Embolization of uterine leiomyomata: current concepts in management

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Transcatheter bilateral uterine artery embolization is a relatively new, but fast increasing modality being offered as an alternative to surgery for the treatment of symptomatic uterine fibroids (myomata). Since its introduction in 1995, it is estimated that over 5000 procedures have been performed, despite little objective evidence of its efficacy in comparison with more traditional surgical procedures, e.g. hysterectomy, abdominal or laparoscopic myomectomy or hysteroscopic procedures. The enthusiastic uptake of uterine artery embolization is partly due to the fact that it can be performed as a day case, and is a means of avoiding surgery especially hysterectomy. However, the procedure is not without significant risks, and these are becoming clearer as more procedures are being reported. This review examines the procedure, its use and purported efficacy and discusses its complications and potential hazards.

Key words: complications/uterine artery embolization/uterine leiomyomata

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Introduction

Hysterectomy is the most common surgical operation performed by gynaecologists, with ~77 000 being performed in the UK annually (Effective Healthcare, 1991) and ~591 000 being performed annually in the USA, of which about one third are performed because of fibroids (National Centre for Disease Control and Prevention, 1998). However, some women with myomata, especially those of childbearing age, may wish to retain their uterus and request myomectomy as an alternative form of treatment especially when fibroids are multiple and not amenable to more conservative forms of surgical treatment, e.g. hysteroscopic resection (Sutton, 1996). Estimates of the number of abdominal myomectomies undertaken in proportion to hysterectomies is difficult to estimate but is believed to be ~35 000 to 40 0000 in the USA. Abdominal myomectomy is not without risk of hysterectomy, although once again the exact rate is difficult to estimate.

Transcatheter bilateral uterine artery embolization is a relatively new, but fast increasing modality being offered as an alternative to surgery for the treatment of symptomatic uterine myomata (Ravina et al., 1995a,b,c). Although only recently used for this purpose, uterine artery embolization has been used successfully for arresting post-partum (Mitty et al., 1993) and operative haemorrhage (Goldin et al., 1978), bleeding in trophoblast disease (McIvor and Cameron, 1996) and to occlude arteriovenous malformations (Nicholson et al., 1999). It has also been used to decrease blood flow to cancers prior to debulking surgery. Indeed, the first use of embolization for the treatment for fibroids was prior to surgery to decrease the amount of bleeding at myomectomy (Ravina et al., 1995a). Since the first report for its use (Ravina et al., 1995b,c), it has been estimated that >5000 procedures have been performed (unpublished data).

The procedure

The procedure is generally performed under sedation rather than general anaesthesia by an experienced interventionist radiologist (for details of method see Ravina et al., 1995a; Bradley et al., 1998; Goodwin et al., 1997; Worthington-Kirsch, 1999). An angiography catheter is guided percutaneously via the patient’s femoral artery into the ipsilateral or contralateral uterine artery (Figure 1).

Due to the commonly found tortuosity of the uterine artery, the catheter is not passed into the vessel directly supplying the fibroid as is commonly believed, but to the point at which angiography demonstrates it to be past major branches supplying non-uterine structures (e.g. superior gluteal and aberrant branches supplying the ovary). Particles of polyvinyl alcohol (PVA) 300–500 μm are injected in boluses until blood flow in the vessel is seen to cease (Figure 2).

The catheter is withdrawn from that uterine artery and passed over the bifurcation of the aorta into the opposite side and the

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procedure repeated. The procedure generally takes 45–135 min, during which the patient is exposed to ~20 cGy of ionizing radiation, compared with 2–3 cGy for a computerized tomography (CT) scan of the pelvis. Patients are generally kept in hospital for 12–48 h for observation and pain control although the procedure may be conducted on a day care basis in some institutions.

**Effectiveness of the procedure for myomata**

To date, there have been no reports of randomized trials of efficacy, and only a handful of case series in the literature, although a number of abstracts have appeared at specialized meetings. Results of some of the published reports (by authors of the same groups) are included in subsequent papers and hence only ~400 cases appear in this literature although more are reported in abstracts of meetings. We have included information from abstracts delivered at the 11th meeting of the Society for Minimally Invasive Therapy held in Boston in September 1999, at which the most up-to-date information was presented by international experts in this rapidly expanding field. We have also included in this discussion, data from >200 embolization procedures carried out by one of the authors (J.R.) at Guy’s and St Thomas’ Hospital and at allied hospitals since June 1996.

**Objective measures**

Shrinkage of fibroids and reduction in uterine volume have been used as measures of embolization efficacy, since many patients complain of bulk symptoms (swelling, urinary or bowel pressure symptoms), and these can be measured subjectively by abdominal palpation, or objectively by ultrasound (Figure 3) (Goodwin et al., 1997; Worthington-Kirsch, 1999) or magnetic resonance imaging (MRI) (Bradley et al., 1998).

In all reports, average fibroid shrinkage or reduction in uterine volume has been substantial but with large individual variations being reported: 46% (0–84) (Worthington-Kirsch, 1999); 69% (Ravina et al., 1997); 40% (22–61) (Goodwin et al., 1997); 52% (Bradley et al., 1998). Where no reduction is seen, especially where the ‘fibroid’ is single, adenomyosis (Smith et al., 1999) or sarcomatous change should be considered. Preoperative MRI will delineate adenomyosis (Reinhold et al., 1998), whereas abnormal vasculature or growth after embolization may herald a sarcoma.

**Menorrhagia and bulk related symptoms**

In the first published report (Ravina et al., 1995b), arterial embolization was used to treat uterine myomata in 16 patients (age range 34–48 years), who were followed for an average of 20 months (11–48). The main indications for treatment were menorrhagia (n = 14) and a mass (n = 2). In nine patients, the menorrhagia had resolved, and three were said to have improved. One hysterectomy and one myomectomy were performed subsequently for persistent heavy bleeding. There was one pregnancy in a patient who was infected with human immunodeficiency virus (HIV) and who died after delivery. In a follow-up of this series enlarged to 88 cases (Ravina et al., 1997), 60 out of 67 patients complaining of menorrhagia had symptom improvement after embolization. In the largest published series (Hutchins...
et al., 1999), the authors interviewed by phone a proportion of 305 patients treated by uterine artery embolization who were asked to rate change in symptoms from complete resolution, great improvement, moderate improvement slight improvement or no change (Table I).

Although the validity of this survey may be criticized as being open to bias because the telephone survey was carried out by members of the therapeutic team, and because of its subjectivity, it gives some indication of relative satisfaction of those seeking this type of treatment and accords with other, as yet unpublished, surveys.

Pregnancy

Few procedures have been carried out in women of childbearing age, since women seeking pregnancy generally have been discouraged from therapy due to the unknown long-term effects of the procedure. Nevertheless some women have accepted embolization where myomectomy may have been hazardous or difficult. In our own series, we are aware of two pregnancies following embolization both of which went to term. One in a patient who became pregnant 8 weeks after her embolization procedure (Bradley et al., 1998), and one who delivered twins following bilateral embolization for a haemorrhaging arteriovenous malformation, similar to a case reported previously (Nicholson et al., 1999). A further successful pregnancy delivered by Caesarean section has been reported from that group (Nicholson and Ettles, 1999). A total of 12 pregnancies in nine women have recently been reported by the Ravina group in their total series of 220 (Ciraru-Vignon et al., 1999). Two pregnancies have been reported (Hutchins et al., 1999). Despite these successes, until more information is acquired about uterine integrity, the effect on growth of the fetus and the likelihood of conception, this procedure is not recommended as a primary treatment for those seeking pregnancy (for review, see Forman et al., 1999). The use of gelatin sponge particles (500 μm) may be an effective alternative to PVA for inducing ischaemia to the myomata while subsequently preserving blood flow to uterus (Katsumori et al., 1999).

Complications of uterine artery embolization

Radiological complications

Besides the exposure to radiation which will be related to the length of the procedure, other possible adverse consequences are haematoma at the puncture site, failure to cannulate both uterine arteries due to anatomical variation, absence of one artery or due to tortuosity of the vessels, inadvertent vessel damage, hypersensitivity to contrast material and non-target organ embolization.

Since the ovaries are in the direct X-ray beam for a considerable part of the procedure, and some of these women may wish to become pregnant subsequently, there is concern about the total dose of radiation that the women may receive. It has been estimated that the total is ~20 cGy, 5–10 times that of a pelvic CT scan (Broder et al., 1999), but will be affected by the total time of the procedure and quality of the equipment used. Thus it is important to take all the necessary steps to keep the X-ray dose to as low as possible by minimising fluoroscopy times, limiting filming of the procedure, and using state-of-the-art angiography equipment with dose reduction features.

In this relatively young age group (as might be expected), we have found that complications directly related to the procedure are rare: we have had no hypersensitivity reactions, no haematoma of any significance, no vessel damage and in only six of >200 patients (2.5%) were there difficulties in cannulating both arteries due to anatomical variation. One group (Hutchins et al., 1999) reported 13 unsuccessful attempts out of 305 (4.2%), either due to anatomical distortion, premature thrombosis, or absence of one artery. Vessel spasm is another cause which is reported to have been overcome successfully by the administration of a glyceryl trinitrate patch and intra-arterial papaverine (Goodwin and Walker, 1998). Where unilateral embolization was performed because of complications or electively, the clinical benefit was variable but usually poor.

Vascular complications

There have been two reports of uterine arterial damage. In the first case, the left uterine artery was successfully embolized, but the
should be warned of the possibility of fibroid expulsion, and need may be an associated prodromal antisocial foul smelling vaginal discharge, or expulsion may occur at inopportune times (one of where the uterus is large and distorted. Prior to expulsion, there associated with significant pain, haemorrhage or if a fibroid passed through the cervix, and expulsion may not be complete, requiring surgical intervention to remove it. It may be argued that such fibroids are best managed initially by hysteroscopic resection rather than by embolization, but resection may not be possible where the uterus is large and distorted. Prior to embolization, there may be an associated prodomal antiscial foul smelling vaginal discharge, or embolization may occur at inopportune times (one of our patients shed two small fibroids during intercourse). Patients should be warned of the possibility of fibroid expulsion, and need only seek medical attention if the passage of the mass is associated with significant pain, haemorrhage or if a fibroid remains attached by a pedicle. In our experience, two patients have required general anaesthesia and hysteroscopic resection of the base of the pedicle of large prolapsed fibroids. This was achieved without difficulty or any other consequence to the patient.

**Pain**

Patients suffer pain to a variable degree after embolization. Ischaemic pain occurs immediately after the second artery is occluded and appears to be similar to that experienced in spontaneous degeneration of fibroids during pregnancy. The addition of local anaesthetic medication intra-arterially does not seem to reduce the pain (Goodwin and Walker, 1998). Treatment is with non-steroid anti-inflammatory drugs, narcotics and antiemetics. Patient-controlled narcotic analgesia (PCA) is effective but is not always required (Bradley et al., 1998). Surprisingly there does not seem to be a clear relationship between uterine size, fibroid size, fibroid number and analgesic requirement. However, pain may be related in part to the particle size used (Goodwin and Walker, 1998). Smaller particles (300–500 μm) reaching deeper into smaller vessels within the muscle mass, may cause a higher ischaemic volume. Use of larger particles (500–700 μm) may be associated with a reduction in the need for PCA. Hospital stay varies from same day discharge to a few days admission. When the patient can manage with oral or rectal analgesia, they may be discharged from hospital. Analgesic requirements progressively decrease; one to two week convalescence is common.

**Amenorrhoea and ovarian compromise**

Amenorrhoea was reported in six out of 81 patients (Ravina et al., 1998); this was transient in two patients and permanent in four. The average age of these patients was 45 years, and amenorrhoea said to be ‘related to menopause’. We reported the development of amenorrhoea due to ovarian failure in one patient, aged 41 years with a FSH concentration of 59.8 IU/l after the procedure (Bradley et al., 1998). Unfortunately the FSH concentration had not been determined prior to uterine artery embolization, so comparison with pretreatment concentrations could not be made. For this reason, we now evaluate the day 3 FSH concentration in all patients prior to the procedure. Two further cases of amenorrhoea have occurred in our series in older women, although in one other the FSH concentration rose from 3.7 to 15.5 IU/l after treatment, without amenorrhoea occurring. Seven cases of amenorrhoea were reported in a series of >200 patients (Walker, 1999), being permanent in three patients aged >50 years, and in two patients ‘in their late 40s’. In three other patients aged <50 years this resolved within 9 months. The mechanism for ovarian failure is unclear but must include redistribution in blood flow as may be seen in earlier menopause in patients following hysterectomy (Siddle et al., 1987), the procedure being coincidental with the perimenopause, and non-target embolization. The presence of aberrant ovarian arteries, and the finding of embolization particles in the ovarian vein after hysterectomy and oophorectomy (Walker, 1999) lends weight to this latter postulate.

**Sepsis**

This is the most serious complication as it may lead to emergency hysterectomy and in at least one case has resulted in death. There is an important line to be drawn clinically between extension of the post-embolization syndrome and life-threatening sepsis. In the post-embolization syndrome, the necrosis of a large tissue mass causes pain and intermittent lowgrade pyrexias, malaise, nausea and lethargy which usually resolves within 1 week. However, significant sepsis can appear relatively early, where it easily may be confused with a marked post-embolization syndrome. One death has already been reported in a 51 year old, which occurred within 10 days of the procedure (Vashisth et al., 1999). The patient was admitted with a pyrexia of 38.5°C with a tender uterus, and rapidly progressed to a disseminated intravascular coagulopathy. Despite early recourse to hysterectomy, the patient

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**Table I.** Response to telephone questionnaire in 305 cases of uterine artery embolization (data taken from Hutchins et al., 1999)

<table>
<thead>
<tr>
<th>Follow-up period</th>
<th>3 months</th>
<th>6 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients interviewed</td>
<td>185/240</td>
<td>121/180</td>
<td>59/109</td>
</tr>
<tr>
<td>Proportion (%)</td>
<td>77</td>
<td>67</td>
<td>54</td>
</tr>
<tr>
<td>No. complaining of menorrhagia</td>
<td>179</td>
<td>116</td>
<td>58</td>
</tr>
<tr>
<td>No. (%) showing clinical success</td>
<td>155 (87)</td>
<td>101 (87)</td>
<td>50 (86)</td>
</tr>
<tr>
<td>No. complaining of bulk symptoms</td>
<td>121</td>
<td>86</td>
<td>42</td>
</tr>
<tr>
<td>No. (%) showing clinical improvement</td>
<td>103 (85)</td>
<td>71 (83)</td>
<td>36 (86)</td>
</tr>
</tbody>
</table>
remained oliguric and acidic and died despite intensive therapy support. Hysterectomies are reported in most series where they have been performed as an emergency for sepsis (Goodwin and Walker, 1998; Ravina et al., 1998). In our own series of >200 cases, we have had to perform four hysterectomies for sepsis, one following a similar course with septic shock and coagulopathy 4 months after embolization, and one in a Jehovah’s witness who appeared with a marked cataba, weight loss and anaemia (6.6 g/dl) 3 months after her uterine artery embolization procedure. A septic pedunculated fibroid involved with the bowel necessitated a 50 cm bowel resection as well. Involvement of a pedunculated septic fibroid with the bowel was reported as part of the French group’s early series (Ravina et al., 1998). One other hysterectomy was performed within 10 days of the procedure because of worsening pyrexia unresponsive to antibiotic therapy similar one reported previously (Goodwin et al., 1997). Walker and Ettles (1999) reported two hysterectomies for infection in their series of 220 patients – one similarly associated with a tubo-ovarian mass, and one with an infected fibroid mass. Fibroid abscesses can be diagnosed most clearly on CT or MRI, where degenerating fibroids can be distinguished from infarcted ones by the presence of gas within them (Figure 4).

We have drained similar abscesses successfully transcervically using a termination suction catheter. Alternatively CT percutaneous drainage may be tried (Goodwin et al., 1997).

The factors predisposing to the likelihood of sepsis are not fully quantified, nor whether pretreatment with antibiotics or post treatment therapy is effective. However, pre-embolization screening for intrauterine infection may be appropriate. Clearly, for a woman having embolization as an alternative to surgery in order to preserve her fertility, hysterectomy is a real risk (1:50 in our series) which may exceed that of hysterectomy following myomectomy.

Conclusions

Bilateral uterine artery embolization has been taken up enthusiastically as an alternative treatment for fibroid disease. Although preliminary observational reports look impressive, with marked reduction in uterine volume and resolution of many symptoms, there are few objective data to support its efficacy in comparison with myomectomy, or hysterectomy or other surgical or medical means of controlling menorrhagia. Formal objective quality of life surveys are yet to be conducted and need to be undertaken in comparison with equivalent surveys on other modalities of treatment. Furthermore, the outcome of pregnancy following this procedure is yet to be established, especially the effects on fertility, fetal growth, and uterine integrity.

Although patient satisfaction seems to be high, embolization is not without serious complications including hysterectomy, a devastating outcome for patients seeking pregnancy. Indeed the risk following embolization may indeed be higher than the risk of hysterectomy following abdominal myomectomy, but equivalent data where myomectomy is undertaken on large multiple fibroid uteri is not available. For this reason alone, it is probably inappropriate that these procedures are undertaken by radiologists working in isolation, but patients should be investigated prior to the procedure and followed up afterwards, by a team including a surgically competent gynaecologist. Since it is likely that gynaecologists and radiologists will continue to adopt and practice uterine artery embolization for the treatment of fibroid disease, it is appropriate and timely that societal or national registers of cases should be organized in order to understand the benefits and hazards of the procedure until information from randomized trials is available (Broder et al., 1999).

References


Received on January 11, 2000; accepted on August 18, 2000