An Evidence-based Guideline for the Management of Uterine Fibroids Working Party of the New Zealand Guidelines Group*

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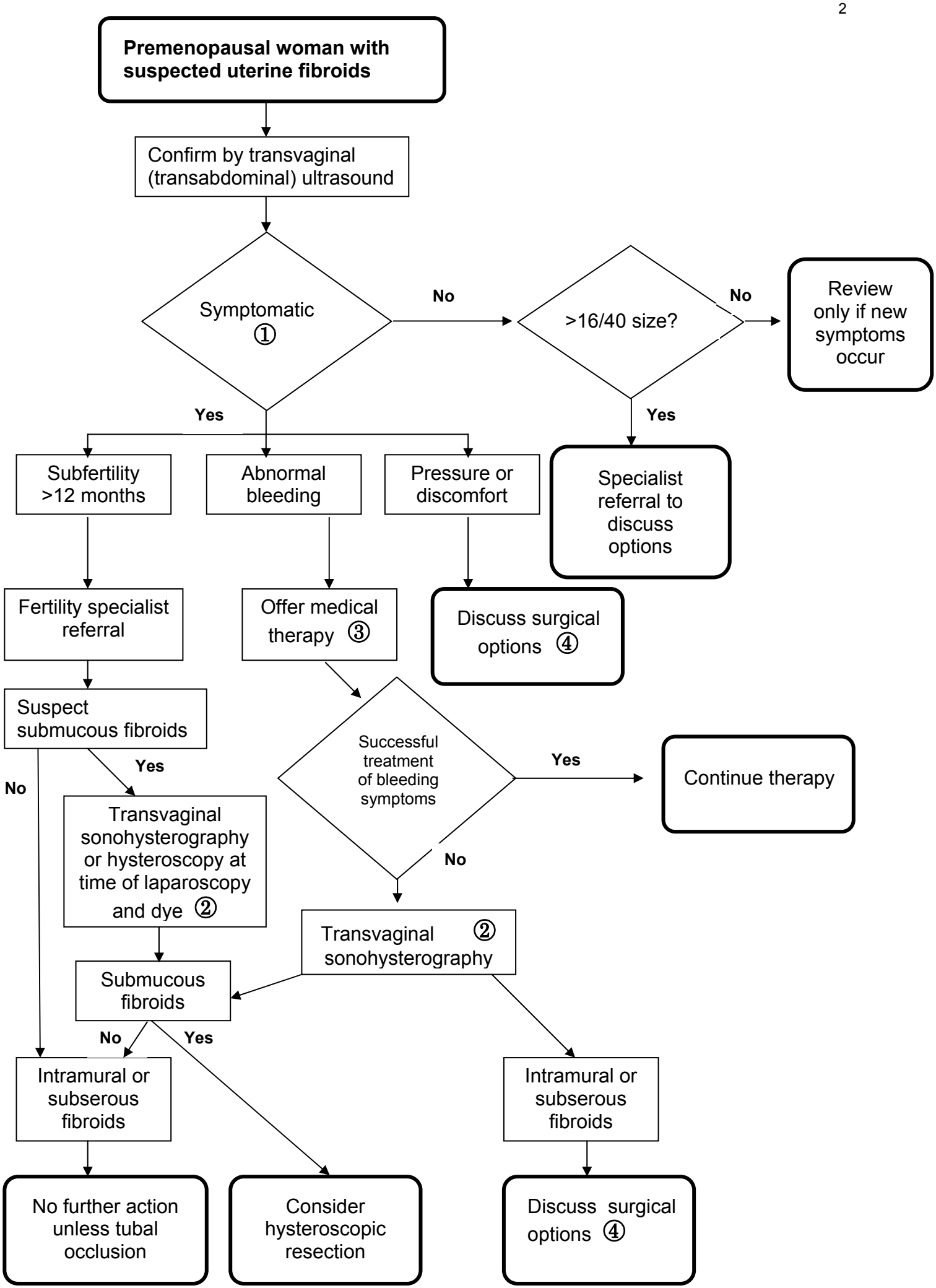
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Premenopausal woman with suspected uterine fibroids
Confirm by transvaginal (transabdominal) ultrasound
Symptomatic ①
No
>16/40 size?
No
Review only if new symptoms occur
Yes
Yes
Subfertility >12 months
Abnormal bleeding
Pressure or discomfort
Specialist referral to discuss options
Fertility specialist referral
Offer medical therapy ③
Discuss surgical options ④
Suspect submucous fibroids
Successful treatment of bleeding symptoms
Yes
Continue therapy
No
Yes
No
Transvaginal sonohysterography or hysteroscopy at time of laparoscopy and dye ②
Transvaginal ② sonohysterography
Submucous fibroids
No
Yes
Intramural or subserous fibroids
Intramural or subserous fibroids
No further action unless tubal occlusion
Consider hysteroscopic resection
Discuss surgical options ④

NOTES TO ALGORITHM

NOTE 1 Symptomatic for Uterine Fibroids

- Asymptomatic women with fibroids where the uterine size is less than 16 weeks in size (and where other causes of pelvic mass have been excluded) do not need further investigation but should be advised to seek help if symptoms occur (D).

- Although there is no evidence that asymptomatic women with a fibroid uterus greater than 20 weeks will have future health problems, hysterectomy or myomectomy is an option (D).

NOTE 2 Use of Transvaginal Sonohysterography

- Transvaginal sonohysterography (TVSH) should be considered prior to hysteroscopy in women where intrauterine pathology such as submucous fibroids and polyps are suspected as diagnostic hysteroscopy can be avoided in up to 40% of cases (A).

- MRI should be considered for women in whom the location or nature of the fibroids remains uncertain after transvaginal ultrasound and transvaginal sonohysterography or who wish to avoid the possible discomforts of a TVSH (D).

NOTE 3 Medical Treatment

Rx	Level of evidence	Improving symptoms	Shrinking fibroid	Maximum duration	Side effects
OC pill (HMB only)	2+	✓	X	Unlimited	Nausea, headache, breast tenderness
Danazol	2-	Not studied	✓ 57%**	6 months	Androgenic side effects
Gestrinone	1+	Not studied	✓ 15-36%	6 months	Androgenic side effects
GnRH analogues	1+	✓	✓	6 months	Androgenic side effects
LNG IUS	2+	Not studied	Not studied	5 years	Irregular menses, perforation, expulsion
RU486*	2+	Not studied	✓ 49%***	Not yet investigated	Not studied

Abbreviations:

OC=oral contraceptive; HMB=heavy menstrual bleeding; GnRH=gonadotrophin-releasing hormone; LNG IUS=levonorgestrel intrauterine system; RU486=mifepristone.

Symbols: * not yet licensed in New Zealand; ** result based on one trial; *** result based on one small non-randomised study

NOTE 4 Surgical Treatments

- The decision whether a hysterectomy or myomectomy is undertaken is dependent on: the woman's preference, the age of the woman, the desire to retain reproductive potential and the position and number of the fibroids (D).

- Medical therapy is an option if the woman is not considered fit for surgery or does not wish to undergo surgery; however, fibroids will return to pretherapy size within 6 months of stopping therapy (D).

- Administration of GnRH analogues for 2 to 4 months prior to surgery for uterine fibroids is recommended for women with a large uterus (> 18 weeks size) or pre-operative anaemia (B).

- Further imaging with MRI prior to surgical procedures may assist with decision making (D).

SUMMARY OF RECOMMENDATIONS

Assessment

- Asymptomatic women with fibroids where the uterine size is less than 16 weeks in size (and where other causes of pelvic mass have been excluded) do not need further investigations but should be advised to seek medical advice if symptoms occur (D).
- Asymptomatic women with fibroids >16/40 should have specialist referral to discuss options including observation (D).
- Women who have fibroids detected during pregnancy should be referred to a specialist for a consult but do not require additional surveillance unless symptoms arise during the pregnancy (D).
- Although there is no evidence that asymptomatic women with a fibroid uterus greater than 20 weeks will have future health problems, hysterectomy or myomectomy is an option (D).
- Transvaginal sonohysterography (TVSH) should be considered prior to hysteroscopy in women where intrauterine pathology such as submucous fibroids and polyps are suspected as diagnostic hysteroscopy can be avoided in up to 40% of women (A).
- Transvaginal ultrasound of the endometrium is accurate in excluding endometrial hyperplasia but is often unable to distinguish submucosal fibroids and polyps (A).
- Transabdominal ultrasound may be required for uteri greater than 12 weeks' size as these will be beyond the reach of the transvaginal ultrasound (D).
- Transvaginal ultrasound and transvaginal sonohysterogram are both more accurate in diagnosing the location of fibroids than hysteroscopy (A).

- When recommending hysteroscopy the following should be considered:
    - Normal saline should be used as it offers advantages (shorter and less discomfort) over carbon dioxide instillation (A).
    - Local anaesthetic should be offered as either a paracervical block, uterosacral block or uterine instillation (A).

- There is insufficient evidence to recommend magnetic resonance imaging (MRI) scanning as an initial diagnostic test for uterine pathology (D).

- MRI should be considered for women in whom the location or nature of the fibroids remains uncertain after transvaginal ultrasound and transvaginal sonohysterography or who wish to avoid the possible discomforts of a TVSH (D).

- There is insufficient evidence to recommend CT scanning in the assessment of fibroids (D).

Medical Treatments

- Progestogens should not be recommended in the treatment of uterine fibroids as there is insufficient evidence of benefit (D)

- Oral contraceptives are not effective in shrinking uterine size but may reduce menstrual blood loss with a resultant improvement in haematocrit (C).

- Hormone replacement therapy (HRT) should not be used to treat fibroids as it is not effective in reducing uterine fibroid size (A).

- Women who bleed while on continuous combined HRT and who are known to have fibroids should have adjustments made to their HRT by either decreasing the oestrogen dose or increasing the progesterone dose (D)

- Transdermal oestrogen formulations should not be given to women with fibroids (A).

- RU486 is effective in reducing uterine fibroid size without causing a reduction in bone mineral density (D)
- Danazol should not be recommended as initial treatment for fibroids as it is not as effective as gonadotrophin-releasing hormone analogues and has androgenic side effects which limit its use (C)
- Gestrinone is effective in reducing uterine and fibroid size but androgenic side effects may limit its use (A)
- Nonsteroidal anti-inflammatory drugs (NSAIDs) are not effective as a treatment for women with fibroids in reducing heavy menstrual bleeding (B)
- Gonadotrophin-releasing hormone analogue (GnRHa) treatment effectively reduces uterine and fibroid size but unpleasant side effects and a reduction in bone mineral density limit its sole use to 6 months (A).
- Gonadotrophin-releasing hormone (GnRH) analogue treatment for 3 months followed by combined 'addback' therapy (oestrogen plus progestin) result in fibroid shrinkage and are an alternative for women who have contraindications to surgery or who do not wish to undergo. Once therapy stops then the fibroids will return to pretherapy size. (B)
- There is insufficient evidence to recommend progestogen-releasing intrauterine systems to reduce uterine fibroid size (C)

Surgical Management

- Administration of GnRH analogues for 2 to 4 months prior to surgery for uterine fibroids is recommended for women with a large uterus (> 18 weeks size) or pre-operative anaemia (B).

- Women who are diagnosed with submucous uterine fibroids and heavy or abnormal menstrual bleeding should be offered hysteroscopic ablation or resection as an alternative to hysterectomy (C).

- Women with subserous and intramural fibroids associated with symptoms such as heavy menstrual bleeding and pressure symptoms should be offered a myomectomy as an alternative to hysterectomy (D).

- Laparoscopic myomectomy should not be undertaken in women who wish to conceive because of case reports suggesting increased risk of uterine rupture (D).

- There is insufficient evidence to recommend the routine use of adhesion barriers (B)

- There is insufficient evidence to recommend the routine use of vasopressin in reducing operative blood loss . (C).

- There is insufficient evidence to support the introduction of laser induced interstitial thermotherapy, myolysis or cryomyolysis technique (D).

- Embolisation of uterine fibroids may be an effective alternative to myomectomy or hysterectomy but RCTs are awaited (D).

- The low incidence of leiomyosarcoma discovered incidentally in asymptomatic women with uterine fibroids does not support operative management of fibroids as prevention of leiomyosarcoma (D).

- The decision whether a hysterectomy or myomectomy is undertaken is dependent on: the woman's preference, the age of the woman, the desire to retain reproductive potential and the position and number of the fibroids (D).

- Women with fibroids associated with symptoms such as heavy menstrual bleeding and pressure symptoms should be offered a myomectomy as an alternative to hysterectomy (D).

- Women who have fibroids detected during pregnancy should be referred to a specialist for a consult but do not require additional surveillance unless symptoms arise during the pregnancy (D).

INTRODUCTION

Uterine fibroids (myomas or leiomyomas) are benign growths of uterine muscle that occur commonly in women of reproductive age. Symptoms often attributed to uterine fibroids are heavy menstrual bleeding and pressure symptoms. When heavy menstrual bleeding occurs in association with uterine fibroids, hysterectomy has long been considered the definitive treatment. A fibroid uterus is one of the most common indications stated for hysterectomy (1,2,3). One in five New Zealand women will, by the age of 54, undergo hysterectomy (4), an operation that usually requires 4-6 weeks of convalescence (5). Yet, while the exact proportion is unknown, many cases of uterine fibroids are asymptomatic and surgical interventions may therefore be unjustified and unnecessary. Even if the fibroids are associated with symptoms, there are new management options that may reduce the need for hysterectomy.

Objective of the Guideline

The objective of this guideline is to provide evidence-based recommendations to assist decision making for the management of women who have uterine fibroids. It is aimed at general practitioners, obstetricians and gynaecologists and at women seeking information on management options for uterine fibroids. It does not provide recommendations for the investigation of undiagnosed abdominal masses.

Guideline Development Process

A multidisciplinary working party as listed in the authors with representation from both professional and consumer groups undertook the preparation of this guideline in association with the New Zealand Guidelines Group. After three meetings over 8 months in 1999, a draft document was widely distributed for comment and a final document prepared. This guideline has received endorsement from both the RNZCGP and the RANZCOG (NZ Committee). The full document including the evidence tables and the appendices is available on the New Zealand Guidelines Group Web Site (http://www.nzgg.org.nz/library/gl_complete/gynae_uterinefibroids/index.cfm#contents).

Clinical Questions

The following clinical questions were identified by the working party:

- How common are uterine fibroids?
- What are the risk factors for uterine fibroids?
- What clinical symptoms are attributable to uterine fibroids?
- What is the natural history of uterine fibroids?
- What is the best diagnostic test for uterine fibroids?
- Are there effective non-surgical interventions for uterine fibroids?
- Is pre-operative medical therapy helpful?
- What are the best surgical techniques?
- Is there an impact of fibroids on fertility and assisted reproductive technologies?
- What is the best advice to give asymptomatic women with uterine fibroids?
- What is the best advice to give women who have uterine fibroids during pregnancy?
- What is the best advice to give menopausal women with uterine fibroids who are receiving hormone replacement therapy ?

Identifying and Sifting the Evidence

For each question and topic, evidence was sought from original scientific publications, systematic reviews or meta-analyses. Comparative studies and randomised controlled trials (RCTs) were sought for evidence for diagnostic tests. Electronic searches were undertaken using MEDLINE (1966-1999), EMBASE and smaller databases such as Current Contents, Biological Abstracts, Social Sciences Index, PsychLIT and CINAHL. A full description of the process including the evidence summaries is available from the website. The Working Party agreed to rank the evidence and grade the

recommendations using the Revised Sign Grading System (Scottish Intercollegiate Guidelines Network 2000) (See Box 1):

BOX 1 Scottish Intercollegiate Guidelines Network Levels of Evidence and Grading of Recommendations

1^{++} 1^{+} 1^{-}	High quality meta analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias Well conducted meta analyses, systematic reviews, or RCTs with a low risk of bias Meta analyses, systematic reviews, or RCTs with a high risk of bias
2^{++} 2^{+} 2^{-}	High quality systematic reviews of case-control or cohort studies High quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, eg. case reports, case series
4	Expert opinion

Grade A*	At least one meta-analysis, systematic review, or RCT graded as 1++, and directly applicable to the target population; *or* A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
Grade B	A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; *or* Extrapolated evidence from studies rates as 1++ or 1+
Grade C	A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; *or* Extrapolated evidence from studies rates as 2++
Grade D	Evidence level 3 or 4; *or* Extrapolated evidence from studies rates as 2+

(SIGN, 2000)

Symbols: * In addition, our grading system differs from that of the SIGN in that we have graded comparative cross sectional studies that meet criteria for quality diagnostics as Grade A.

SUMMARY OF THE EVIDENCE

Prevalence

Fibroids are benign smooth muscle tumours found in the submucous, intramural and/or subserosal regions of the uterus (Fig 1). They are often asymptomatic, which may explain the paucity of prevalence data. They are frequently quoted as occurring in 25-40% of women of reproductive age, although the original sources of these data are not clear (6 (3)).

Fibroids were found at routine histological examination in 40% of New Zealand women (aged less than 46 years old) at hysterectomy (3 (2-) although the true frequency may be even higher. The application of gross serial sectioning at 2 mm intervals in 100 consecutive total hysterectomy specimens revealed an incidence of 77% (649 leiomyomas in 77 of 100 uteri) compared to 52% at routine histology (7 (3)).

Hysteroscopic series have reported finding submucous fibroids in 6-34% of women investigated for abnormal uterine bleeding (8,9,10,11,12(all 3)), in 2-7% of women investigated for infertility (13,14 (all 3)),, and in only 1.5% of asymptomatic women undergoing hysteroscopic sterilisation (15 (3),), suggesting that the site of the fibroid may be important in determining symptoms. Some 10 to 15% of women will undergo hysterectomy for fibroids between the ages of 25 and 64 years, according to data from the Oxford Family Planning Association Study (16 (2-)) and the Healthcare Cost and Utilisation Project, USA (17 (2-)). Studies designed to identify the prevalence of polycystic ovaries in women aged 18-45 years reported fibroids on ultrasound in less than 3% of cases (18 (2-); 19 (2-); 20 (2-)).

Risk Factors

Increasing age is associated with increasing prevalence of fibroids until menopause when oestradiol levels begin to fall (16 (2-)). After the menopause the uterus contains fewer and smaller fibroids (7 (3)). Family history is associated with increased

prevalence, with up to a 3-fold higher risk in first degree relatives (21,22 (all 2-)). African- and Caribbean-American women have a higher prevalence of fibroids, are more likely to undergo hysterectomy and at a younger age, and have larger and greater numbers of fibroids compared to white women (23 (2-)). No differences in prevalence were found among Maori, Pacific Islands or Asian women undergoing hysterectomy at National Women's Hospital (3 (2-). Obesity is strongly associated with fibroids (24), with the risk being three times greater in women weighing >70 kg compared with those weighing <50 kg (16 (2-)).

There is an association between nulliparity and fibroids, and an inverse relationship between number of pregnancies and fibroids. The risk for women with five or more children is a quarter that of nulliparous women (16 (2-)). The risk is not related to maternal age at birth of the first child but is reduced by a later age at last pregnancy (16 (2-)). It is not clear whether the association between parity and fibroids is a true protective effect or a result of a contribution by fibroids to infertility. Infertility has been associated with a doubled risk of fibroids (25 (2-)).

Oral contraceptive pill use, sterilisation, frequent PAP smears, and higher education are associated with an increase in fibroid prevalence. These factors are also markers of access to health care and probably reflect increased detection rates (21,26,27 (all 2-)). In contrast, the Oxford Family Planning Association Study showed that the risk of fibroids decreased with increasing duration of oral contraceptive use (16(2-))., while Parazzini and colleagues (25) (2-) reported no association between oral contraceptive use and fibroid prevalence. A large case-control study found no overall increase in fibroid detection after more than 3 months of combined oral contraceptive pill (COC) use (26 (2-)). These conflicting studies provide no clear evidence of an association between COC use and fibroids. The use of Depo-Provera (medroxyprogesterone acetate) was associated with a relative risk of fibroids of 0.44 (i.e. a protective effect) (21 (2-)).

Table 1: Risk factors for uterine fibroids

Ethnicity *African – Caribbean women	Increased risk
Family history First degree relatives with fibroids	Increased risk
Low parity/infertility	Increased risk
Obesity	Increased risk

Symbols: *In a study of NZ women (n=350), Maori and Pacific Islands women had the same rates of fibroids as European women.

Natural history

Little is known about the natural history of asymptomatic fibroids. However, their growth appears to be slow and they are often undetected until a woman presents for cervical screening or in pregnancy. The most common age at presentation is 30 to 40 years (16 (2-)).. Once detected there is some evidence that fibroids in symptomatic women are associated with ongoing health problems. For example, in a group of symptomatic pre-menopausal women with fibroids initially choosing conservative management, approximately 25% subsequently decided to have a hysterectomy within 12 months (28 (2-)). After myomectomy, fibroids may recur in up to 27% of women over a 10-year period. (29 (3)). The recurrence rate was lower (15%) for women who gave birth after myomectomy than for women who did not conceive (30%). Recurrence rates were also lower in women with fewer fibroids at the time of surgery.

Prospective studies of uterine fibroids in pregnancy report that 80% of fibroids reduce or show no change in size (30,31,32,33 (all 3)). When they do increase in size the increase is rarely greater than 25%. Although degeneration is commonly suspected this is infrequently found at histology. A reduction in the size and number of fibroids occurs after the menopause (7 (3)).

Leiomyosarcoma (a malignant tumour of fibroids) is rare. It is not known how often these tumours arise in fibroids but, given that many women with fibroids do not undergo hysterectomy, it has been estimated at less than 1 per 1,000 (13 (3)). These tumours are more common in postmenopausal women and present with rapid growth, pain, and postmenopausal bleeding. In a review of 20 years of cases of leiomyosarcoma at National Women's Hospital, 60% occurred in postmenopausal women with abnormal bleeding (34 (3)). The American College of Obstetricians and Gynaecologists do not consider the risk of leiomyosarcoma to be sufficiently high to justify hysterectomy (35).

Clinical Associations

Although it is commonly stated that an unknown proportion of uterine fibroids are probably asymptomatic (36 (4)), it is difficult to establish this as fact because no prevalence studies have been identified that specifically address this issue.

Heavy Menstrual Bleeding. The contribution of uterine fibroids to heavy menstrual bleeding is unclear. Approximately 50% of women with heavy menstrual bleeding have no identifiable uterine pathology and 30% of women with fibroids have been reported to have menstrual abnormalities (13 (3)). In a prospective study of premenopausal women undergoing hysterectomy for a variety of indications, uterine fibroids were identified in 40% of women but there was no association with complaints of heavy menstrual blood loss (MBL) (3). However, there is some evidence that women with higher volumes of MBL have an increased frequency of uterine fibroids; in one study 40% of women with MBL greater than 200 ml (less than 80 ml is considered within the normal range) had uterine fibroids whereas only 10% of women with MBL between 80-100 ml had fibroids (37 (2-)). There is also limited evidence that the site of the uterine fibroids may be responsible for certain clinical symptoms as menstrual blood losses of >350 ml appear to be associated with submucous fibroids in particular (38 (2-)). The incidence of submucous fibroids in 323 consecutive

asymptomatic women undergoing sterilisation was reported at 1.8% (15 (2+)) whereas in a series of women with abnormal uterine bleeding, submucous fibroids were reported more frequently (6-34%) (8,9,10,11,12 (all 2-)).

The association of fibroids with heavy or abnormal menstrual bleeding is most likely to be due to increased endometrial surface area. Both submucous and intramural fibroids have the potential to cause this to occur. Another explanation is that fibroids alter the production of local endometrial factors such as prostaglandins (36 (3)).

Anaemia is more common in women with fibroid-associated menorrhagia than in women with menorrhagia from other conditions (38 (2-)).

Hysterectomy Fibroids were found in 21.7% of uteri at hysterectomy in Australia (6 (3)), 27% in the USA (17 (3)), 50% in Finland (39 (3)) and 40% in New Zealand (3 (3)).

Infertility The extent to which infertility is attributable to fibroids is unclear. In a review of nine case series of women undergoing myomectomy, Buttram and Reiter (13 (3)) found that 27% reported a history of infertility. This figure is likely to be inflated by those women whose myomectomy was performed because of infertility, and includes women who may have had a co-existing cause for infertility. No RCTs of myomectomy for infertility exist. The impression that fibroids are related to infertility arises from a number of reported case series where removal of fibroids resulted in subsequent conception rates between 30 and 80% (13,36,40 (all 3)). Although there is an inverse relationship between the number of term pregnancies and uterine fibroids (16 (2-)), age may be a confounding factor.

Fibroids have been associated with poor outcomes in artificial reproductive technology cycles and myomectomy improves outcome (41,42,43 (all 3)). In

order to establish whether fibroids cause infertility and whether myomectomy is an effective treatment, RCTs need to be undertaken.

Pressure Symptoms Pressure symptoms are often described with uterine fibroids but no reports were found to support this symptom as being a true clinical feature. Occasionally fibroids can prolapse through the cervix.

Pelvic Pain Although fibroids are thought to be an infrequent cause of pelvic pain, RCTs of therapeutic interventions gonadotrophin-releasing hormone (GnRH) analogues report a reduction in pelvic pain (particularly dysmenorrhoea) when the fibroid volume reduces (44 (2-)). Other explanations for the reduction in pain are also possible.

Pregnancy The reported prevalence of fibroids in pregnancy (detected by ultrasound) is 4-5% (14,45 (all 3)) although this figure is strongly influenced by maternal age. Most fibroids remain uncomplicated and do not increase in size. Up to 10% undergo degeneration, typically in the second trimester. This is usually a self-limiting process occasionally requiring only bedrest, adequate hydration and analgesia (45 (3)). It is not clear whether fibroids are implicated in miscarriage, placental abruption, preterm birth, preterm premature rupture of the membranes, outlet obstruction, and caesarean section. Fibroids lying over the lower segment may prove a challenge at the time of caesarean birth.

Causality Applying the criteria necessary to prove causality between pathology and symptoms (46 (1991)) results in the following conclusions: Fibroids probably do not cause infertility in most cases, submucous fibroids probably increase menstrual bleeding but other types of fibroids probably do not and fibroids may cause pressure symptoms and pain although little research has addressed this question.

Assessment

The accurate assessment of the number, size and location of fibroids, especially when myomectomy is planned, is important because it often influences the type of surgical approach. There is no single correct approach to evaluating uterine fibroids. A number of options are available which vary considerably both in cost and inconvenience to the woman.

The true prevalence of fibroids is unknown as clinical populations - by their very nature - may include women with higher rates if fibroids do, in fact, cause gynaecological symptoms and signs. Post-test likelihood of a positive result (also known as the positive predictive value) rises as the prevalence rises (46). In the evidence tables provided in this guideline, the prevalence ranges from 10% (47) to 94% in a pre-selected study group (48) For most of the clinical populations the rates are below 60% ensuring that a positive test will have a high probability of being truly positive and a negative test will have a low probability of being falsely negative. The quality of the comparative studies in the following sections was assessed according to the following criteria: independent assessment by 2 individuals, prospective study and consecutive recruitment of cases. Diagnostic tests were assigned a 1- level of evidence or higher if they had 1 or more of these criteria.

Transvaginal ultrasound (TVS)

In a large prospective study of 770 premenopausal women, transvaginal ultrasound (TVS) had a sensitivity of 0.8 and a specificity of 0.7 for diagnosing submucous myomas (12 (1+)). Six submucous fibroids were missed and 31 cases of intramural fibroids were incorrectly diagnosed as submucous fibroids. While TVS is able to rule out endometrial hyperplasia in premenopausal women (negative likelihood ratio of 0.02) it is of limited use for the exclusion of submucous fibroids and polyps (negative likelihood ratio of 0.29). In another prospective study, had TVS been used as the first step to decide on the need for further examination, further assessment (usually

hysteroscopy) would have been avoided in approximately 40% of women (9 (1+)).). Transabdominal ultrasound (TAUS) in combination with TVS may be undertaken as TAUS will allow large fibroid uteri or pedunculated fibroids to be imaged (49 (3)).

Transvaginal sonohysterography (TVSH)

The technique of transvaginal sonohysterography (TVSH) involves uterine injection of saline during a TVS. Seven comparative studies comparing TVSH (or transabdominal sonohysterography [TASH]) with either TVS (8,50) or hysteroscopy (47,51,52,53,54) have been undertaken. (The quality of these studies is mixed and the assigned levels of evidence varies from 1+ to 1-). For diagnosing fibroids the positive likelihood ratios are excellent - ranging from 17.9 to infinity (47,51,53,54 (1+)). Negative likelihood ratios ranged from 0.06 to 0.12 (47,51,53,54 (1+)).. Some discomfort from the distension may be experienced. The procedure takes slightly longer than TVS (maximum 15 mins) (51 (1-)). Infective complications are rare (50 (1+)).. It is estimated that 29 to 47% of women could avoid diagnostic hysteroscopy as a result of a negative TVSH (8,51 (all 1+)).. All cases of fibroids and polyps were diagnosed and although three endometrial cancers were not initially picked up in this study there were abnormalities that indicated the need for diagnostic hysteroscopy (51 (1+)). Cervical stenosis may result in some failures (8 (1+)). Concern about the spread of adenocarcinoma in the peritoneal cavity is debated. Peritoneal lavage in the four cases of endometrial carcinoma was negative for cancer cells (8 (1+)). Survival rates of women with endometrial carcinoma who underwent standard hysterosalpingography with radiopaque contrast media (a procedure similar to TVSH) were not different between women who demonstrated intraperitoneal spill of the contrast medium and those who did not (55 (3)).

Hysteroscopy

Hysteroscopy involves inserting a telescope (usually 2.7-4 mm) into the endometrial cavity. The procedure may be performed in an outpatient setting without anaesthetic,

although some women (approximately 25%) will require local anaesthesia and some women may prefer general anaesthesia (56,57 (3)).. Two methods of uterine distension are used – carbon dioxide and normal saline instillation. A RCT of carbon dioxide versus normal saline instillation during hysteroscopy found that normal saline provided comparable visualisation to carbon dioxide with reduced procedure time and patient discomfort (58(1+)).

A large comparative study (quality A) of hysteroscopy and TVS has been undertaken (12 (1+)). Hysteroscopy was well tolerated with only 3.6% (28/770) of women reporting that they would not have the procedure done again due to the pain they experienced. Complications were rare and tubal infection following the procedure was infrequent (1/770 cases). Both TVS and hysteroscopy detected the 2 cancers present in the study but hysteroscopy was superior to TVS in detecting submucous fibroids.

In a comparative study of TVSH and hysteroscopy, TVSH was marginally better than hysteroscopy for diagnosis of submucous fibroids although hysteroscopy detected one additional case of hyperplasia (6/7) than did TVSH (5/7) (54 (1+-)). However, in other comparative studies (12,47 (1+)) hysteroscopy (without biopsy) is not considered reliable in the identification of endometrial hyperplasia; this emphasises the need for a biopsy in the presence of endoscopically normal mucosa. In another comparative study (quality A) both TVS and hysteroscopy had similar positive and negative likelihood ratios for submucous myomas (10 (1-)) but TVS was better at mapping and sizing submucous and intramural fibroids than hysteroscopy. In a further report (quality C) comparing TVSH with hysteroscopy the authors concluded that TVSH avoided the need for diagnostic hysteroscopy in 47% of women who could then proceed to planned operative hysteroscopy (8 (1+)).

Computerised tomography (CT)

Computerised tomography (CT) provides complete visualisation of the female pelvis including non-gynaecological structures, but offers limited resolution of the internal architecture of the female pelvic organs and requires the use of ionising radiation (59 (4)). It is not as specific as ultrasound in differentiating uterine masses from ovarian masses or the surrounding bowel. Its current use in gynaecology is in staging or following up gynaecological malignancies (60 (4)). No comparative studies of CT scanning and TVS or hysteroscopy that enabled calculation of both sensitivity and specificity were found, although one study did compare TVS with CT and magnetic resonance imaging (MRI) (61 (2-)). While only the sensitivities could be calculated MRI was found to be more accurate than TVS or CT at detecting both benign and malignant disease. The authors concluded that ultrasound would still be used as a screening tool, with MRI used when there is a significant difference of opinion between the clinical and ultrasonic findings.

Magnetic Resonance imaging

Magnetic resonance imaging (MRI) is claimed to have superior contrast resolution compared with CT or ultrasound and better spatial resolution compared with CT (59,60,62 (all 3 or 4)). Studies comparing MRI with other modalities do not involve many women: of the 31 studies identified, none had more than 43 participants and most had considerably fewer (63,64,65,66,67,68; other references not listed (all 2- or 3)). One large study using MRI in 93 women undergoing either hysterectomy or myomectomy reported a sensitivity of 1 and a specificity of 0.94 (69 (1+)). Smith and colleagues (61) performed a comparative study of MRI, CT and TVS and reported that MRI was more accurate than CT or TVS (see section 2.2.4)(1+). Other pathologies such as endometriosis may also be diagnosed (64). Until further large studies comparing ultrasound or hysteroscopy with MRI are undertaken it is not possible to make a recommendation regarding the use of MRI as a diagnostic tool.

Medical Management (not followed by surgery)

Treatment options for women with large or symptomatic uterine fibroids have traditionally been hysterectomy or myomectomy. As many women are delaying child-bearing into their thirties or forties and there is a desire for less invasive treatment, alternative options to surgery have been developed. As understanding of the factors that contribute to the growth of uterine fibroids has developed, a number of different medical treatments have been tested. Since fibroid growth and maintenance are stimulated by oestrogen and are affected by hormonal cyclic changes, many of these treatments are based on the suppression of oestrogen. Gonadotropin-releasing hormone (GnRH) analogues are most commonly used for the medical management of uterine fibroids but other treatments have also been investigated. Although complete regression of fibroids is the ideal outcome of medical treatment, in practice the main objective is symptomatic relief resulting from the reduction in uterine and fibroid size.

Progestins

There is little evidence to support the use of progestins in the treatment of uterine fibroids. Fibroids contain progesterone receptors (70) and, as such, progestins should in theory be effective; however, no studies were identified. Progestins are often used in practice to halt the growth of fibroids and to improve symptoms but there is no evidence from clinical trials to support their use.

Combined oral contraceptives

There are no RCTs of the combined oral contraceptive (COC) pill for the treatment of fibroids. Data is available from a several large cohort studies (16,26,27,71 (all 2-)). Unfortunately both selection and detection bias limit the usefulness of the findings. [NB. In a non-randomised 1 year study of women with fibroids those taking COCs were compared to women not on the pill for 1 year. No significant change was found in uterine size though the duration of the period decreased significantly (5.8 to 4.4

days) in women taking COC with a significant increase in haematocrit (71). However, this study was completely retracted one month later (72).

Antiprogestogens

Mifepristone (RU486) is a synthetic steroid with antiprogestogen activity that has been shown to inhibit ovulation and disrupt endometrial integrity. Because fibroids are ovarian steroid dependant, RU486 may cause regression of fibroids. In a non-randomised study, fibroid volume was reduced 49% in 12 weeks and side effects were mild and infrequent (73 (3)), while bone mineral density (BMD) was not affected. While early results are promising, longer follow-up studies are required before this treatment can be recommended. RU486 is not currently available in New Zealand.

Androgens

In a non-randomised study, Danazol caused a regression in fibroids over 3 months of therapy (74 (2-)). In another non-randomised study, Danazol was less effective than a GnRH analogue, buserelin, in shrinking fibroids (75(2-)). Danazol has also been reported to prevent rebound growth after GnRH analogue treatment (76 (2-)). However, Danazol's usefulness as a treatment option is limited because of its androgenic side effect profile and restricted duration of use (6 months).

Gestrinone

Gestrinone is an antiprogestogenic and anti-oestrogenic agent that may have a role in the treatment of fibroids. In one study total uterine volume as measured by ultrasound decreased in 73% of women and amenorrhoea occurred in 53% of women by 8 weeks (77 (1+)). The decrease in fibroid size lasted up to a year following treatment. Other benefits included increases in haemoglobin. Most women experienced androgenic side effects such as acne, hirsutism and weight gain although these reversed on cessation of treatment. Whether these side effects are acceptable to women seeking treatment for their fibroids is unclear. The long-lasting effects of reduced fibroid volume after stopping treatment may be a major advantage for gestrinone.

Non-steroidal anti-inflammatory drugs

NSAIDs can be useful in reducing heavy menstrual bleeding not associated with uterine fibroids but they are not effective as a treatment for women with fibroids (78 (1-); 79 (1-)).

GnRH analogues

The reduction in the size of fibroids during the menopause, a naturally occurring hypo-oestrogenic state, led researchers to consider GnRH analogues as a therapeutic option. These treatments have been the most commonly investigated in RCTs. By suppressing the pituitary and thereby blocking ovarian function, GnRH agonists induce a state of hypo-oestrogenism with the consequent effects being a reduction in fibroid and uterine volume and control of bleeding. Multiple studies have confirmed a regression of fibroids - typically to 50% of their initial volume - with complete regression occurring only in smaller tumours. The reduction in total fibroid/uterine volume seems to be dependent on the level of oestrogen suppression (80,81), with heavier women (having elevated levels of circulating estrone) requiring larger doses of GnRH analogues (82). Nevertheless, the decrease in uterine volume in studies ranged from 25 to 80% and is achieved maximally at 12 weeks.

Although as many as 50% of women with uterine fibroids are asymptomatic, a diagnosis of fibroids is usually made when a woman seeks help for symptoms such as pressure, heavy menstrual bleeding, pelvic pain and dysmenorrhoea. Pressure symptoms may be relieved by GnRH analogue treatment (83). GnRH analogue treatment relieves heavy menstrual bleeding by inducing anovulation and endometrial atrophy, although the bleeding recurs rapidly upon ceasing therapy. Pelvic pain and dysmenorrhoea are also common symptoms in women with fibroids. In a RCT of 3 months' treatment with buserelin or placebo, 26.5% of women receiving placebo had relief of dysmenorrhoea compared with 91% of women receiving the GnRH analogue (44 (A+)). Comparable figures for reduction in pelvic pain were 45% and 72% in the placebo and buserelin groups, respectively. Significant reductions in pain symptoms

can thus be achieved in women with uterine fibroids receiving GnRH analogue treatment.

However, there are significant disadvantages to the use of GnRH analogues as a sole treatment for uterine fibroids. The duration of treatment with these agents is limited to 6 months because of the rapid bone demineralisation associated with oestrogen withdrawal (84). Furthermore, the occurrence of subjective side effects associated with the hypo-oestrogenic state, particularly hot flushes and vaginal dryness, are unpleasant and can reduce quality of life. After GnRH analogue therapy is stopped, there is regrowth of both fibroids and uterus to almost pre-treatment size and a recurrence of symptoms in most women (84). For this reason, the use of GnRH analogues as a sole treatment for uterine fibroids is disappointing.

Concerns about bone loss and the poor tolerability of GnRH analogues led to a number of studies on oestrogen and progestin 'addback' therapy in conjunction with GnRH analogue treatment. With the addition of progestins alone to GnRH analogue treatment, there is a reduction in hot flushes and other symptoms but no reduction in uterine or fibroid volume (85). However, with combined addback therapy (oestrogen plus progestin), the reduction in uterine and fibroid size is maintained while the annoying side effects of GnRH analogue treatment are controlled (86 (1-)). Addback therapy is usually administered at about 12 weeks after the beginning of GnRH analogue treatment by which time the maximum reduction in uterine size has occurred. This regimen may provide the answer to long-term GnRH analogue treatment where surgery is not desired or feasible; however, a cost benefit analysis needs to be undertaken. GnRH analogues are not currently funded in New Zealand for this indication.

Levonorgestrel intrauterine system (LNG-IUS)

No RCTs of levonorgestrel intrauterine system (LNG-IUS) in women with fibroids were identified. As fibroids may distort the uterine cavity, their presence has usually been a contraindication to IUS use. However, in a large multicentered study comparing the

LNG-IUS (Mirena) and the TCu 380AG intrauterine contraceptive device, LNG-IUS users experienced a lower rate of myoma development and less uterine surgery and hysterectomy after 5 years of use (87 (1-)). In a small prospective pilot study of 5 women fitted with the LNG-IUS, fibroid volume regressed after 6 to 18 months of use (88 (3)). The LNG-IUS may have an effect on fibroid growth by inhibition of endometrial growth factors (89,90). Further studies are required to confirm these preliminary findings.

Hormone replacement therapy (HRT)

There are limited data on the effect of HRT on fibroid growth. A RCT of postmenopausal women with small asymptomatic fibroids (diagnosed by TVS) compared the effect on fibroid size of treatment of 50 μg transdermal oestrogen and 5 mg medroxyprogesterone acetate (MPA) given continuously, or 0.625 mg oral conjugated equine oestrogen plus 2.5 mg MPA given continuously (91 (1+)). At one year of follow up there was a significant increase in fibroid size with transdermal oestrogen but no change in fibroid size with oral oestrogen. A one year RCT of tibolone versus placebo compared fibroid growth by TVS in 40 asymptomatic postmenopausal women with at least one fibroid >20 mm (Gregoriou et al. 1997(1+)). No significant difference was found in the mean volume of fibroids after treatment with tibolone compared with placebo.

The extent to which HRT increases the frequency of abnormal bleeding in pre and postmenopausal women with fibroids is not known, and the different findings are in part due to dissimilar study definitions of abnormal bleeding and different treatment regimens.

Pre-operative Management

GnRH analogues induce a state of hypo-oestrogenism by suppressing pituitary function; the consequent shrinkage of fibroids and uterus and reduction in uterine blood flow have led to investigations of their role as a pre-operative adjunct to surgery.

A number of RCTs have formed the basis of a Cochrane systematic review evaluating the role of GnRH analogue pre-treatment prior to either hysterectomy or myomectomy for uterine fibroids (5). Outcomes evaluated in these trials included the pre-operative assessment, such as the change in blood count parameters and reduction in uterine and fibroid volume, as this is likely to have an impact on the forthcoming surgery. Intra-operative (duration of operation and hospital stay, blood loss, frequency of blood transfusions) and post-operative (complications, recurrence of fibroids) outcomes were evaluated separately according to whether hysterectomy or myomectomy was performed.

Pre-operative outcomes

Blood count parameters (haemoglobin and haematocrit) were significantly increased and uterine and fibroid volume and gestational size were significantly reduced when women were treated with GnRH analogues for 2 to 4 months prior to surgery for their uterine fibroids. Pelvic symptoms were also reduced but women were more likely to suffer uncomfortable adverse events relating to treatment such as headaches, hot flushes and vaginal symptoms.

Intra-operative outcomes

Blood loss during surgery was reduced by an average of 60 ml in women pre-treated with GnRH analogues and the duration of hysterectomy and hospital stay after hysterectomy were reduced by an average of 6 minutes (less than 10% of total operating time) and 1 day, respectively. The rate of blood transfusions was not affected by pre-treatment but fewer operations were rated as difficult by the surgeons. The odds of vertical as compared to transverse incisions during both types of surgery was reduced by at least two thirds in women with GnRH analogue pre-treatment and these women were eight times more likely to have a vaginal rather than an abdominal hysterectomy.

Post-operative outcomes

Haematological parameters after surgery were marginally higher in women with GnRH analogue pre-treatment compared to women with no pre-treatment but the rate of complications or quality of life did not appear to be affected. However, there is some evidence to suggest that women with pre-treatment may be more likely to have their fibroids recur (an average of 4 times the odds), presumably because small fibroids are not seen at the time of surgery. There was no evidence of pre-treatment leading to an improvement in fertility outcomes after myomectomy; this issue has yet to be conclusively evaluated.

Regardless of the benefits shown, there is inadequate evidence to support the use of GnRH analogues for all women with fibroids undergoing hysterectomy or myomectomy. In one small study uterine size was reduced by 350 ml in women with uteri 14 to 18 gestational weeks, but by 1304 ml in women with uteri greater than 18 weeks (93 (1-)). Thus GnRH analogues can be recommended for pre-operative use in women with a greatly enlarged uterus, pre-operative anaemia or where a midline rather than transverse incision would be planned. In addition, some women undergoing hysterectomy would be able to avoid an incision as their uterus may be able to be removed via the vaginal instead of the abdominal route (5 (1+)).

Surgical Management

Hysteroscopic treatment of fibroids

There is an association between submucous fibroids and heavy menstrual bleeding. Submucous fibroids are suitable for hysteroscopic management by either ablation or resection because of their site within the uterine cavity. The degree of damage to the endometrial cavity will depend on the depth of extension of the fibroid into the myometrium.

Eleven case series of submucous fibroid resection have been reported (clinical subjective improvements only). These series were summarised by Brill (94 (3)) and

showed a failure rate (i.e. continued heavy menstrual bleeding) of 0-35%. The largest series retrospectively reports long-term follow-up of consecutive participants with abnormal menstrual bleeding in association with submucous fibroids (n=196) or endometrial polyps (n=65) (95 (3)). Postoperative woman satisfaction was 86% for polyps and 81% for fibroids. Derman and colleagues (96) constructed a life-table analysis which showed that the cumulative chance of avoiding further surgery four years after initial surgery was 84% (3). In a prospective study of 51 women with abnormal uterine bleeding and submucous fibroids, it was found that, in order to achieve control of bleeding, up to 3 procedures were necessary if there was more extensive intramural extension (97 (3)). Overall 69% of women had a resolution of their bleeding after one resection and 88% were symptom free following three resections. Hart and co-workers (98) reported that 79% of women (n=122) who underwent hysteroscopic myomectomy did not require further surgery over the first four years of follow-up (3). The degree of extension of the fibroid into the endometrial cavity and the size of the fibroid (<4cm) determined the likelihood of success of hysteroscopic resection. Operative complications included incomplete resection (n=9), fluid absorption > 2000ml (3), cervical tear (1), blood transfusion (1) and uterine perforation (1). 86% of women reported an improvement in menstruation and 72% reported an improvement in dysmenorrhoea. Only 10% of women were dissatisfied with the procedure. Pretreatment of the endometrium is considered unnecessary.

Only one study measured menstrual blood loss before and after hysteroscopic myomectomy (size 1-4 cm) (99 (3)). In 4 women, measured menstrual blood loss was reduced from a mean of 261 ml (range 127-454 ml) preoperatively to 57 ml (range 41-100) at 6 months.

Myomectomy

Myomectomy is an operation that aims to remove fibroids and conserve the uterus. It is an alternative operation to hysterectomy. The aims of myomectomy are to preserve

reproductive function and gain improvements in symptoms such as heavy menstrual bleeding, pressure symptoms and reduction in an abdominal mass.

Heavy menstrual bleeding

There are no RCTs of myomectomy for improving menstrual blood loss or fertility outcomes. In reviews of case series of myomectomy for heavy menstrual bleeding, 80% or more of women report subsequent resolution or improvement in menorrhagia (13 (3)). It is not clear from this report the site from which the fibroids were removed.

Recurrent miscarriage

In women with known fibroids who are planning a pregnancy, myomectomy is not indicated as the presence of fibroids does not usually influence the pregnancy outcome (45,100 (both 3)). In women with recurrent miscarriage and known fibroids the role of myomectomy is unknown. In a large series a miscarriage rate of 19% was reported in women following myomectomy compared to 41% for the same group of women prior to myomectomy (13 (3)).

Pregnancy following myomectomy

Pregnancy outcomes following myomectomy are largely favourable but, rarely, scar rupture in late pregnancy or in labour may occur (0.5% of cases) (85 (3)). Caesarean section is recommended if multiple uterine incisions had been required or if the uterine cavity had been entered but no evidence was found to support this recommendation (101 (4)).

Recurrence of fibroids following myomectomy

One series of 622 women who underwent myomectomy reported a 10-year recurrence rate of 27% (102 (3)). Women who gave birth were less likely to have a recurrence than women who did not (15 *vs* 30%).

Techniques of myomectomy

Until the advent of advanced laparoscopic surgery all myomectomies were performed by laparotomy. The use of the laparoscope to remove intramural fibroids has been described but the surgery takes longer than open laparotomy and requires a high level of suturing skill (103,104 (both 3)). Usually fibroids >6 cm in diameter are considered unsuitable for a laparoscopic approach (105,106 (3); 107 (1-)). In one RCT of open versus laparoscopic myomectomy no differences in surgical time, blood loss or postoperative complications were reported (107 (1-)).

Uterine rupture during pregnancy following laparoscopic myomectomy has been reported (106,108,109 (all 3)) and is attributed to a lack of deep suturing. Thus its role in women who wish to retain fertility is limited.

Procedures to reduce adhesions following myomectomy

Although the use of adhesion barriers (Interceed, GorTex) is associated with reduced adhesions at second-look laparoscopy, there were problems with study design within the RCTs and no RCTs have included pregnancy as an outcome measure (110 (1-). New liquid products (e.g. Intergel) are currently under evaluation. The use of saline instillation immediately at the end of the surgical procedure does not improve subsequent pregnancy rates (111(1-)).

Procedures to reduce blood loss at myomectomy

The use of vasopressin resulted in a greater reduction in operative blood loss at the time of myomectomy than tourniquet or placebo (112,113 (both 1-)) although another study did not report any difference between vasopressin and tourniquet (114 (1-)).

New surgical techniques of fibroid management

Laser-induced interstitial thermotherapy (LITT)

Laser-induced interstitial thermotherapy involves inserting a laser fibre into the blood supply of the fibroid via the laparoscopy. The fibroid either shrinks considerably or disappears altogether (115 (3)). Further reports are awaited.

Myolysis

During laparoscopy a bipolar probe (electrocoagulation) is inserted into the fibroid and diathermy applied (116 (3)). This technique has not been assessed in clinical trials. Further surgery was avoided in 95% of women with uterine fibroids (117 (3)). Uterine rupture at the site during pregnancy has been reported (118 (3)) and as a result the technique is not widely used (119 (4)).

Cryomyolysis

In this technique a cryoprobe is inserted into the fibroid to freeze the fibroid. No large studies have been identified.

Hysterectomy

Hysterectomy is the most common operation for fibroids. It is obviously curative but has the drawback of removing future fertility. It is one of the treatment options for women with symptomatic fibroids. Previously a uterus >12/40 size was considered a

recommendation for hysterectomy because of concern over leiomyosarcoma, compromise of adjacent structures (the ureter) and difficulty with surgery performed at a later date. There are no data to support this approach but there is limited evidence that performing hysterectomy on women with larger uteri to detect a future ovarian cancer has not been demonstrated to lead to any benefit for the woman (120 (3)). The surgery has not been shown to be more difficult when the uterus is large (121 (2-)). With respect to identifying leiomyosarcomas earlier in their natural history, the risks of hysterectomy outweigh the risk of leiomyosarcoma in women with fibroids (120,121 (both 3)).

Embolisation of fibroids

A potential future treatment for symptomatic fibroids in women who wish to retain their fertility may be uterine artery embolisation (UAE). This procedure was first carried out in France in 1991 for the treatment of fibroids. The procedure is performed by interventional radiologists and entails cutting off the blood supply to the fibroid so that it shrinks.

A reduction of uterine blood flow by arterial embolisation has been shown to reduce the growth of fibroids (123). Particles of 300-600 microns are injected into the feeder arteries supplying the fibroids by catheterising the femoral artery using radiological imaging under local anaesthesia. Seven case series of UAE have been published (123,124,125,126,127,128(all 3)) and 11 abstracts. Over 1000 women have now undergone this procedure. There have been no RCTs of UAE versus other surgical procedures such as myomectomy or hysterectomy although two are planned (129,130). Menorrhagia is reported as resolving or improving in 64 to 96% of cases (minimum follow-up time 2 months; maximum follow-up time 48 months). Woman satisfaction has been reported only infrequently but data available from 80 women indicate a range from 71 to 94%. Complications were reported in 4 to 25% of cases and included fibroid expulsion through the cervix (requiring hysterectomy), fibroid necrosis, severe pain and fever requiring hospital admission. Discomfort may occur in

the first weeks following the procedure (125 (3)). Only one pregnancy has been reported following the procedure.

Although the technique has been widely used to halt bleeding, there is a need for further trials to clearly establish the efficacy of UAE in removing fibroids so that fertility is preserved and/or restored. It appears to be a promising alternative to surgery but follow-up is needed to evaluate the long-term effects and to determine the women for whom the procedure is most suitable (124).

Management during Pregnancy

It is becoming quite commonplace for previously unknown fibroids to be detected by obstetric ultrasound during pregnancy. In many of these women the fibroids had not caused any problems or symptoms that could be attributed to them. An increasing number of women are delaying childbearing until their late thirties which is also the most likely time for fibroids to develop (45).

Obstetric risks

A retrospective review of the ultrasounds and medical records of 12,708 pregnant women concluded that the mode of delivery, foetal growth and premature rupture of membranes appear to be generally unaffected by the presence of fibroids (45). However, a statistically significant increase in threatened preterm labour was reported in women with fibroids and required treatment with intravenous tocolysis.

The likelihood of developing particular complications appears to be related to the position, location and size of the fibroid/s (45).

Placental abruption has been identified as a particular risk in women with fibroids larger than 20 cm where the fibroid is in direct contact with the placenta (45). Another study which recorded the increased risk of an abruption noted that the size of the

fibroid/s was not relevant (131). These researchers also noted that caesarean birth was more likely in women with submucous fibroids.

Pelvic pain also appears more likely to occur in women with fibroids larger than 20 cm (45). The pain may become severe as the pregnancy progresses and pain management may be required. The pain is thought to be caused by an acute disruption of blood supply to the fibroid.

There are reports of urinary retention and obstruction of the urethra due to the combination of fibroids and pregnancy (132) and a case of a fibroid changing its position resulting in a uterine rotation (133), but these are very rare complications.

Termination of pregnancy

Surgical termination of a pregnancy can very occasionally present a problem in women with fibroids particularly if they are particularly large or numerous. There has been some success in the use of RU486 to carry out a medical termination when a surgical procedure is indicated (134 (3)). This treatment is not currently available in New Zealand.

Surgery during pregnancy

Surgery during pregnancy for the removal of fibroids is not recommended because of the increased risk of haemorrhage. Occasionally myomectomy at the time of caesarean birth will be performed if the fibroid is over the lower segment. In one study (45 (3)) 19 women had surgery at the time of the delivery. Nine had myomectomies performed at the time of a caesarean. Three of these had severe bleeding complications requiring hysterectomy. Another nine hysterectomies were carried out during caesarean operations and one after a vaginal birth.

Pre and Postnatal sequelae

There was no significant difference in the course of pregnancy, mode of delivery or postnatal outcome when women with subserous or intramural fibroids were compared to controls (131 (3)). However, postpartum sepsis was found to occur in 3.5% of women with fibroids compared to only 0.4% of the control group.

A rare case is reported of a woman who developed a severe puerperal fever due to extensive necrotic degeneration of her fibroids that was attributed to the hormonal changes of pregnancy and the puerperium (135).

Recommended management

Although fibroids are associated with increased complications during pregnancy, there is a prevailing view in the literature that these risks and complications have been exaggerated (36).

There is no evidence to challenge the current approach that prophylactic intervention is seldom warranted (126) and that surveillance during pregnancy with a referral to an obstetrician is sufficient for most women who are found to have a fibroids.

Effect of fibroids on pregnancy associated with assisted conception therapies

A 1998 Australian retrospective comparative study found that pregnancy and implantation rates were significantly lower in groups of women with intramural and submucosal fibroids even when the uterus was not altered or misshapen (41 (2-)). Pregnancy and implantation rates were not influenced by the presence of subserosal fibroids. The recommendation from this and a similar earlier study (43) was the need to consider surgical or medical treatment in women who have intramural and/or submucosal fibroids with a history of infertility before attempting assisted reproductive therapies. No evidence from RCTs is available.

Alternative Therapies

A number of alternative therapies have been suggested for the treatment of fibroids. These include herbal preparations, homoeopathic remedies and lifestyle changes. Although some report promising responses to treatment, most have not been subjected to the scrutiny of conventional research methodologies. No RCTs have been carried out to evaluate the effectiveness of any of these treatments.

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