ASSESSMENT OF VOLUME REDUCTION OF UTERUS AND UTERINE FIBROIDS USING ARTERIAL EMBOLIZATION

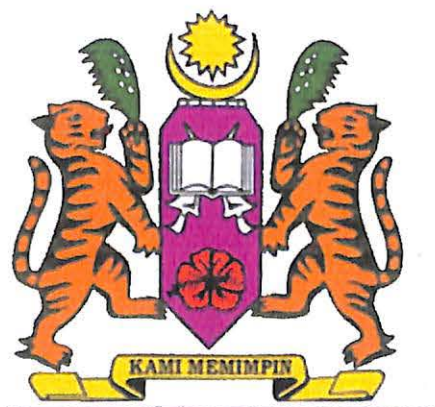
By

DR.GURMIT KAUR A/P SARDARA SINGH

Dissertation Submitted In Partial

Fulfillment Of The Requirements Of Masters

Of Medicine (Radiology)



UNIVERSITY SAINS MALAYSIA

2006

To,

My beloved husband Dr.Kuljit Singh Gill and my beautiful daughter Ravneet Kaur Gill

for their patience and understanding

Acknowledgements

I would like to express my heartfelt gratitude and love to my family, for all their sacrifices, love and support.

Special thanks for Dr. Mohd Shafie Abdullah my supervisor as well as my lecturer for his effort, patience and support.

Not forgetting all the lecturers of Radiology department for their advice, assistance and support during the four years of the Masters of Medicine program.

I would also like thank my co-supervisor of this study Dr.Nik Haslina Nik Hussin (from the Department of Obstetrics and Gynecology) and Dr.Nor Azwany Bt Yaacob (from the Department of Community Medicine) for their help and support to make this study a success.

Last but not least I would like to thank all my colleagues and my friends for their support and love during these four tedious years of joy, tears, hard work and emotional distress.

Table of contents

List of figure

List of tables

List of abbreviations

ACOG	American College of Obstetricians and Gynecologists
BMI	Body Mass Index
CT	Computed Tomography
HUSM	Hospital Universiti Sains Malaysia
JVIR	Journal of Vascular and Interventional Radiology
MRI	Magnetic Resonance Imaging
OCP	Oral Contraceptive Pill
PS	Power and Sample Size Calculation
SCVIR	Society of Cardiovascular & Interventional Radiology
TAH	Total Abdominal Hysterectomy
UAE	Uterine Artery Embolization
US	Ultrasound

Abstract

Bahasa Malaysia

Tajuk: Penilaian pengecutan isipadu fibroid dan rahim selepas "embolisasi" salur darah.

Tujuan: Tujuan kajian in adalah untuk mengukur peratus pengecutan isipadu fibroid dan rahim selepas 'embolisasi'. Kami juga mengkaji apakah komplikasi yang timbul selepas penyekatan salur darah rahim dan mengkaji manakah gejala pesakit berkurang selepas embolisasi.

Metodologi:

Dua belas (12) pesakit telah menjalani penyekatan kedua-dua salur darah rahim bagi ketumbuhan fibroid yang bersimtomatik. Kajian in dijalankan selama 21 bulan di Hospital Universiti Sains Malaysia. Semua pesakit in telah menjalani pemeriksaan Magnetic Resonance Imaging (MRI) sebelum "embolisasi" salur darah rahim tetapi hanya sepuluh (10) pesakit mengulangi pemeriksaan MRI tiga bulan selepas "embolisasi" salur darah rahim. Seorang pesakit mengalami pendarahan selepas "embolisasi" salur darah rahim dan histerektomi telah dilakukan. Seorang lagi pesakit telah hamil sejurus selepas "embolisasi" salur darah rahim dan melahirkan seorang bayi perempuan yang sihat melalui pembedahan. Isipadu rahim dan isipadu fibroid yang terbesar telah diukur sebelum dan selepas "embolisasi". Bandingan isipadu sebelum dan selepas "embolisasi" dibuat untuk mengukur

peratus pengecutan. Pemulihan gejala dan komplikasi yang timbul disebabkan oleh penyekatan salur darah rahim juga dicatat.

Keputusan:

Keputusan menunjukan isipadu fibroid berkurang sebanyak 63.82% dengan interquartle range sebanyak 36.78. Isipadu rahim berkurang sebanyak 47.85% dengan interquartile range sebanyak 33.96. Pengurangan gejala adalah sebanyak 85-100%. Komplikasi yang diperhatikan adalah komplikasi yang ringan dan hanya satu komplikasi yang rumit yang memerlukan pembedahan histerektomi.

Kesimpulan:

"Embolisasi" salur darah rahim adalah satu cara yang efektif dan selamat untuk merawati fibroid. Ia menunjukkan kekurangan gajala pesakit dan isipadu rahim serta fibroid yang memuaskan.

English

Title: Assessment of volume reduction of uterus and uterine fibroids using arterial embolization

Objective: The objective of this study was to assess the volume reduction of the uterus and the uterine fibroid using artery embolization for patients with symptomatic fibroids. This study was also aimed to determine the complications of uterine artery embolization and to document improvement of the symptoms post UAE.

Materials and Methods: Twelve patients had bilateral uterine artery embolization(UAE) for symptomatic uterine fibroids. This study was conducted over a period of 21 months in Hospital Universiti Sains Malaysia. All the patients had a pre-embolization Magnetic Resonance Imaging (MRI) and ten of the patients had a repeat MRI three months post uterine artery embolization. One patient developed bleeding post-embolization and had a hysterectomy done. The second patient got pregnant immediately post-embolization and delivered a healthy term baby girl by caesarean section. Volume of the uterus and the dominant fibroid was calculated pre-embolization and post-embolization. Comparison was done between the volume pre-embolization and post-embolization, to see the percentage of reduction. Symptom improvement and the complication due to uterine artery embolization were also noted.

Results

Results show fibroid volume reduction median to be 63.82% with interquartile range of 36.78 and uterine volume reduction median to be 47.85% with interquartile range of 36.99. Symptom improvement at three months was 85-100%. The complications which occurred were mostly minor complications with one major complication requiring hysterectomy.

Conclusion:

UAE is an effective and a safe method of treatment for symptomatic uterine fibroids. There is significant symptom and volume reduction of both the uterus and the dominant fibroid.

INTRODUCTION

1.0 INTRODUCTION

Uterine artery embolization was initially used in the management of life threatening gynaecological bleeding. In 1995, Ravina et al first described the use of uterine artery embolization as an alternative treatment of symptomatic uterine fibroids. The basic principle of this procedure is intravascular occlusion of the uterine arteries causing hypoxia and necrosis of the fibroids. Subsequently the fibroids shrink and there is symptomatic relief. Uterine necrosis is avoided since there is adequate collateral circulation.

In the past twelve years, uterine artery embolization has been gaining increasing acceptance as a minimally invasive treatment for symptomatic uterine fibroids. The less invasive nature of the procedure, shorter recovery period and preservation of the uterus, has made uterine artery embolization a popular alternative to hysterectomies or myomectomies.

Multiple studies have shown that menorrhagia and bulk-related symptoms improve in 80–97% of patients who undergo uterine artery embolization (Brunereau *et al.*, 2000, Chrisman *et al.*, 2005, Goodwin *et al.*, 1999, Ravina *et al.*, 1995, Spies *et al.*, 1999, Spies *et al.*, 2001b, Siskin *et al.*, 2000a, Worthington-Kirsch *et al.*, 1998, Worthington-Kirsch *et al.*, 1998). There is also a reduction in volume of the fibroids of between 50% -70% post-embolization. (mean reduction 45%-55%) (Burn *et al.*, 1999, Goodwin *et al.*, 1999, Spies *et al.*, 1999, Ravina *et al.*, 1995, Pelage *et al.*, 2000, Siskin *et al.*, 2000a, Worthington-Kirsch *et al.*, 1998). However, all the data available and the studies done are from developed countries where the quality of care and technology available differs from our

local set up. Hence there is a need to establish new data applicable to our local population and environment.

UAE does not vary very much from center to center. It has been extensively described in many of the studies done and recently in the year 2001 there were guidelines given in the Journal of Vascular and Interventional Radiology (JVIR) by the SCVIR. Variation may be seen in the technique where some approached the uterine artery directly with a 5F catheter or some used microcatheters; some prefer unilateral femoral approach and some prefer bilateral approach and the other possible variation is the preference of embolic material. Current imaging modality of choice for pre and post-embolization is MRI since it is not operator dependent, images are reproducible, signal intensities can somewhat predict the outcome of volume reduction and other comorbid disease can be ruled out. Post-embolization MRI displays the infarcted fibroids clearly and allows the detection of any residual enhancing tissue.

The focus of this study was to determine the volume reduction of the fibroid and the uterus post UAE. The short term efficacy and safety of this procedure was also evaluated by assessing the symptom relief and the complication rates. Fibroids are the major cause of hysterectomies in Malaysia representing 47.6% of the indications for surgery (Ravindran and Kumaraguruparan, 1998). UAE has been proven to be an alternative treatment which when compared to hysterectomies, UAE has a lower morbidity and mortality rates. Pinto et al (2003) reported that UAE had a shorter hospital stay and resulted in fewer major complications when compared to hysterectomies.

To our knowledge there is no published data regarding UAE and the success of UAE in treating uterine fibroids in Malaysia. The purpose of this study was also to provide local data and also to start a new service in our hospital. Since UAE is considerably a new technique of treating uterine fibroid; it is not well known among our patients and treating doctors. This turned out to be our main limitation in acquiring our sample size. We only had a total of twelve patients of which one was referred from Terengganu, two were referred from Kota Bharu and the rest were from USM. This was despite the introduction of this study to the Obstetrics and Gynecology department of the respective hospitals. This was done via a presentation to them by us. However referrals were limited as the treating doctors preferred to perform hysterectomies. Referrals were also limited due to the refusal by the patients for UAE as this mode of treatment is still new in our country. The knowledge regarding this procedure is still limited as we observed our own medical staffs who have not heard of it. Our imitation of including patients who had completed their families and only including patients with symptomatic fibroids further limited our sample size. The other problem faced was the pre-embolization and post-embolization procedural MRI which had to be performed. This was because of the cost being very high and also had a long waiting list (3 months) for an appointment. Discussion regarding our study is severely limited due to our small sample size.

LITERATURE REVIEW

2.0 LITERATURE REVIEW

2.1 General Overview

Uterine fibroids have been a leading caused of hysterectomies all over the world. Up to 1995 uterine fibroids were either treated medically or surgically. However since 1995, with the development of uterine artery embolization (UAE), many extensive studies have been done to determine the role of UAE as a viable option.

2.2 Anatomy

2.2.1 Vascular anatomy of the uterus

The uterus is primarily supplied by the uterine arteries which arise from the internal iliac arteries (Fig. 1). Other than that the uterus is also supplied by the branches of the ovarian arteries, vaginal arteries and direct branches of the internal iliac arteries. It is important to know the vascular supply of the uterus as the fibroid may be supplied by any of the above branches.

The fundus of the uterus is supplied by the uterine artery in 90% and by the ovarian artery in 10% of cases. Vice versa, the ovary is supplied by the ovarian artery alone in 40%, by the uterine artery and the ovarian artery in 56% and by the uterine artery alone in 4 % of cases (Binkert *et al.*, 2001). The duality of supply of the uterus and the ovaries requires angiographic assessment of the vascular supply prior to embolization.

A dual blood supply also suggests the possibility of anastomosis between the uterine and the ovarian arteries. Anastomosis between uterine arteries and ovarian arteries have been classified into three groups (Razavi *et al.*, 2002), Type I, Type II and Type III. In Type I,

the ovarian artery supplies the fibroids by way of connections to the intramural uterine artery. A subgroup is noted in Type I where, when flow in the tubal artery is low, the pressure generated during selective uterine angiography is sufficient to overcome it and cause reflux into the ovarian artery (Type Ib). In Type II, the ovarian artery feeds the fibroids directly. In Type III, the ovarian supply appears to be from the uterine artery. Evaluations of these anastomoses are important as they affect the final outcome of UAE and also to avoid non target embolization.

The normal ovarian artery which measures less than 1mm in diameter is usually not visualized on a flush aortography. However in a diseased state, the ovarian artery tends to get larger. Arteries which are larger than 1.5mm are usually detectable on a flush aortography. Binkert et al (2001) reported visualizing an ovarian artery in 25% of patients with uterine fibroids in the flush aortography done pre-embolization. The visualization of the ovarian arteries in the generally used angiographic technique; where a non selective pelvic arteriography is carried out with a catheter placed at the aortic bifurcation and followed by direct selective catheterization of the uterine arteries is unlikely. To detect the presence of ovarian collateral blood supply, an application of nonselective flush arteriography with the tip of the catheter at the level of the renal arteries and imaging centered over the pelvis is required.

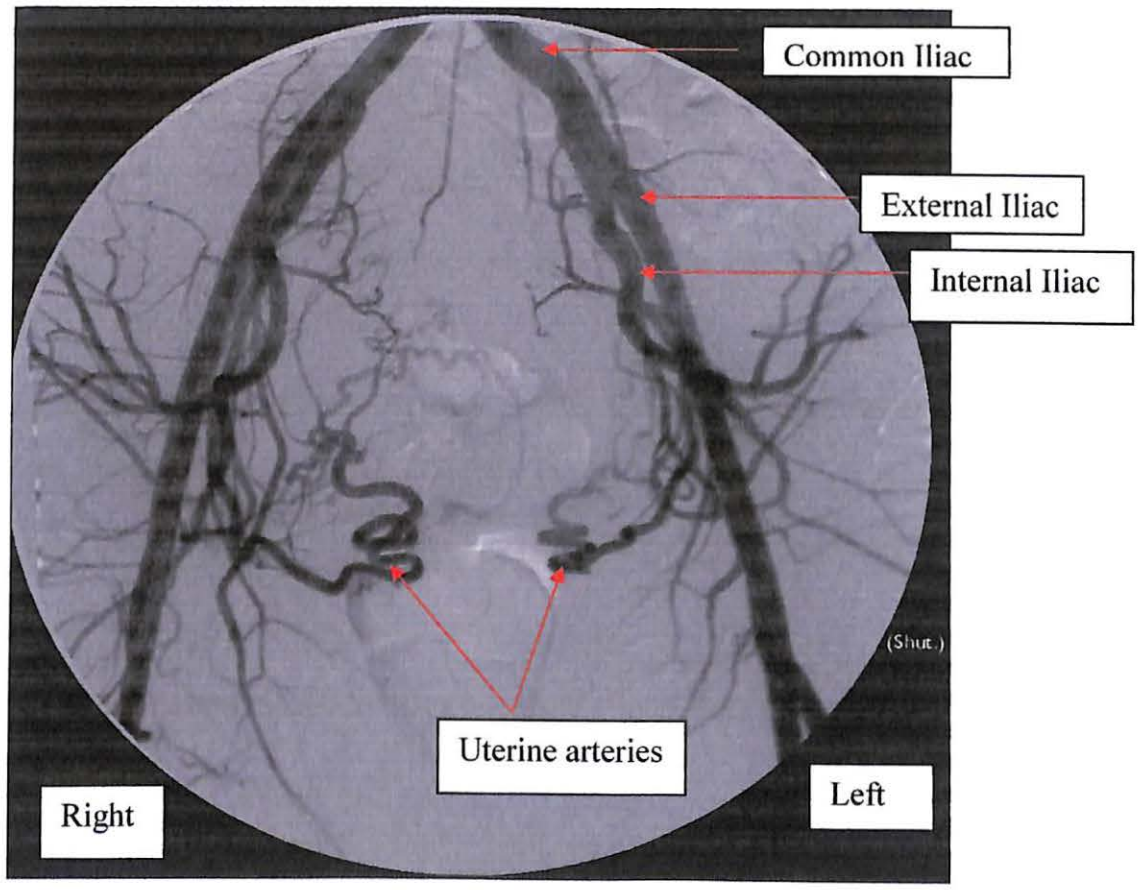


Figure 1 : Vascular anatomy of uterus

2.2.2 Classification of fibroids

Fibroids are divided according to their locations and are grossly classified into submucosal, intramural and subserosal (Fig. 2). Subserosal and submucosal fibroids can become pedunculated. The subserosal fibroid can protrude into the pelvic cavity and the submucosal fibroid can protrude into the uterine cavity. Pedunculated fibroids can undergo torsion and post UAE there can be stalk necrosis. In view of the possibility of stalk necrosis, UAE was initially considered unsuitable for pedunculated subserosal fibroids.

Goodwin et al (2001) further classified fibroids as

1. Pedunculated submucosal: a submucosal fibroid attached by a stalk narrower than 50% of the diameter of the fibroid.
2. Broad-based submucosal or mixed intramural/submucosal: a broad-based fibroid that substantially distorts the endometrial lining of the uterus.
3. Intramural: fibroid that is centered in the wall of the uterus with or without mild to moderate distortion of the endometrial or serosal surface.
4. Transmural: fibroid centered in the myometrium but substantially distorting both the endometrial and serosal surfaces of the uterus.
5. Subserosal: a fibroid centered in the outer myometrium with substantial distortion of the serosal surface of the uterus.
6. Pedunculated Subserosal: subserosal fibroid with its center outside the uterus attached to the uterus by a stalk narrower than 50% of the diameter of the fibroid.

Occasionally the subserosal fibroid can detach from the uterus and deposit elsewhere in the peritoneal cavity as a parasitic fibroid.

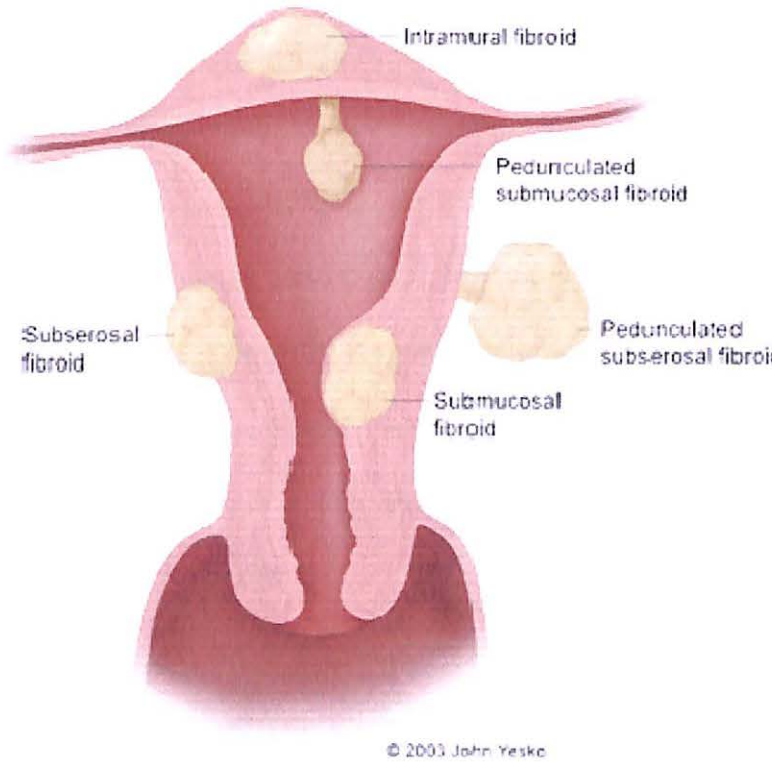


Figure 2 : Classification of fibroids

Image was downloaded from the following site from the internet on the 06-05-2006.

mailto:info@ask4ufe.com

2.3 Uterine Fibroids

2.3.1 Prevalence

Leiomyomata, better known as fibroids, are the most common benign tumors of the female genital tract, occurring in about 25% of women of childbearing age (Lupattelli *et al.*, 2005). Some literature mention rates as high as 40% in women aged 40 years or older (Tulandi, 2003). The true prevalence of these tumors has not been truly calculated as many patients with these tumors are clinically asymptomatic. Histological examinations of 100 consecutive hysterectomy specimens were carried out by Cramer and Patel. They found 649 leiomyomas in 77 of those specimens, with multiplicity of leiomyomas found in 84% of cases (Cramer and Patel, 1990).

A prospective cross-sectional study involving 14 government hospitals was undertaken over a period of 6 months in Malaysia to study the patterns of hysterectomy for gynaecological indications. A total of 707 patients were enrolled in the study consisting of 612 abdominal hysterectomies and 95 vaginal hysterectomies. Fibroids (47.6%) formed the main indications for surgery (Ravindran and Kumaraguruparan, 1998).

2.3.2 Histopathology

Fibroids are smooth muscle tumors, arising from the smooth muscle and the fibrous connective tissue of the uterus. Fibroids are generally benign proliferations. However, they can undergo malignant transformation into uterine sarcomas. The total incidence of uterine sarcomas among patients operated on for uterine leiomyomas, is extremely low and a study done showed the incidence to be 0.23% (Parker *et al.*, 1994).

Morphologically, the fibroid is composed of whorled rubbery pink white tissue with no true capsule. A fibroid can be calcified, degenerated or cystic. Gross appearance of the fibroid can be altered by either haemorrhage, where there will be dark red areas, or by necrosis, where we can see sharply demarcated yellow areas. Microscopically, fibroids are composed of smooth muscle cells with interspersed fibrous connective tissue.

Prior to embolization two thirds of all myomas show some degree of degeneration. Three most common types of degeneration are hyaline degeneration, myxomatous degeneration and calcific degeneration (Stenchever *et al.*, 2001).

Immediately post-embolization, the fibroids show thrombosis and necrosis. Thrombosis is caused by the embolic material within the vessels. Ultimately, thrombosis results in arterial occlusion, leading to interstitial oedema within the fibroid. This is followed by ischemic necrosis and later hyaline degeneration (Siskin *et al.*, 1999, Lipman *et al.*, 2002). Several weeks post-embolization, fibroids show coagulative necrosis and acute inflammatory changes. A few months after embolization, fibroids show features of hyaline necrosis and dystrophic calcification. Gross morphology post-embolization shows dusky red softening in contrast to the characteristic firm, white whorled appearance of a myoma. Histologically, foreign body emboli can be seen in blood vessels at the periphery. Microscopic examination shows coagulative necrosis characterized by cytoplasmic eosinophilia and fragmentation of the nuclei. (Tulandi, 2003)

2.3.3 Radiological imaging

The role of imaging is for the diagnosis of the uterine fibroids, to rule out any other factors causing uterine enlargement and to differentiate other possible pelvic masses. MRI is the choice imaging modality as it unequivocally demonstrates the myometrial origin of the fibroids, where other investigation techniques such as transvaginal ultrasounds, are indeterminate. Other imaging modalities include transabdominal ultrasonography, which is very much operator dependant and computed tomography which involves radiation to the pelvis and ovaries.

a) MRI of the pelvis.

MR images depict the uterine zonal anatomy clearly. On T2 weighted images, the central zone which includes the endometrium and any fluid in the endometrial cavity, is depicted as high signal intensity. Surrounding this there is the junctional zone which is a region of low signal intensity. Adjacent to this is the myometrium which is depicted as a region of intermediated signal intensity. At the periphery there is a thin hypointense zone observed. On T1 weighted or proton density images, the zonal anatomy is poorly differentiated due to the isointensity of the uterine zones.

A fibroid is composed of tightly bound smooth muscle cells and fibrous tissue, which is seen as a well defined low signal intensity area on T2 weighted images. On T1 weighted images, the fibroids have intermediate signal intensity; hence there is difficulty in distinguishing it from the myometrium. MRI features of fibroids also depend on the presence or absence of degenerative changes such as haemorrhagic, hyaline, mucinous,

fatty, myxomatous and cystic degeneration. In addition to this the fibroid may also calcify. Degenerative changes may account for the increased signal intensity on T2 weighted images and T1 weighted images may be useful in depicting hemorrhagic degeneration. Post-intravenous gadolinium, the enhancement of the fibroid is less in comparison to the surrounding myometrium. MRI is also useful to differentiate adenomyosis and sarcomatous change of the fibroid prior to the embolization.

Pre-embolization assessment of the fibroid with a MRI of the pelvis is important for assessment of viability of the fibroid, volume pre-embolization, enhancement pattern (Nikolaidis *et al.*, 2005), anatomical location and the vascular supply of the fibroid. Assessment of the fibroid post-embolization is best done with MRI where the volume reduction of the fibroid (Burn *et al.*, 2000), the significance of signal intensities pre and post-embolization, vascularity of the fibroid and changes to the myometrium can be assessed. MRI also allows the precise quantitative assessment of the response to therapy (Jha *et al.*, 2000) .

b) Ultrasound (US) of the pelvis

US of the pelvis can be done either trans abdominal or trans vaginal. It is useful in the diagnosis of uterine fibroids and other uterine pathologies. The limitation of US is that it is operator dependant and there is difficulty in accurately defining the location of the uterine fibroid.

c) Computed tomography (CT) of the pelvis.

CT scan has limited role in the imaging of the uterine fibroids as it involves radiation to the pelvic structures and has relatively limited contrast resolution.

Imaging of the fibroid is important as it is required for confirmation of the diagnosis, for selection of patients for appropriate management, to monitor the outcome of the therapy and also for follow up.

2.3.4 Treatment

Treatment of uterine fibroids for many years was either medical or surgical. Medical treatment includes anti-estrogen drugs such as tamoxifen, which is a combination of gonadotropin-releasing hormone agonists which often relieve the patient of their symptoms temporarily (used only for 3-6 months). Other drugs are progesterone and androgenic agents like gestrinone.

Other options like surgical procedures including myomectomies (which preserves reproductive function but recurrence is seen in 25% of the patients), and hysterectomies (a radical procedure that is associated with some surgical risks to the patient and results in infertility) often are needed later despite the medical treatment.

The latest treatment option for symptomatic uterine fibroid became available in 1995 when Ravina et al used UAE for management of fibroids. The study done was on 16 patients with a mean follow up of 20 months. Results showed that there was 20-80% volume reduction and symptomatic relief was noted.

2.4 UAE

2.4.1Technique

a) Pre-embolization assessment

Patient selection is based on confirmation of the diagnosis and the indication of the UAE. Most patients undergoing UAE are patients who wish to preserve their uterus or to avoid a surgical procedure. Many of them have either had failed medical or surgical treatment.

Goodwin et al (1999) analyzed possible prognostic factors such as age, race, size, vascularity of fibroid and previous medical or surgical therapies. Only age and earlier myomectomy were significant prognosticators of the outcome. Co-morbid diseases which may also affect the outcome of UAE have to be considered. Studies done in the previous years suggested that there is clinical failure after UAE in patients with underlying adenomyosis. Other co-morbid factors that have to be considered are ovarian cyst, tubal inflammation, endometriosis or diverticulosis. Chances of a life threatening infection are increased with chronic salpingitis or endometriosis (Goodwin *et al.*, 1999, Smith *et al.*, 1999).

Pre–embolization imaging should be done to provide information on the type, number and size of the fibroids. Pre-embolization MRI is an ideal tool for assessment. In a study done by Nikolaidis et al (2005); MRI in 94 patients prior to embolization, showed the prevalence of non viable fibroids to be 20% however in approximately two thirds of these cases, the non viable fibroids were not dominant. Only 6% were dominant nonviable fibroids hence MRI helps in omitting UAE as an option for treatment in these instances.

MRI imaging also excluded another 16% of patients from proceeding with UAE based on the number of fibroids, uterine size, adenomyosis, dominant submucosal fibroids and endometrial lesions. Thus MRI imaging can be used to determine the viability of the tumors and to detect other findings that preclude UAE.

Studies done show that large fibroids and pedunculated fibroids are not an absolute contra-indications for embolization. Katsumori et al evaluated 152 patients of which, 47 patients had fibroids larger than 10cm and the rest had fibroids smaller than 10cm. They studied the possibility of a large fibroid being a high risk for UAE. Complications posts UAE were analyzed. There were 30 complications, 25 of which were minor complications. In comparison between the two groups, there were no statistical differences noted in the complication rates. Hence they concluded that there is no increased risk on the basis of tumor size in patients undergoing UAE. The largest tumor embolized was 19cm in diameter (Katsumoril *et al.*, 2003).

Katsumori et al (2005) also reported that UAE can be a safe and effective treatment for pedunculated subserosal fibroids with stalk diameters of 2cm or larger. One hundred and ninety six patients consecutive women were studied of which 12 showed one or more pedunculated fibroids. Fifteen pedunculated fibroids were identified. Mean stalk diameter before embolization was 3.1cm (range 2.0-5.5cm) and mean tumor volume was 279ml. The mean baseline uterine volume was 976ml. Four months post-embolization, MRI was performed and showed tumor volume reduction of 41%, and at one year it was 53%. The mean stalk diameter was 3.2cm at 4 months and 2.9cm at one year post-embolization.

Uterine volume reduction at 4 months was 35% and at 1 year was 47%. This study has excluded patients with a stalk diameter of less than 2cm hence concluding that any peduculated subserosal fibroids with a stalk of more than 2cm have successful outcome post-UAE (Katsumoril *et al.*, 2005).

MRI signal intensity prior to embolization can predict the response to UAE. Multiple studies done (Burn *et al.*, 2000, deSouza and Williams, 2002, Jha *et al.*, 2000) reported that fibroids which had high signal intensity on T1 weighted images show a poor response to UAE. This is because high signal intensity on T1 images indicated hemorrhagic degeneration in which the fibroid had outgrown the blood supply, hence the poor response to UAE. Fibroids which have high signal intensity on T2 weighted images showed good response to UAE.

b) Embolization

Embolization techniques have been extensive described in various studies done previously. (Goodwin *et al.*, 1999, Pelage *et al.*, 2000, Ravina *et al.*, 1995, Spies *et al.*, 1999, Worthington-Kirsch *et al.*, 1998). The techniques vary from centre to centre but do not differ vastly. The basic concept is placement of a catheter into the uterine artery and injection of embolic material to occlude the lumen. Subsequently there will be an infarction and shrinkage of the fibroid. Technical variation may be in the choice of catheters, as some use 5F catheters ((Pelage *et al.*, 2000, Worthington-Kirsch *et al.*, 1998) to directly cannulate the uterine arteries and some prefer microcatheters (Goodwin *et al.*, 1999).

c) Embolic material

The debate regarding the ideal embolic material is still on going. Non spherical polyvinyl alcohol (PVA) particles were the first embolic material used successfully for UAE. (Goodwin *et al.*, 1999, Ravina *et al.*, 1995, Spies *et al.*, 1999, Worthington-Kirsch *et al.*, 1998). PVA has limited potential for recanalization and it is a permanent occlusive agent. Tris-acryl gelatin microspheres (TAGM), which are spherical embolic particles, have been developed and used in France since 1994. By November 2002, tris-acryl gelatin microspheres gained popularity as non spherical PVA had the tendency to clump and had unpredictable levels of arterial occlusion. However a randomized comparative study done by Spies et al in year 2004, to compare PVA and TAGM showed no differences between the outcomes of UAE. The study showed microcatheter occlusion was more common with use of PVA and larger volumes of TAGM were used in comparison to PVA (Spies *et al.*, 2004).

PVA particles used are of various sizes ranging from 150um-750um. Smaller particles cause better devascularization of the fibroids and higher rates of complete resolution of symptoms. Larger particles do not cause good devascularization of the fibroid, however the risk of uterine infarction and non target embolization is reduced (Lupattelli *et al.*, 2005).

A recent advancement is the development of spherical PVA in March 2004. A study done by Spies et al in year 2005 to compare spherical PVA and TAGM showed unacceptably high rates of failed tumor infarction when using spherical PVA.

Other embolic materials used are gelatin sponge particles. A study done in 60 patients who underwent UAE using gelatin sponge particles successfully showed that the post-embolization outcome bears comparison with those UAE with PVA as reported in literature (Katsumoril *et al.*, 2002).

d) Radiation doses

UAE is performed under fluoroscopic guidance which involves exposure of the gonads to ionizing radiation. Nikolic et al (2000) conducted a study using dosimeters which were placed in the posterior fornix of the vagina in 20 patients who underwent UAE. The screening times ranged between 9 and 52 min (mean 22 min). The radiation dose of the fluoroscopy varied between 2.9 R/min (0.75 mc/(kg min)) and 4.4 R/min (1.13 mc/(kg min)), and 21–62 (mean 44) screenings were performed. The mean estimated ovarian dose was 22.34cGy and the mean absorbed skin dose was 162.32cGy. In comparison to the pelvic radiation received in treatment of Non Hodgkin's lymphoma(absorbed ovarian dose 263-3500cGy), the dose received during UAE is much lower than the dose needed to cause any acute or long term injury or increase the genetic risk to the patient's future children.

Nikolic et al (2000) did another study on influence of radiographic technique and equipment on absorbed ovarian dose associated with UAE. The absorbed ovarian dose during UAE can be reduced by limiting fluoroscopy time and the use of magnified fluoroscopy.

Pron et al (2003) reported procedure time and fluoroscopy time averaged 61minutes (95 % CI; 58-63 minutes) and 18.9 minutes (95 % CI; 18-19.8 minutes). The fluoroscopic time is lower than that reported by Nicolic et al (2000). This varied significantly among interventional radiologist. There is an average reduction of 27% in procedure time and 24 % reduction in fluoroscopy time with increasing UAE experience of the interventional radiologist.

The embolization technique for uterine fibroids has been decisively optimized in recent years. Screening times range between 14 and 15 min on average. The radiation dose is minimized by applying pulsed fluoroscopy, dispensing with magnification factors and placing diaphragms.

2.4.2 Complications

Complications are divided into those which occur during the procedure (incidence is less than 1 %.) and those that occur after the procedure (Sterling *et al.*, 2002). Complications from UAE have been arbitrarily divided into three categories based on the interval from the procedure to the onset of the complication: immediate (related to the technical aspects of the procedure itself), acute (within 30 days), and long term (after 30 days). Each complication has also been categorized as major or minor complications. The rating of the severity of each complication was according to the standard definitions of outcome created by the Society of Cardiovascular & Interventional Radiology (SCVIR).

a) Complications during the procedure

Complications that occur during the procedure are arterial catheterization related complications such as arteriovenous fistulas, pseudoaneurysms, haematomas, arterial thrombosis and infections.

Haematoma and bleeding from the puncture site requires compression. Sometimes if the bleeding is excessive, a transfusion may be required. Pseudoaneurysms if small are treated conservatively, and if large may require percutaneous thrombin injections. Arteriovenous fistulas and arterial thrombosis may be managed with percutaneous techniques or may require open surgical repairs. Infections can be avoided by using aseptic techniques and prophylactic antibiotics.

Other vascular complications include arterial dissection, vasospasm, non target embolization and vessel perforation. Arterial dissection is managed conservatively. Embolization of the ipsilateral vessel is usually done at a later date; however embolization of the contralateral vessel can be attempted. Sometimes embolization on the ipsilateral vessel can also be attempted in the same setting if there is still antegrade flow and the true lumen is identified.

Vasospasm can be avoided by using microcatheters however if it still occurs, intra-arterial vasodilators such as verapamil and nitroglycerin can be used. During the spasm of the vessel, embolization should not be performed as there are high chances of non target embolization due to absent antegrade flow. Embolization performed during a vascular

spasm has also high chances of failure due to the recanalization of the embolic material when the vessel relaxes.

Non target embolization should be avoided using meticulous technique. Areas most likely affected by non target embolization are the pelvic organs and both the lower limbs. Management would depend on the severity of the non target embolization. Vessel perforations can be managed with coils or gelfoam embolization may be required. Other procedural complications include contrast reaction which is managed according to practice guidelines.

b) Post procedural complications

i) Expulsion of fibroids or large fibroid fragments

This is a known phenomenon that occurs in patient with submucosal fibroids. Post-embolization the fibroid is necrotic and sloughs off into the uterine cavity .Fragments are usually passed out however in some cases the cervical canal may be obstructed and there can be pyometra formation. Patients will present with abdominal pain, fever and raised total white count. These patients will require referral to the gynecologists for cervical dilatation and removal of the impacted fragments.

ii) Uterine ischaemia and infarction

This is a known complication as both the uterine arteries are embolized. However this does not occur in most of the patients as there is a rich collateral supply to the uterus. Several hours post-embolization the collaterals open up and follow up MRI of the pelvis shows re-

perfusion post-embolization (Katsumori *et al.*, 2001). Post-embolization necrosis of the fibroid is a sequelae and this can cause the uterine wall to thin out and subsequently rupture. Patients having multiple intramural fibroids and still considering on getting pregnant post-UAE should be advised of this risk.

If post-embolization, the patient presents with abdominal pain, raised total white cell count and fever, the possibility of uterine ischemia should be considered. MRI is the best imaging modality to confirm the diagnosis. There have been case reports where patients have presented with uterine ischemia. In the reports uterine ischemia was proven by hysterectomy and subsequent histopathology reports (Gabriel *et al.*, 2004, Godfrey and Zbella, 2001, Torigian *et al.*, 2005).

ii) Infection of the necrotic fibroid and /or the uterus

Patients which present with low grade fever on and off, purulent per vaginal discharge, abdominal pain and raised total white counts more than 7 days post UAE should raise the suspicion of infection. The infection may involve the uterus or the infarcting fibroid. Symptoms may sometimes present as late as three months post procedure hence patients have to be followed up closely for three months. Patients presenting with the above symptoms have to be investigated with abdominal imaging, cultures and blood counts. Imaging evidence of the persistent presence of gas within the myometrium, inflammatory changes of the uterus or presence of free fluid surrounding the uterus have to be looked for. Prophylactic antibiotic can be given to patients who have higher risk of infection or to all patients either pre or post-embolization. There is no consensus regarding the antibiotic

cover. No prospective studies have been done to answer the question of need of antibiotic cover.

Spies et al (2002) reported the frequency and severity of complications that occur as a result of UAE. The study population was 400 consecutive patients who had UAE. They found most of the complications were minor complications, the most common being allergic reaction which comprised 21% of all adverse events. There was 64% of a variety of other minor complications which did not require hospitalization. The most common complication requiring hospitalization was fibroid tissue passage. Thirty four patients experienced periprocedural complications at the rate of 8.5% (95% CI 6%-11.7%) and there were 5 major complications (SCVIR class D) comprising of 1.25 % (95% CI 0.3%-2.5%) of the study population. Using American College of Obstetricians and Gynecologists (ACOG) definitions of perioperative complications, the overall morbidity was 5 % (95% CI 3.1%-7.7%). Findings suggested short term complication rate was low in women undergoing UAE.

Pron et al (2003) reported procedural rate of complication of 5.3% (95% CI 3.6%-7.4%). There were 30 adverse events of which only three were major complications requiring extended hospital stay or additional care.