* (1995) Recurrence of fibroids after myomectomy: a transvaginal ultrasonographic study. *Hum. Reprod.*, **10**, 1795–1796.

Friedman, A.J. (1993) Use of gonadotropin-releasing hormone agonists before myomectomy. *Clin. Obstet. Gynecol.*, **36**, 650–659.

Friedman, A.J., Daly, M., Juneau-Norcross, M. *et al.* (1992) Recurrence of myomas after myomectomy in women pretreated with leuprolide acetate depot or placebo. *Fertil. Steril.*, **58**, 205–208.

Friedman, A.J., Daly, M., Juneau-Norcross, M. *et al.* (1994) Long-term medical therapy for leiomyomata uteri: a prospective, randomized study of leuprolide acetate depot plus either oestrogen-progestin or progestin 'add-back' for 2 years. *Hum. Reprod.*, **9**, 1618–1625.

Garcia, C.R. and Tureck, R.W. (1984) Submucosal leiomyomas and infertility. *Fertil. Steril.*, **42**, 16–19.

Golan, A., Bukowsky, I., Schneider, D. *et al.* (1989) D-Trp6 LH-RH microcapsules in the treatment of uterine leiomyomas. *Fertil. Steril.*, **52**, 728–733.

Hasson, H.M., Rotman, C., Rana, N. *et al.* (1992) Laparoscopic myomectomy. *Obstet. Gynecol.*, **80**, 884–888.

Mais, V., Ajossa, S., Guerriero, S. *et al.* (1996) Laparoscopic versus abdominal myomectomy: a prospective, randomized trial to evaluate benefits in early outcome. *Am. J. Obstet. Gynecol.*, **174**, 654–658.

Nezhat, C., Nezhat, F., Silfen, S.L. *et al.* (1991) Laparoscopic myomectomy. *Int. J. Fertil.*, **36**, 275–280.

Nezhat, F., Seidman, D.S., Nezhat, C. and Nezhat, C.H. (1996) Laparoscopic myomectomy today. Why, when and for whom? *Hum. Reprod.*, **11**, 933–934.

Nezhat, F., Roemisch, M., Nezhat, C.H. *et al.* (1998) Recurrence rate after laparoscopic myomectomy. *J. Am. Assoc. Gynecol. Laparosc.*, **5**, 237–240.

Semm, K. and Mettler, L. (1980) Technical progress in pelvic surgery via laparoscopy. *Am. J. Obstet. Gynecol.*, **138**, 171–177.

Sudik, R., Husch, K., Steller, J. and Daume, E. (1995) Fertility and pregnancy outcome after myomectomy in sterility patients. *Eur. J. Obstet. Gynecol. Reprod. Biol.*, **65**, 209–214.

Tulandi, T. and Labarge, P. (1997) Laparoscopic myomectomy. *Hum. Reprod. Update*, **3**, CD ROM, Item 3, video.

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