DEBATE

Emboliization versus myomectomy versus hysterectomy

Which is best, when?

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Uterine fibroids are the commonest tumour affecting the female reproductive tract. In many instances they are asymptomatic, but in some women there does appear to be an association with heavy menstrual blood loss and, possibly, subfertility. Classically, treatment has been surgical with hysterectomy the most common approach for women who have completed their fertility and myomectomy for those who wish to conceive. The surgery can be carried out laparoscopically, vaginally and abdominally, although all routes are associated with an appreciable rate of morbidity. Myomectomy can also be achieved hysteroscopically. Hysterectomy is associated with a high rate of satisfaction and is likely to relieve menstrual problems in virtually all women. The success of myomectomy is less certain since no randomized trials against expectant management have ever been carried out. In addition, myomectomy may lead to adhesion formation within the abdominal cavity, which may impair fertility further. Since myomectomy is not the ideal answer, other treatments for fibroids are being sought. Medical treatment may be useful in specific instances and for the short-term, but does not lead to a cure. Consequently, other modalities are being developed, one of which is uterine artery embolization. This procedure involves occluding the vessels using either foam or coils. The normal myometrium rapidly develops a new blood supply from collateral circulations, whereas the fibroids do not. The procedure leads to fibroid shrinkage of ~30–50% and appears to lead to relief of fibroid-associated symptoms, although it is too early to determine the effect on fertility. However, it is associated with significant complications and requires further evaluation before being accepted as a useful alternative to surgical therapy in the management of women with uterine fibroids.

Introduction

Uterine fibroids are the most common tumour in the female reproductive system. They are estimated to occur in 25% of women of reproductive age. Forty percent of women who are still menstruating beyond the age of 50 years (Buttram and Reiter, 1981) and 89% of uteri removed at hysterectomy from women of Afro-American origin, a group in which they occur with a particularly high incidence (Kjerulff et al., 1993, 1996), have fibroids. Their presence maybe associated with infertility, miscarriage, pressure effects and menstrual problems. For women who have completed their families, the established treatment is abdominal hysterectomy. In the USA, 30% of women will have had a hysterectomy by the age of 60 years and 60% will be performed to treat fibroids (AHRQ, 2000). Of these, at least 75% will be performed by the abdominal route. Abdominal hysterectomy is a major operation, involving a hospital in-patient stay of 3–5 days and a convalescence time of several weeks. A recent study carried out in Glasgow suggests that it is associated with significant morbidity in 3% of cases and minor morbidity in ~14%, the total cost of operation being £2400 (Lumsden et al., 2000). However, hysterectomy is a very successful operation with as many as 85–90% of women being satisfied with the operation and reporting improved quality of life. There have now been several studies comparing it with conservative treatment for menorrhagia in the absence of fibroids, suggesting that long-term satisfaction is very high (Dwyer et al., 1993; Pinion et al., 1994).

Presenting symptoms

The prevalence of asymptomatic fibroids is unknown. In those attending their gynaecology clinics, menstrual problems and pressure symptoms are common. Fibroids also occur in those with reproductive dysfunction, although the exact relationship between the two is uncertain. It is unusual for symptoms to appear prior to the age of 30 years and these will usually disappear at the time of the menopause. However, for some, the impact on quality of life is significant.

The mechanisms controlling the growth of fibroids are unclear, but almost certainly involve steroid hormones (estrogen and progesterone), peptide growth factors (epidermal growth factor) and the availability of an adequate blood supply (Wallach, 1981; Lumsden et al., 1988a,b).

There are numerous unsubstantiated theories as to why fibroids cause symptoms and these have been extensively reviewed (Lumsden and Wallace, 1998). It is probable that increased menstrual loss is associated with the presence of submucous or intracavity fibroids. Pain may result from tissue...
necrosis or torsion and the relationship with infertility is discussed further below.

**Treatment options**

The standard medical treatments for menorrhagia are less effective in the presence of uterine fibroids. Prostaglandin synthetase inhibitors are effective in a proportion of women and GnRH agonists or danazol (agents that produce amenorrhoea), can be useful in some instances (Stovall et al., 1991; Maheux and Lemay, 1992; West et al., 1992; Davis and Schlaff, 1995). For women who wish to maintain their fertility, myomectomy is the usual option. In most centres, the majority of operations are performed by the abdominal route. However, if the fibroid protrudes into the uterine cavity, myomectomy can be achieved hysteroscopically. Subserosal fibroids can also be removed laparoscopically. With the exception of units serving a large Afro-American population, the number of myomectomies performed is small, which calls the overall success of the operation into question and explains why alternatives are being sought. These alternatives include uterine artery embolization and myolysis. The former will be considered further in this debate.

Embolization is a well established radiological technique, which has been in clinical practice for the last 25 years. It has been used successfully in the female pelvis in cases of trauma and post-partum haemorrhage to good effect (Ledee et al., 2001). Uterine fibroids appear to be particularly sensitive to the effects of the acute ischaemia produced by embolization and undergo necrosis. Consequently, they usually shrink significantly and occasionally even disappear. The integrity of the uterus is preserved by collateral blood flow from other vessels with revascularization of the normal myometrium, but not of the fibroids. This treatment is becoming wide-spread throughout the world and is being considered by many women who find hysterectomy unacceptable. However, its efficacy and safety are still under review. The observational data available so far will be summarized to allow some comparison to be made with the surgical options.

**Surgical treatment**

There are various key questions that might be useful to consider when assessing surgical treatment for fibroids. These are listed in Table I. Consideration will be given to these questions during the discussion of surgical options.

**Table I. Key questions that might be useful to consider when assessing surgical treatment for fibroids**

<table>
<thead>
<tr>
<th>Key questions</th>
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<tr>
<td>What are the risks and benefits of hysterectomy and myomectomy in the treatment of symptomatic and asymptomatic fibroids?</td>
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<tr>
<td>Are outcomes different after myomectomy in women with a single clinically detectable fibroid compared with women with multiple fibroids?</td>
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<tr>
<td>Who are appropriate candidates for the various treatment options?</td>
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<tr>
<td>How often do women need additional procedures after conservative therapy for fibroids?</td>
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<tr>
<td>Does additional treatment result in significantly increased morbidity compared with immediate definitive therapy?</td>
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<tr>
<td>What are the risks and benefits of alternative treatments?</td>
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**Risks and benefits of surgical treatment**

Hysterectomy is the most common major gynaecological operation in the world and fibroids are the commonest cause of hysterectomy (Vessey et al., 1992). In the USA, 177–366 000 hysterectomies are performed each year to treat fibroid-associated symptoms (National Center for Health Statistics, 1996; Levine et al., 1997). For benign indications, many countries have favoured either the abdominal (Harkki-Siren et al., 1997) or the vaginal approach (Querleu et al., 1994). These traditions have prevailed unaltered for decades. However, since the late 1980s, the new option of laparoscopic hysterectomy (Reich et al., 1989) has raised questions about the most suitable type of approach. The prospective observational study of >10 000 hysterectomies carried out in Finland (Harkki-Siren and Kurki, 1997; Makenin et al., 2001), suggested that the overall rate of complications was 17.2% for abdominal, 23.3% for vaginal and 19% for the laparoscopic approach, with infection the most common problem. Haemorrhage occurred in 2.1, 3.1 and 2.7% of abdominal, vaginal and laparoscopic hysterectomy respectively. The significant difference between the different routes was that ureteric injury was seven times more common during operations performed by the vaginal than the abdominal route.

There is a small but significant mortality associated with hysterectomy. Studies estimate this to be between 10 and 20/1000 operations (Bernstein et al., 1997). The VALUE (Vaginal, Abdominal, Laparoscopic Uterine Excision) study of 37 000 hysterectomies carried out for benign indications and excluding post-partum hysterectomy, recorded 14 deaths in total, of which eight were in women aged ≤51 years (M.Maresh and K.McPherson, unpublished data). Overall, the incidence of significant complications is low. A randomized comparison of laparoscopic and abdominal hysterectomy carried out in Scotland suggested that significant complications occurred in only 1% of women following abdominal hysterectomy and ~3% of women following laparoscopic hysterectomy. Minor complications occurred in 8 and 14% of those having laparoscopic and abdominal hysterectomy respectively. Since the complication rate was lower than expected, this study was too small to identify any difference in complication rate between the two routes (M.A.Lumsden et al., 2000). However, it was observed in this study, as well as in both the audit carried out in Scotland and the VALUE study, that complications were more likely when hysterectomy involved the removal of a fibroid uterus (Brechin et al., 2000). Although the complication
rate is relatively low, it must be borne in mind that these women are usually young and fit prior to the operation. The risk/benefit equation is different in this group than when the operation is life saving, for example in the presence of malignant disease. In addition, the operation is performed not to prolong life, but to improve its quality, a factor that should now be assessed in studies involving hysterectomy (Rowe et al., 1999).

Hysterectomy has been compared with endometrial ablation in the treatment of menstrual problems in several studies, which have suggested that as many as 95% of women will be satisfied (Pinion et al., 1994; O’Connor et al., 1997). Our own study cited above would support these data. Long-term satisfaction is high even in those experiencing pre-operative or early post-operative complications. This means that an alternative treatment has to be extremely good in order to have a higher satisfaction rate than hysterectomy itself. For women who do not wish to retain their uterus, there are gynaecologists who would suggest that there is no necessity to seek an alternative.

Hysterectomy will cure problems associated with menstrual bleeding in most cases and, since this is the commonest presentation for uterine fibroids, it explains why the operation is so often successful. However, in women with other symptoms, there is a less consistent response.

Myomectomy

For women who desire future pregnancies or who wish to retain their uterus for other reasons, myomectomy is the operation of choice. For multiple myomas or a significantly enlarged uterus, this will be achieved, most often, by the abdominal route. Where fibroids impinge on the uterine cavity, hysteroscopic resection is possible and smaller fibroids can also be removed laparoscopically. This is a much less common operation than hysterectomy, with about one-tenth of the number being performed annually.

However, the fundamental question is whether the fibroids need to be removed at all. Many women have a myomectomy with the aim of improving fertility. Fibroids are common in a naturally subfertile group, i.e. women >40 years, and their causality is unproven. In some instances the myoma can cause tubal occlusion and it is possible that there may be a foreign body reaction with endometrial inflammation, altered vascularity or altered contractility (Buttram and Reiter, 1981; Stewart, 2001). This might suggest that the location, size and number are of importance, although data for the assertion are lacking.

The relationship between fibroids and fertility was reviewed by Vercellini, with consideration of data from nine prospective studies (Vercellini et al., 1998). Since data from randomized controlled trials (RCTs) or cohort data are lacking, no conclusive relationship could be identified. The pregnancy rate following laparoscopic myomectomy is ~50%, although this is less for women with multiple fibroids (Wood and Maher, 1998). The most robust data that suggest myomectomy does improve the chance of fertility come from studies of the success of IVF where a decrease in fertility was noted in those with fibroids (Bajekal and Li, 2000). Most available information is derived from observational studies where women who have difficulty conceiving are assessed before and after myomectomy. Unfortunately, many of these studies are flawed in that other causes of infertility are not considered.

Difficulty achieving haemostasis can occur at myomectomy. This can result in the formation of post-operative adhesions that may impair fertility further. Occasionally, the bleeding can be sufficiently heavy as to require hysterectomy. Also, the uterus may be weakened following the incision or incisions required. One of the major disadvantages of myomectomy is the risk of new myoma formation. The risk of recurrence is difficult to assess because, since fibroids are of a clonal nature, it is possible that these are new fibroids rather than recurring old ones. It would appear from the data that the recurrence rate after abdominal myomectomy is less than after laparoscopic myomectomy, suggesting that the former route is more likely to be associated with achieving a pregnancy. It would appear that after abdominal myomectomy, the recurrence rate varies from 5.7–11.1% (Fauconnier et al., 2000). However, the accumulative rate at 5 years for laparoscopic myomectomy may be as high as 51% with 2 years being the mean time before this tends to occur (Nezhat et al., 1998). However, unless serial ultrasound scans are used, it is difficult to be clear whether recurrence has occurred or not (Fedele et al., 1995). Accrued rate of re-operation tends to vary from one study to another, but as many as one patient out of two will require a further procedure (Iiverson et al., 1996). For studies where there have been 5 years of follow-up, up to 16.8% of women having myomectomy may require hysterectomy, although Loeffler suggested that it may be as high as 26% (Loeffler and Noble, 1970).

Myomectomy appears to be an effective treatment for menstrual problems in many instances, although overall these studies have used subjective means of assessment with variable length and enthusiasm of follow-up (Derman et al., 1991). For women with submucous fibroids, hysteroscopic myomectomy maybe the most appropriate route. Accessible myomas can be resected with an operating endoscope through the cervix. Symptom relief appears to be good, with only 16% of women requiring a second procedure after 9 years. Good pregnancy rates have also been reported (Goldenberg et al., 1995). In conclusion, myomectomy can relieve the symptoms associated with myomas, but does not affect the underlying process.

It is possible to have a healthy pregnancy after myomectomy since the risk of uterine rupture is very low (0.002%), considerably less than that after previous Caesarean section (0.1%) (Garnet, 1964). There is doubt as to whether the closure of the incision at laparoscopic myomectomy is as effective as during abdominal myomectomy, with reports of uterine rupture as early as 33 weeks (Nezhat, 1996). Subsequent fertility rates are good after hysteroscopic myomectomy and it would appear that uterine rupture after this procedure is unlikely (Derman et al., 1991; Ubaldi et al., 1995).

Uterine artery embolization

This novel technique for the treatment of uterine fibroids was first performed by Ravina, a French gynaecologist, in 1995.
It is an established treatment for post-partum haemorrhage and bleeding at the time of gynaecological surgery. For reasons not fully understood, the normal myometrium receives a new blood supply from the vaginal and ovarian vasculature, whereas the fibroids become avascular and shrink.

There have been a large number of observational studies and some of the published studies are summarized in Table II, which gives an overview of the success and problems associated with the procedure. The subject has also been the topic of review (Reidy and Bradley, 1998; Braude et al., 2000; Lipman, 2000). It is thought that >10 000 procedures have now been performed, although it is difficult to get an accurate figure. Although analgesia is required for 24–48 h after the procedure, studies suggest that recovery is rapid and a day-case or short in-patient stay are required at most (Siskin et al., 2000). Initial studies suggest that uterine artery embolization is useful in controlling menstrual blood loss (Table II) (Yamashita et al., 1994). We have performed a small observational study of 50 women, with objective assessment of blood loss. A highly significant decline in menstrual blood loss was noted in virtually all women with the complaint of menorrhagia and this is maintained at 1 year (M.A.Lumsden, unpublished observation). The response of the fibroids in terms of decrease in size is extremely variable, but is probably similar to that achieved following administration of GnRH agonists, with a mean of 30–50% (Goodwin et al., 1999; Reidy et al., 1999; Spies et al., 1999). However, in contrast to the shrinkage achieved with the agonists, the decrease in size following embolization continues and does not slow down after 3 months. However, since the fibroids do not usually disappear, symptoms related to the size of the fibroid alone may not be as well treated as those related to the menses themselves.

In the initial series, there have been few women treated who have desired pregnancy, so most information is anecdotal. Ravina has published the results of 12 pregnancies (Ravina et al., 2000). The median age of the women at the time of embolization was 40 years, with a delay before pregnancy of 9 months. Five early miscarriages occurred and the seven other pregnancies were uneventful. Delivery prior to 37 weeks occurred in three instances and there was one case of toxaemia. No recurrence of the myoma or abnormalities in uterine function was observed at the time of Caesarean section in the four women delivered by this route. However, it is important that studies are carried out to investigate the incidence of uterine rupture and possible problems with placentation, although this has not been reported in women who have had embolization for other causes.

Although uterine artery embolization has obvious benefits, it is also associated with a significant incidence of morbidity and mortality. There have been reports in the literature of two deaths, one occurring from sepsis and a second, not related to the procedure, but due to ovarian cancer that might have been treated had the women in question had a hysterectomy (Vashisht et al., 1999; Armstrong and Caird, 2001). There has been a further anecdotal report of a death, in Italy, of a woman who had pulmonary embolus after embolization. However, she had breast cancer and death may not have been due to the procedure.

The procedure of uterine artery embolization (UAE) itself is not difficult for interventional radiologists with the appropriate skills. It involves canulization of the femoral artery, which may be achieved on one or both sides at the same time. Catheters are then fed into the iliac vessels followed by the uterine artery and angiography is used to confirm the correct position. The embolic agent is then introduced. Since complications of the catheterization procedure itself are unusual, the first problem that is usually noted is that of post-embolization pain due to ischaemia. It can be well controlled using parenteral analgesia similar to that used after laparotomy, but is usually the reason why an in-patient stay is required.

One significant complication associated with the procedure is a post-embolization syndrome similar to that following myocardial infarction and possibly related to the release of cytokines and toxins from the ischaemic tissues. This syndrome manifests itself with a flu-like illness, high temperature, high white blood cell count and a feeling of general malaise. It is extremely difficult to distinguish from sepsis itself and is normally treated with antibiotics.

Inevitably, sepsis is a major problem, although it is possible that this may be related to the site and size of the fibroids and also to the patient groups in question, although insufficient data are available to confirm this. The data for a relationship between infection and size are sparse. A report of eight cases of embolization of large fibroids was published from St

### Table II. Results of published case series

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample size</th>
<th>Technical success (%)</th>
<th>Menorrhagia resolved (%)</th>
<th>Patient satisfaction (%)a</th>
<th>Complications (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ravina, 1995</td>
<td>16</td>
<td>87</td>
<td>64</td>
<td>No data</td>
<td>12</td>
</tr>
<tr>
<td>Goodwin, 1997</td>
<td>11</td>
<td>100</td>
<td>86</td>
<td>87</td>
<td>9</td>
</tr>
<tr>
<td>Bradley, 1998</td>
<td>8</td>
<td>No data</td>
<td>80</td>
<td>71</td>
<td>25</td>
</tr>
<tr>
<td>Worthington-Kirsch, 1998</td>
<td>53</td>
<td>98</td>
<td>96</td>
<td>94</td>
<td>4</td>
</tr>
<tr>
<td>Hutchins, 1999</td>
<td>305</td>
<td>96</td>
<td>87</td>
<td>84</td>
<td>4</td>
</tr>
<tr>
<td>Spies, 1990</td>
<td>61</td>
<td>98</td>
<td>89</td>
<td>82</td>
<td>18</td>
</tr>
<tr>
<td>Goodwin, 1999</td>
<td>60</td>
<td>100</td>
<td>95</td>
<td>88</td>
<td>21</td>
</tr>
<tr>
<td>Siskin et al., 2000</td>
<td>49</td>
<td>98</td>
<td>No data</td>
<td>94</td>
<td>16</td>
</tr>
</tbody>
</table>

aModerately or very satisfied.

The incidence of complications is difficult to calculate accurately due to the varying detail in each publication and length of follow-up.

(Ravina et al., 1995).
Thomas’ Hospital and concluded there should be no additional problems (Bradley et al., 1998), but great care must be taken in women with large fibroids. Subserosal fibroids may be particularly prone to problems because of adhesions to the bowel leading to necrosis of the bowel wall and to peritonitis and systemic sepsis. Infection may ascend from the vagina, which may be particularly important after treatment of intracavity fibroids. These might be treated more appropriately by hysteroscopic resection.

Infection may be more prevalent in certain racial groups. Fibroids per se are much commoner in Afro-American women, where they also tend to be larger. This is thought to be associated with cyto-genetic abnormality. If pelvic inflammatory disease is also a problem in the same group of women then this could lead to an increased incidence of infection. Some units screen for infection although, since it may occur some weeks after the procedure itself, the value of this is debatable. Women who have uterine artery embolization require extremely careful and long-term follow-up as complications have been reported as long after the procedure as 4 months.

The effect on ovarian function is another contentious issue and is of importance to women keen to maintain their fertility. Because of the anastomosis between the uterine and ovarian vessels, it is possible for contrast material to enter the ovarian circulation with a decrease in its blood supply. However, women who have conservation of their ovaries at the time of hysterectomy may also go through an earlier menopause (Siddle et al., 1987), possibly due to interference in the blood supply. The significance of this is less since these women do not wish to maintain their fertility. In most series, including our own, ovarian failure after UAE was found to occur most often in women in their late forties, when already nearing the menopause, with an overall incidence of 5%. An additional problem is that amenorrhoea may occur even in the presence of normal ovarian function. This is probably related to the development of intruterine adhesions, a potential issue for those wishing to conserve fertility. Also, it is as yet unknown whether the incidence of fibroid recurrence will be similar to that after myomectomy since there are no studies with sufficient long-term follow up.

Prolapse of the uterine fibroid through the cervix can be a distressing symptom for women after embolization (Abbara et al., 1999; Berkovitz et al., 1999). This has been reported following administration of GnRH agonist and is probably associated with a rapid change in size of an intracavity of submucous fibroid. This will lead to passage of the fibroid per vaginam along with a rather unpleasant discharge that has been described by some as being like ‘chicken soup’. It may also require surgical intervention to evacuate the necrotic fibroid.

The Royal College of Obstetricians and Gynaecologists and the Royal College of Radiologists formed a working party to discuss uterine artery embolization and met in November 2000 (RCOG/RCR Report 2001). Uterine artery embolization has been classified as a C1 procedure by the Safety and Efficacy Registrar of New Intervventional procedures of the Medical Royal Colleges (SERNIP). Category C1 is defined as, ‘Safety and/or efficacy not yet established; procedure requires a fully controlled evaluation and may be used only as part of systematic research—an observational study in which all interventions and their outcomes are systematically recorded’. The working party go further and recommend that for women wishing to maintain their fertility, that the procedure should only be performed as part of a RCT against myomectomy. Many units within the UK’s National Health Service are adhering to these guidelines, with patients being referred into centres whereby detailed audit can be performed. Our own unit in Glasgow has achieved a high level of follow-up, which includes observational assessment of blood loss and completion of questionnaires related to quality of life.

It is essential that the radiologists involved in the procedure are experienced in this type of technique and also have appropriate equipment. If more than one radiologist is available at any given time, then it is possible to cut the radiation dose considerably using a bilateral approach (McDonald et al., 2001). A vast majority of those being treated have completed their families. Prior to the procedure, all patients receive a detailed information sheet outlining all the possible treatments for uterine fibroids as well as the pros and cons of each one. Both patient and GP also receive information as to what should be expected after the procedure with the phone number of an individual to contact at any time. This is onerous for the staff in terms of time and commitment.

The working party also recommended that a registry should be set up similar to that in the USA. This is not yet available, but it is possible for UK centres to contribute to the US database if they wish to do so. The ultimate test for uterine artery embolization will be the completion of a RCT (Broder et al., 2000a,b). There are two currently planned or in progress. Our own in Scotland, which is a randomized controlled trial of UAE against surgical treatment, which will assess all aspects of the gynaecological and social problem, as well as including a detailed cost analysis. A second study is due to get underway in Holland.

In summary, uterine artery embolization is a promising new approach for the treatment of uterine fibroids. However, information is lacking as to the effectiveness in women who wish to maintain fertility. The morbidity and mortality must be compared with surgical treatment, since no new intervention should be introduced that is less safe than this effective, acceptable treatment for menstrual problems. Funding should be made available to establish a UK register and it is vital that people are honest and submit their problems as well as their successes. This is more likely when the register is local and most of the participants carrying out this procedure are known. RCTs are very difficult to perform and appropriate funding must be made available so that enough interested units can be involved with appropriate staffing. Much more information must be gathered before we can conclude which is the most acceptable treatment for uterine fibroids and we look at the appropriateness of different treatments in different patient groups. It is only then that the questions posed in Table I and in the title, can be answered.

Key Points

(i) Results of different treatments are comparable.
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