A descriptive study of uterine artery embolisation for leiomyoma in an African population in a low-resource setting

A research report submitted to the Faculty of Health Sciences,

University of the Witwatersrand, Johannesburg,

in partial fulfilment of the requirements for the degree of Master of Medicine

in the branch of Obstetrics and Gynaecology

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Date: 22 September 2015

DEDICATION

I lovingly dedicate this work to my family, who inspire me to do my best because of their faith in me.

To my dad, Ahmed, for his confidence in my abilities, to my mum, Zaibie, for her unwavering support, reassurance and encouragement, to my sister, Zaheera, for being the biggest believer in my abilities and to my husband, Ahmed, for being so patient with me and whose determination, discipline and drive motivates me.

ACKNOWLEDGEMENTS

I would like to express my deep gratitude to the following people for their assistance with this research report.

1. Dr K.A Frank - my supervisor. Her guidance, sound advice, refreshing honesty and genuine interest in my research made her indispensable. The generosity of her time, approachability and experience was invaluable to me and helped me reached this milestone.
2. Professor E.J Buchmann - for assisting me with the statistics.
3. Dr Mauthoor - Hosanee - for trusting me with her patient records.
4. Dr Oyebajo - for exposing me to uterine artery embolisation and allowing me access to his patient records.
5. Department of Radiology (CHBAH) - for performing the uterine artery embolisation procedure on the patients referred to them by the Gynaecology Department as well as for educating me on the technical process of performing uterine artery embolisation.

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LIST OF ABBREVIATIONS

ACOG	American College of Obstetrics and Gynecology
AMH	Anti-mullerian Hormone
BMI	Body Mass Index
CHBAH	Chris Hani Baragwanath Academic Hospital
DSA	Digital subtraction angiography
EMMY	Embolization versus hysterectomy study
FIBROID	Fibroid Registry for Outcomes Data
FSH	Follicle Stimulating hormone
GnRH	Gonadotrophin Releasing hormone
Hb	Haemoglobin
HIFU	High-Intensity Focused Ultrasound
HOF	Height of fundus
HRQOL	Health Related Quality of Life scores
MRI	Magnetic Resonance Imaging
NICE	National Institute for Clinical Excellence
NSAIDs	Nonsteroidal anti-inflammatories
PES	Post-embolisation syndrome
POF	premature ovarian failure
QOL	Quality of life
RCOG	Royal College of Obstetricians and Gynaecologists
REST	Randomised controlled trial comparing uterine artery embolisation with surgical treatment
SPRM	Selective progesterone receptor modulators
UAE	Uterine artery embolisation

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ABSTRACT

Introduction

Uterine leiomyomas are the commonest benign tumours in women of reproductive age. Fibroids have a significant impact on the womanôs quality of life as well as her fertility. Women who have symptomatic fibroids can present with abnormal uterine bleeding, pressure symptoms, pain, infertility, miscarriage or pregnancy complications. This necessitates treatment. There are many available options, apart from medical and surgical management, such as uterine artery embolisation. This alternative to surgical treatment in an African population, who have a higher risk of fibroids, within a low resource setting is assessed in this study. Uterine artery embolisation (UAE), is an interventional radiologic procedure that has developed over the last 10 years and is gaining popularity. It involves occlusion of the uterine arteries thereby decreasing the blood supply to the fibroid, thus improving symptoms in patients. The complications and outcomes of this procedure was assessed.

Objectives and Methods

The four objectives in this study were

1. To describe the demographics of the women who have attended the Uterine Artery Embolisation clinic from January 2004 till December 2011.
2. To describe the presenting complaints of the women attending Uterine Artery Embolisation clinic.
3. To quantify the response of the fibroid to Uterine Artery Embolisation in terms of size.
4. To document complications and outcomes associated with the procedure.

There were 100 women in the study sample ultimately who had UAE done after specific inclusion and exclusion criteria were met. The procedure was performed by interventional radiologists. This was a longitudinal descriptive study where the data was collected retrospectively.

Results

The mean age of women in this study was 34.5 years. Thirty four women (46%) had never conceived. The mean gravidity was 1 but 57 women (70%) were nulliparous. Pain was the most common symptom experienced, followed by menorrhagia. Fibroids were located intramurally in 94% of cases. Most patients experienced overall symptomatic relief at follow-up visits.

The commonest complication immediately post-UAE was pain. Post-embolisation syndrome occurred in 24% of women. At follow-up visits PV discharge, pain and bleeding were complications present.

Incidental outcomes which could be defined as adverse events were assessed post-UAE procedure in a total of 24 patients over the 5 follow-up visits, although the questionnaire applied to all the women who underwent UAE. Two patients were discharged (8%), 8 patients became amenorrhoeic (33%) and 5 patients became pregnant (21%). Three patients were referred for hysterectomy (13%) and 5 patients for myomectomy (21%).

The mean height of fundus (HOF) at presentation of women in this study was 17.8cm and the final mean HOF after UAE was 12.5cm. There was a 5.3cm difference in the mean height of fundus after treatment which was statistically significant.

The mean area of the dominant fibroid at initial presentation was 109.8cm^2 and at final visit was 71.9cm^2. There was a mean area difference of 40.0cm^2, this was also statistically significant.

Conclusion

Symptomatic fibroids occur more commonly in younger African women with more severe symptoms, that impact on quality of life and have a high disease burden, yet conservative treatment that preserves the uterus is a sought after alternative. UAE provides a safe and effective alternative to invasive surgery. After the results shown in this study, patients, gynaecologists and interventional radiologists should be encouraged to use UAE as a modality for the conservative management of fibroids in suitable candidates.

1. LITERATURE REVIEW

Uterine leiomyomas, also referred to as fibroids, are the commonest benign tumours in women and are the most common tumour in women of reproductive age.[1,3,4,5,7,9,12] The symptoms caused by fibroids are often distressing and have a significant impact on the womanôs quality of life as well as her fertility.[6] The emphasis of conservative treatment in women of reproductive age is ideally to retain their childbearing ability while controlling the symptoms caused by fibroids, and minimising the risks of invasive surgery. Fibroids can be asymptomatic or cause distressing symptoms such as abnormal uterine bleeding, pressure symptoms, pain, infertility, miscarriage and pregnancy complications.[10] Once symptoms are present, treatment is necessary and presents a significant burden of disease to the health sector.

Leiomyomas are tumours of the smooth muscle cells of the myometrium of the uterus, with each fibroid arising independently.[2,4]The actual incidence of fibroids is difficult to assess as women are frequently asymptomatic and undiagnosed.[2]Between 40 ï 50% of women over 35 years of age may have asymptomatic fibroids with the peak incidence of diagnosis occurring in women between their 30s and 40s.[1,3,4]Clinically apparent fibroids occur in 20% of women of reproductive age but may be as many as 70% present in-uteri at hysterectomies and in 50% of post-mortem examinations.[5,7]Observational evidence in premenopausal women shows an increase in fibroids with age through reproductive years.[2,9]In women over the age of fifty and who are still menstruating, there is a 40% incidence of fibroids.[15]

The Fibroid Growth Study showed each fibroid had its own growth rate. These findings are consistent with studies showing that fibroids are monoclonal in origin.[11]Clinical studies show that multiple fibroids in the same uterus are derived from individual myometrial cells.

Race

Women of African descent have a greater predilection for fibroids.[1,2,3,4,5]Black race has been identified as a risk factor.[2]Wise et al, maintains a 2 ï 3 fold increased incidence of uterine fibroids in black women, than in white women.[8]Higher rates of fibroids among black women are evident across all age groups, and it is not uncommon to encounter fibroids in black women younger than 30 years of age.[9]Further evidence points towards black women having larger and more symptomatic fibroids than white woman at the time of diagnosis.[9]Black women also have a greater propensity to more rapid fibroid growth and are more likely to have multiple fibroids.[17,20]It is however, uncommon for fibroids to occur in any race under the age of 20.

The black-white disparity in fibroid occurrence is not explained by an established risk factor, however it is evidenced that black women are affected disproportionately by this condition.

In the study by Wise et al, the association between hair relaxer use and leiomyomata was prospectively evaluated in a large cohort of premenopausal women involved in the Black Womenôs Health Study. Hair relaxers have been used by millions of black women in the US, often for long periods of time. These hair products may contain hormonally active products such as phthalates, which can be absorbed by the skin or inhaled and have shown to have oestrogenic effects in cell models and experimental animals. Hair relaxers can cause burns and lesions in the scalp allowing entry of hair constituents into the body. Results of the study showed the incident rate of fibroids comparing ever with never use was significant and duration of use and number of burns were positively associated with the risk of uterine leiomyomata. The risk of leiomyomata was unrelated to age of first use or type of formulation. This study raised the hypothesis that hair relaxer use is associated with an increased risk of uterine leiomyomata; however the possibility of increased genetic predisposition among African ancestry could also explain the observed association.[8]

Obesity

Obesity is a risk factor for developing fibroids.[2,7]The increased risk of developing endometrial cancer is thought to be due to the higher level of circulating oestrogens in obese women. Uterine fibroids are also thought to be influenced by oestrogens. Obesity is a major health concern and may cause hyperoestrogenism. Shikora et al assessed the relationship between obesity and uterine leiomyomata and the results suggested that symptomatic uterine fibroids may be another co-morbid disease state associated with obesity.[10]

Higher body-mass indices (BMI) are found in our South African female population compared to those reported in other African countries. In a sample of 7726 South African women,

black women had the highest prevalence of overweight and obesity (58.5%), followed by women of mixed ancestry (52%), white women (49.2%) and then Indian women (48.9%). BMI was also found to increase with age.[36]In the United States of America (USA) the prevalence of obesity is defined as a body mass index (BMI) Ó30 and is nearly twice as high in black women compared to white women therefore obesity may be a contributory cause of increased disease burden among black women.[35]As a result obesity combined with African race suggests a strong association for higher rates of fibroids in our population. In the Ontario trial, there was an association between fibroids and being overweight or obese, with prevalence of fibroids in 35% of overweight women and in 17% of women who were obese.[20]

Hormonal influences

The exact aetiology of fibroids is unknown however risk factors have been identified.[1] Hormones are the strongest factor demonstrating a causal relationship. Oestrogens act as a major promoter of growth as mentioned by Ezeama et al, who also showed progesterone stimulates growth-like factors.[1]There is increasing evidence that progesterone and progesterone receptors also have a major role in the growth and development of uterine fibroids.[10]The growth of fibroids during reproductive life when circulating oestrogen is maximal, suggests a hormonal influence, as well as in pregnancy which is also associated with an increase in blood supply. Sex steroids act via receptors which are found in higher concentrations in fibroids.[3]Post-menopausally, myomas shrink or fibrose.

Nulliparity

Nulliparity is associated with uterine fibroids and parity decreases the risk of developing fibroids with the number of term pregnancies.[1,3]The relationship between the number of term pregnancies and risk of developing fibroids is inversely proportional.[2,7]

Diet

A study from Nigeria reviewing case records of 117 patients with fibroids over 5 years showed that a high intake of red meat increased the incidence of fibroids.[1]

Pelvic infection

An increased risk of fibroids was also linked to a history of pelvic infections, with the risk of fibroids increasing with the number of infectious episodes.[1]

Genetics

There seems to be an increased familial incidence.[4]Uterine leiomyomas appear to have a genetic basis for their presence and growth.[5]Cytogenetic abnormalities occur in 50% of cases.[3]Abnormal gene expression of myomas suggest dysregulated differentiation and resemble the myometrium of pregnancy.[5]

Malignant transformation is extremely rare.[3,5]

The risk of developing fibroids decreases with long term contraceptive use as well as with smoking.[2,3,7]

Diagnosis

The gold standard of diagnosis is histological confirmation, however diagnosis with the use of ultrasound is clinically accepted and is the most suitable initial test as it is the least invasive and most cost effective investigation.[2]Magnetic Resonance Imaging (MRI) can be used but it is an expensive investigation. A bimanual examination is usually the first indication that a patient may have fibroids but other investigations need to be done to differentiate them from other masses of pelvic origin.

Fibroids found during myomectomy can be in multiple sites, but can also occur singularly.[1,3]Fibroids range in size, and the determining factor of the final size is unknown.[3]The consistency varies from hard and stony (calcified) to soft (cystic degeneration) but they are usually firm or rubbery.

Clinical presentation

Presentation is variable and symptoms relate to size, location and number of fibroids. Patients can present with menorrhagia or symptoms of anaemia, dysmenorrhoea, infertility, recurrent miscarriages, pressure symptoms or an abdominal mass. A palpable mass is usually a late presentation; however in the study in Nnewi, Nigeria, this was the commonest presentation (67.7%), followed by menorrhagia (41.7%) and then infertility (30.1%).[1]Evans and Brunsell found pressure symptoms (34%) were the most frequent presenting symptom, followed by menorrhagia (30%), infertility (27%) and recurrent pregnancy loss (3%).[2]Abnormal uterine bleeding accounted for 30% of symptoms and was described as the most common and important clinical feature leading to iron deficiency anaemia as well as having associated dysmenorrhoea.[6, 17]

Fertility and pregnancy

There is a definite association between fibroids and difficulty in conceiving but the relationship between infertility and fibroids is still unclear and controversial.[3,17]Hillard quoted a study stating a 10% rate of pregnancy complications in women with fibroids. The risk of complications appears to be influenced by location and size.[4]Some studies show low pregnancy rates when the cavity is distorted by fibroids, affecting implantation, but Eldar-Geva et al disputed this observation and concluded that pregnancy rates are affected by fibroids even when there is no distortion of the cavity. Yet some women with fibroids conceive without difficulty.[17]

Spontaneous miscarriage rates due to fibroids are unknown ï some authors suggest that they may be possibly twice as common compared with normal pregnancies. Miscarriages occur 40% more frequently, prior to a myomectomy compared to spontaneous miscarriages occurring in 20% of women after a myomectomy.[6]Pregnancy rates seem to have improved after myomectomy in many studies.[17]

Management

Various treatment options are available. Expectant management is the treatment of choice in patients that are asymptomatic, where patients are followed up at intervals and growth of the fibroid is monitored.

Medical treatment

Medical options have been developed in the last 20 to 30 years and are available to treat symptoms, but are usually for short term use due to side effects. Medical management is not curative; it is usually to tide patients over until menopause or until surgery. It is also used preoperatively to shrink tumours as well as in patients who are surgically unfit.

The medical agents used to control symptoms include gonadotrophin-releasing hormone (GnRH) agonists that lead to the down-regulation of the pituitary receptors and ultimately cause a decrease in gonadotrophin output and consequently in ovarian steroid output.[3,5] Although effective, long term use is limited due to bone density loss, reduction in breast size, vaginitis, sweating and hot flushes.[10] Use is restricted to a maximum of 6 months.[17]

Selective progesterone receptor modulators (SPRM) cause amenorrhoea without causing anovulation, having a direct effect on the endometrium.[3,5]SPRMs are characterised by a tissue-specific partial progesterone antagonistic effect. The exact mechanism of action is still unclear.[10]The side-effect of this drug is endometrial thickening which limits its use to 3 or 4

months. It is licensed as a preoperative treatment for fibroids. Progestins produce a hypoestrogenic effect by inhibiting gonadotrophin secretion and oppressing ovarian function.

The combined oral contraceptive pill is also prescribed and recently the levonorgestrel-secreting intrauterine system is being used to treat menorrhagia, in uteri smaller than 12 weeks in size and where there is no distortion of the uterine cavity, because of the high expulsion rate.[3,17]

Surgical options

Surgical options involve hysterectomy or myomectomy. For just over a century since the treatment of leiomyoma came into practice, hysterectomy is still the commonest option for treatment and leiomyoma are still the leading indication for hysterectomy in the USA.[3,7,8,9,,11,17,35]According to the American College of Obstetrics and Gynecology (ACOG) fibroids were accountable for 33% of hysterectomies performed in the United States of America in 1994.[5]Hysterectomy remains the only cure. Before the 20th century there was no effective treatment and death from this benign disease was not uncommon. Drs Kelly and Cullen, who worked together at the John Hopkins Hospital, gradually developed the technique of an abdominal hysterectomy that has been so successful in preventing and controlling intra-operative haemorrhage. In 1907 they published the paper ñMyomata of the Uterusò.[7]This major milestone eliminated the mortality from leiomyoma today, unfortunately the morbidity is still present.

Myomectomy has become popular for women who want to preserve their fertility and their uterus. Myomectomy is the surgical removal of fibroids that can be done via a laparotomy or using a laparoscopic approach or in specific cases (submucosal fibroids entering the endometrial cavity) hysteroscopically.

Laparotomy is preferred for larger fibroids. Methods of removal of fibroids involve a linear or elliptic incision over the largest myoma. The plane of cleavage is identified between the myoma and the myometrium. Sharp dissection or blunt dissection is required to enucleate the myoma from its bed. Ideally other myomas should be removed from the same incision, preferably anteriorly and avoiding the endometrial cavity. Myomectomy is ideal in a solitary pedunculated fibroid. However if there are multiple fibroids, it is a time consuming and difficult surgery, with a substantial risk of bleeding as well as adhesion formation and there is a risk of recurrence of 15 to 30% at 5 years.[2]It may not be possible to remove all fibroids, nor will the operation prevent new fibroids from growing. It also escalates the recommendation for pregnant patients to have an elective caesarean section after a myomectomy, because of an established risk of uterine rupture in later pregnancy as with any uterine surgery, however the exact magnitude of the associated risk remains uncertain and data to support this recommendation is limited.[2]

There is a trend towards more conservative treatment of symptomatic fibroids and changing attitudes of women to uterine preservation and childbearing. Thus minimal access surgery and non-surgical techniques with less morbidity must be evaluated.[6]

Surgery in women with higher BMIs is often technically more challenging may be associated with more post-operative risks due to the risk profile accompanying adiposity.

Other Interventions

Myolysis is the in-situ destruction of tumours by heat, laser or cryotherapy. Advantages are ease and speed of procedure, minimal blood loss and rapid recovery. However there is an unknown risk of recurrence and risk of prolonged vaginal bleeding. Myolysis can cause pelvic adhesions and there may be a delay in reduction of uterine size.[2]

High-Intensity Focused Ultrasound (HIFU) therapy is a non-invasive modality. It involves an extracorporeal source of focused high frequency ultrasonic energy that causes precise thermo-ablation of the pathological tissue.[18]Tissue is destroyed by coagulative necrosis.[19]

Another recent method of therapy involves uterine artery embolisation (UAE), an interventional radiologic procedure that has developed over the last 10 years and is gaining popularity. It involves occlusion of the uterine arteries thereby decreasing the blood supply to the uterus and ultimately to the fibroid.[3,7]

Patients presenting with symptomatic fibroids in need of surgical management do not always have the access to surgery due to long waiting lists, sometimes averaging 6 months, especially in resource depleted public sector hospitals. Medical treatment is also not always a suitable alternative either due to side effects of treatment, availability of the drugs and logistical difficulties for the patient.

On discovering that there was an operational Uterine Artery Embolisation clinic at the at Chris Hani Baragwanath Academic hospital, I was encouraged to learn that this relatively new mode of treatment was available to our patients.

Embolotherapy was first reported for use in 1970 for the control of haemorrhage. In the 1980s Phis and colleagues used it for postpartum haemorrhage. In the early 1990s Ravina and co-workers began using embolotherapy as a preoperative measure to decrease intra-operative blood loss during myomectomy. Embolotherapy was done 24 hours prior to surgery, but in some cases, it was done a few days or weeks before the surgery and patients experienced such marked improvements in symptoms that many surgeries were cancelled and UAE became a primary curative procedure.[12]After Ravina published a paper suggesting the usefulness of UAE, this procedure has become reasonably widespread.[17]

In October 1993, Ravina suggested using arterial embolisation as an alternative to surgery in women over 35 years of age, who did not desire fertility and in whom major surgical treatment was indicated. A small experimental study of 16 patients aged between the ages 34 to 49 years with symptomatic fibroids was carried out and embolisation was offered as a palliative treatment in women with a high operative risk with a mean follow-up of 20 months. This study sought to investigate whether arterial embolisation of myomata might decrease or eliminate symptoms as an alternative to surgery; however it was not a randomised study. The results showed that menorrhagia resolved in 9 out of 14 women, 12 out of 16 women had a 20-80% reduction in fibroid volume after 3 months and 2 cases were unsuccessfully treated (1 was a submucosal fibroid that was expelled and the other case of multiple interstitial and submucosal fibroids that later required a myomectomy). The main consequence was pelvic pain approximately12-16 hours after the procedure with 14 out of the 16 women requiring analgesia. The hospital stay did not exceed 36 hours. Both uterine arteries needed embolisation, due to arterial anastomoses. Complete and lasting devascularisation was needed to prevent revascularisation. In this series there were no technical complications. In their experience UAE did not induce massive necrosis of the myoma and the decrease in volume of myoma were due to vascular changes and a decreased blood supply.[12]

UAE can be done as a day procedure under sedation, after informed consent has been obtained and iodine allergy excluded. Pre-procedural blood tests include a full blood count, coagulation screen and serum creatinine value.[15,16]Overnight admission may be necessary, but in the large multicentre Ontario Uterine Fibroid Embolisation Trial, 18% stayed longer than one night and 5% stayed longer than two nights.[17]

The procedure originally done by Ravina is described later in the Methods section. Embolisation can be done with a variety of embolic agents, such as acrylic co-polymer beads (500 to 700Ûm) that are infused under fluoroscopy until slow flow or stasis occurs and fibroid

vasculature is occluded or polyvinyl alcohol particles (300-500Ôm) are injected into the vessel until blood flow ceases.[13,14,17] After completion of embolisation, a fragment of Spongel (absorbable sponge gel) is left in the trunk of the uterine artery to ensure stability of this devascularisation.[12] Supplemental metal coils have also been used by some radiologists.[14] The embolisation procedure generally lasts between 60 to 90 minutes, with procedure time currently averaging 61 minutes.[12,14] The irradiation to the woman associated with this procedure is negligible.[12]

The National Institute for Clinical Excellence (2004) evidence on UAE shows it is safe for routine use and that there is symptomatic benefit in the majority of patients in the short term. However more evidence is required about the degree and duration of the benefits as well as effects on fertility.[15]

The Royal College of Obstetrics and Gynaecology (RCOG) and American College of Obstetrics and Gynaecology (ACOG) recommend that UAE not be offered to women who wish to retain their fertility.

Contraindications to UAE include pregnancy or menopause, active pelvic infection, contrast medium allergy, arterio-venous malformations, desire for future fertility, an undiagnosed mass, and suspicion of adenomyosis.

Proving efficacy of UAE could make it a more feasible option than surgery, that deserves better ñmarketingò to our patients.

In an article by Goldberg, Pennsylvania, UAE was reported as a primary treatment for fibroids since 1995, and has been used to treat > 50 000 women till 2005 when the article was written. It is a safe and effective procedure in well selected patients. It has the additional benefit of being a potentially outpatient procedure, avoiding theatre time, having minimal

blood loss and a short recovery time. Spies et al found UAE improved heavy bleeding in 90% and reduction of bulk-related symptoms in 91% of women respectively. Another prospective study by Spies et al, found UAE and hysterectomy to have similar benefits in improving quality of life, but significantly fewer complications with UAE than those who had undergone surgery. Spies concluded that UAE was safe and effective compared with hysterectomy, had fewer complications and was associated with a shorter hospital stay.[13,17]

An article in The Wall Street Journal of 2004, titled ñHysterectomy alternative goes unmentioned to many women,ò insinuated that gynaecologists choosing not to discuss the option of UAE were protecting their own financial interests or were unfamiliar with the procedure or lacked long term data on the treatment. Further, because radiologists do not provide post-procedural care, the complications of UAE fall to the treating gynaecologists thereby causing reluctance to use this modality of treatment.[13]

Symptom Relief & Quality of Life

As in most studies, menorrhagia was controlled or improved.[12]In the Ontario trial there was a significant improvement in menorrhagia by 83% which was unrelated to the initial fibroid size or volume reduction after UAE. Dysmenorrhoea, bulk symptoms/size and urinary frequency/urgency improved by 77%, 84% and 86% respectively. Patient satisfaction was significantly associated with the degree of improvement in menses.

In a study of 200 patients Spies et al found that heavy menstrual bleeding improved by 87% at 3 months and in 90% at 1 year. Bulk symptoms improved in 93% of patients at 3 months and in 91% of patients at 1 year.[22]

Walker et al showed a satisfactory subjective improvement in menstrual flow and fibroid related symptoms 5 to 7 years post-UAE, demonstrating long term satisfaction was

sustained.[21,28]A long-term follow-up study by Scheurig-Muenkler et al, found that symptom severity scores decreased and Health Related Quality of Life scores (HRQOL) increased, with a significant improvement compared with short term results. Symptom control ranged between 70 to 93%.[26,27]

Most patients had improvement of symptoms in 3 months and persisted in most cases for 2 years, thus stability of symptom improvement did not change over time.[22]

UAE was the subject of a systematic review commissioned by the National Institute for Clinical Excellence (NICE). Studies in the review indicated that there was a mean fibroid volume reduction between 45% to 70%, but these reductions did not correlate with change in symptoms. Improvements in symptoms were reported in 62% to 95% of the women.[15]

In the Ontario trial only 17% of women self-reported excellent health, with young women more likely to complain about poor health compared to older women.[20]Depending on size and location of the fibroid, 88% of women found it bothersome and were embarrassed by the appearance of pregnancy. Almost all women reported heavy life impact, however the mean life impact score were significantly decreased after UAE and 91% of women expressed satisfaction with UAE treatment.[14]Thus patient satisfaction paralleled symptom relief.[22] Reassuringly, 86% of women who had UAE would recommend it to family or friends.[29]

Complications

In a long term follow-up study in Germany in 2011 involving 82 patients over a median of 6.3 years (range 5 to 7.6 years), there were no major complications according to the Society of Interventional Radiology.[27]There was also a low periprocedural complication rate of 8.5% and serious complications were less than 1%.[24]The low rate of adverse events are consistent with many large multicentre trials, and major adverse events are significantly lower than after

surgical interventions.[28]In a study by Spies et al there were no complications in 90% of women.[24]

Complications can be immediate or delayed. Immediate complications include post-procedural vaginal discharge (21%), spotting(22%) and vaginal bleeding(32%). The development of a haematoma at the site of catheterisation and damage to femoral artery have also been reported.[17]

Delayed complications include hot flushes and mood swings in 30% of women. Fibroid expulsion in 10% of women can cause pain. Amenorrhoea may follow in 1% of women, either transiently or permanently.[17]

Abdominal and/or pelvic pain is normal sequel of UAE but was reported as a complication by some authors.[15,26,28]The pain is as a result of fibroid ischemia. The onset of pain is immediate and usually lasts about 12 hours. The pain requires analgesia administration; most women experience abdominal pain and cramps that requires oral analgesia only. Non-steroidal anti-inflammatories (NSAIDs) usually suffice but in certain studies patient controlled intravenous morphine was administered.[26,28]This pain was significant enough for women to have reservations for a repeat procedure.[14]On examining the Fibroid Registry for Outcomes Data (FIBROID), Worthington-Kirsch et al found the commonest adverse event after discharge was inadequate pain relief that required additional hospital treatment in 2.4% of patients and the risk of extended hospital stay for post-procedure pain was of concern.[30]

Post-embolisation syndrome (PES) is a recognised event that occurs in 30 to 50% of patients.[5,28]It is associated with leucocytosis, pyrexia, nausea, vomiting, malaise and occasionally severe abdominal pain due to cytokine release secondary to necrosis, in the absence of infection.[5]It can occur for a few hours to a few days.[28]These symptoms are thought to be an immune-mediated response occurring after embolisation of any solid organ.

In anticipation of this syndrome anti-emetics, anti-pyretics and anti-inflammatories should be administered routinely post-procedure to control it.[17]

Vaginal discharge is a common and important complication, due to shedding of fibroid material into the endometrial cavity. The cure would be hysteroscopic resection of dead fibroid material when the persistent discharge is a major problem. In long term follow-up studies 48% of patients complained of a vaginal discharge post-UAE; some experienced it continuously and others cyclically. In a study by Walker et al, 71% of women reported it to be a major irritant and 5% thought it was major problem, 31% of women felt it was offensive and 19% said it interfered with their sex life. Passage of fibroid material was reported in 29% of women and passage of a whole fibroid in 5%. This was usually associated with pain and bleeding and occurred around 6 weeks post-UAE.[21]Expulsion of fibroids occurred mostly when fibroids were located submucosally. If partially infarcted fibroid material remains attached to myometrium then hysteroscopic resection or dilatation and curettage can be performed. MRI can assist to visualise size of infracted fragment, degree of extrusion and extent of adherent tissue.[28]

Late expulsion of a fibroid can occur up to a year later, in 2% to 8% of women and can be followed by pelvic infection and fever.[15]

Serious infections occur in less than 1% of cases, but must be treated aggressively to avoid systemic infection and the need for hysterectomy.[28]Infection must be distinguished from PES and should the symptoms of PES last longer than 5 days, infection should be investigated.[26]

Amenorrhoea

Amenorrhoea can be viewed as either a complication or a successful outcome depending on the patientôs desire. In older women it may be a treatment success but in younger women it is

a significant complication resulting from premature menopause and resulting in infertility. If amenorrhoea develops in women over 45 years it is difficult to distinguish between natural menopause and early menopause induced after UAE.

Most studies in which ovarian dysfunction occurred post-UAE resulting in amenorrhoea and an increase in follicle stimulating hormone (FSH), were in women over 45 years of age. Data from the Embolization Versus Hysterectomy (EMMY) study confirmed that there is an increase in FSH associated with a decrease in anti-mullerian hormone (AMH) following both UAE and surgery, although the impact of age itself was not determined.[16]AMH is shown to decrease after UAE, consistent with damage to the ovarian reserve. Pelvic vasculature is variable. If embolic material inadvertently lodges in the ovarian vasculature during UAE, blood supply may be compromised and loss of follicles may result; this loss of oocytes may go undetected because women may still have normal menstrual patterns.[30]Absence of amenorrhoea or normal FSH levels may not reflect the effect of UAE on ovarian reserve. If UAE can independently lead to a decrease in ovarian reserve, the effect may be diminished by youth as these effects are identified less frequently in younger women.[29]Thus in the above 40 age group, when there are fewer oocytes remaining, ovarian failure is detected clinically, however younger women may have oocyte depletion but not menopause.[30]

In the Ontario trial, amenorrhoea post-UAE was highly age-related, averaging from 3% in the under 40 years age group to 41% in women over 50 years.[14]Ovarian failure under the age of 45 years was a rare event.

In a long term follow-up study, in 2011 by Scheurig-Muenkler et al, permanent amenorrhoea occurred in 8% of women with a mean age of 50 years.[27]Another review states a rate of 1% to 7% in over 40 year old women.[26]

In an article on the long term outcomes from the Fibroid Registry, 29% of patients became amenorrhoeic, 79% of which were over the age of 45 and only 6% under the age of 40.[29]It is unknown whether UAE precipitated menopause or if menses ceased independently.

A review article published in 2013 addressed the dose reduction during UAE, to decrease exposure to ovaries, would be beneficial as ovaries are sensitive to radiation. A digital flat panel system can significantly decrease radiation dose in comparison to digital subtraction angiography (DSA).[26]Flat panel detectors are a class of solid-state X-ray digital radiography devices where X-rays pass through the subject being imaged and strike the detectors. DSA is a fluoroscopy technique used to visualise blood vessels using contrast medium, the pre-contrast image is subtracted from the latter image.

Ovarian dysfunction presenting with irregular menses or amenorrhoea as well as menopausal levels of FSH have been reported in some studies, ranging between 3% to 14%. Amenorrhoea following UAE was reported in 3% of women under 40 years and 41% of women over 50 years in the NICE guidelines 2004.[15]A multicentre randomised controlled trial comparing uterine artery embolisation with surgical treatment (REST) evaluated and compared effects of UAE and ovary-sparing surgical treatment on ovarian function and menstrual characteristics and found no significant difference in rates of ovarian failure at 12 months between UAE and surgical patients.[16]The findings in women under 45 years showed no enhanced deterioration of function, however in women over 45 years there was an increase in ovarian failure. Although premature ovarian failure (POF) is a severe complication of UAE for fibroids, its occurrence is unusual when embolisation is performed for other indications, for example when used in cases of postpartum haemorrhage.[16]

Off-target embolisation

Off-target embolisation usually affects the ovaries, but can also affect other vascular supplies. If the vaginal artery is involved it can result in sexual dysfunction and or dyspareunia.[28] Labial necrosis can also occur following UAE.[33]

Pregnancy

Impact on subsequent fertility is not well characterised after UAE and remains contoversial.[16,32]In 3 studies involving 604 women, 4% reported pregnancies following UAE, however it was unclear how many women planned to conceive.[15]A single article documented that although a successful pregnancy can occur after UAE, it may affect myometrial integrity and may lead to uterine rupture during pregnancy.[17]

Younger women are keener on having UAE rather than a hysterectomy, with the intention of preserving fertility, thus studies like the Ontario uterine fibroid trial did not exclude these women, but fully informed them of the uncertain effects of UAE on conception and successful pregnancy outcomes. In this study, 31% of women still expressed a desire for children.

Walker et al suggested UAE be offered in women who were suffering fibroid-related infertility after a failed myomectomy.[21]

A review by Memtsa et al, addressing complications of UAE, found that women can have successful pregnancies after UAE but evidence shows it is risky during the early stages of pregnancy. There is accumulating evidence that women can and do conceive after UAE but because of the greater risk of pregnancy complications it is still a relative contraindication in the majority of facilities in women who desire fertility.[28]

One randomised controlled trial addressing fertility after UAE compared to myomectomy in the short term and suggested a higher likelihood of conceiving with myomectomy (77.5%) versus UAE (50%).[28]

Fertility may be jeopardised if the off-target effect of UAE affects the ovary resulting in ovarian ischemia, depletion of ovarian follicles and risk of premature menopause.[28]

In observational studies the risk of miscarriage after UAE varied from 18% to 64% for spontaneous miscarriage, with a cumulative risk of 35%. This was three fold higher than the entire population. However in another series by Homer et al, where the risk of miscarriage after UAE was compared to the risk of miscarriage in a pregnancy complicated by fibroids, the risk was 35% compared to 16%. This data was contrary to what was expected, where treatment of fibroids should reduce the risk of miscarriage, however it did not and the reason is unknown.[28]

Data collected from 200 pregnancies after UAE on outcomes were analysed and compared to women with untreated fibroids. Higher rates of preterm delivery, fetal growth restriction, fetal malpresentation as well as increased caesarean section rates were found, as well as increased incidence of post-partum haemorrhage were found in the women who had undergone UAE.[28]Similar pregnancy outcomes were illustrated in a study of 50 patients who conceived after UAE.[32]

Recurrence risk

The risk of fibroid recurrence is present after UAE and patients should be made aware of the substantial risk of requiring re-intervention, when deciding initially on which treatment to use.[28]

Although the NICE guidelines deem UAE safe for routine use, recommendations for clinicians undertaking this procedure include taking informed consent and educating patients of the uncertainty of the degree and duration of the procedureôs benefits and the involvement of a multidisciplinary team. Interestingly enough and relevant to my study, the NICE institute acknowledges that upon publication of further evidence this procedure may be reviewed by the institute.[15]

Re-intervention

Treatment failure can be multifactorial. Inadequate fibroid infarction and regrowth due to incomplete embolisation or collateral blood flow can result in UAE failure.[21]

Walker et al found 16% of women underwent other procedures since UAE.[21]Scheurig-Muenkler et al found, in their long term prospective cohort study, with a 6.3 median year follow-up, there was a 17% treatment failure rate that required secondary intervention. This was an acceptable failure rate after long-term follow-up. Up to 29% of patients had recurrence with subsequent surgery or repeat endovascular intervention.[27]In a review by Memtsa et al, recurrence rates averaged 20% at 5 years however the REST and EMMY trial indicate an even higher rate of re-intervention, compared to other long term data, of 28.4% and 32% respectively.[23,28]

Spies et al found gynaecological interventions occurred less frequently in 10.5% of patients. These involved hysteroscopic resection and dilatation & curettage.[22]

In a large study involving 2112 patients over 3 years the long term outcomes from the FIBROID registry were assessed. Further intervention was needed in 14.4% of patients. Repeated UAE was required in 1.8% of patients, hysterectomy in 9.8% of patients and myomectomy in 2.8% of patients.[29]

If a patient is under-embolised, a second UAE may result in success that may decrease the rate of surgical intervention.[21]

Techniques to improve embolisation have been modified and MRI use in some studies have been implemented to confirm totality of fibroid infarction.[21]

Surgical Intervention

Although patients may need a hysterectomy after UAE, it may not always reflect a failure of UAE, but rather after shrinkage of a fibroid post-UAE; surgery may prove easier and successful.[21]

Fibroid size and shrinkage

In the Ontario trial fibroid reduction was found to have a greater percentage volume reduction after UAE, with the mean percentage volume reduction in larger fibroids being twice that of smaller fibroids. The degree of uterine volume reduction was significant relative to baseline size.[14]

In the Ontario trial there was a 42% reduction in mean dominant fibroid volume. However the response of patients to volume reduction was variable.[14]Studies show that even beyond 6 months continued reduction and shrinkage occurs. Patients with bulk symptoms achieve significant reduction between 40 to 69% in uterine volume.[17]

A study in Japan involving 25 patients, showed a 67.9% volume reduction at six months on ultrasound or MRI. At 24 months follow-up, 96% of patients had improvement in symptoms and/or decrease in fibroid size.[23]Of note, the Japanese study demonstrated that UAE done in a woman with a solitary fibroid of more than 10cm or multiple fibroids in a uterus compared to a pregnancy of more than 20 weeks, was ineffective.[23]Data from the long term outcomes from the FIBROID registry found patients with smaller fibroids had better results.[29]

Of note, in the FIBROID registry, symptoms and the severity of symptoms did not correlate with objective measures of uterine and fibroid size.[29]

Spies et al demonstrated the mean fibroid volume decreased by 44% at 3 months and 58% after 12 months, and this was sustained at 1 year post-treatment.[22]

2. PROBLEM STATEMENT

Fibroids are a common gynaecological morbidity as described above, that impacts female health and wellbeing. Definitive cure involves major surgery with its associated complications, time off work and a long recovery period. An alternate treatment such as UAE has offered a cheaper, potentially safer and comparably effective alternative to other existing modalities.

Chris Hani Baragwanath Academic Hospital has a UAE unit that has been in existence since 2004.

The aim of this study was to describe the success in managing troublesome symptoms of fibroids, patient satisfaction with UAE, and determination of actual fibroid size.

3. OBJECTIVES

1. To describe the demographics of the women who have attended the Uterine Artery Embolisation clinic from January 2004 till December 2011.

2. To describe the presenting complaints of the women attending Uterine Artery Embolisation clinic.

3. To quantify the response of the fibroid to Uterine Artery Embolisation in terms of size.

4. To document complications and outcomes associated with the procedure.

4. METHODS

4.1 SETTING

This study was conducted at Chris Hani Baragwanath Academic Hospital (CHBAH), a regional/tertiary academic hospital in South Africa, located in the south west of Johannesburg. This facility provides services to a low income socio-economic group.

The study was conducted using data from the UAE clinic, one of several specialised gynaecological clinics which has been in existence since 2004. Patients who are referred to the UAE Clinic were from the Gynaecology Outpatient Department (GOPD).

4.2 STUDY POPULATION

All patients attending the UAE clinic who had the procedure done at CHBAH since the inception of the clinic in 2004 till 2011 were included in the study.

Patient selection was based on the following criteria:

Women

- who wished to retain their uteri
- who were unsuitable for major surgery
- in whom medical management had failed or who could not tolerate the side effects of medical treatment or where medical treatment was contraindicated or where a recommended drug was not available in the public sector
- with uterine size larger than 14 weeks
- with symptomatic fibroids

Exclusion criteria

- patient refusal for UAE
- allergy to the contrast
- patient who wanted to retain fertility
- submucosal or pedunculated fibroids
- pregnancy
- post-menopausal women
- bleeding diathesis
- pre-existing renal disease
- patients on anticoagulants

4.3 PROCEDURE

Information obtained from the radiologists at CHBAH via personal communication described the procedure as follows. Unilateral (usually right) femoral artery catheterisation is done and angiography of the aorto-iliac arteries to the pelvic arteries is performed, to identify the anatomy of the uterine arteries and visualise tumour hypervascularisation. Angiography is followed by successive selective catheterisation of the right and left uterine arteries, generally with an in-situ catheter. After positioning the catheter in the uterine artery, inert particles of Ivalon® in free flow are introduced; these particles are gradually increased in size until tumour blood flow is eliminated using polyvinyl alcohol particles (500 -700Ôm).

4.4 SAMPLE SIZE

All patients who attended the clinic constituted the sample size. All case notes of women referred were assessed and noted but only those who had UAE procedure done were included in the study.

4.5 STUDY DESIGN AND DATA COLLECTION

This was a longitudinal descriptive study where the data was collected retrospectively. I accessed data retrospectively even though data was collected by clinicians prospectively when the patients presented. Data was accessed from specific UAE clinic records, not from the patientôs original hospital files. Blood results were accessed from the National Health Laboratory Service computers.

4.6 CONTROL GROUP

A control group was not utilised in this study because this study was not comparing UAE to any other treatment modality, but rather focussed on outcomes specific to this treatment. Patients who had hysterectomies constitute an inappropriate control. Ideally comparisons

should be made with patients who received medical treatment however we do not use these drugs routinely and thus such a control group would have been difficult to find.

4.7 RECRUITMANT PROCEDURE

Once the patient had been referred to the UAE Clinic and was found to be eligible for treatment, a detailed history was taken and an abdominal and pelvic examination was performed. Ultrasonography using a Toshiba Ultrasound machine (model number CCISN71MA) was performed to confirm the presence of fibroids, exclude other pelvic pathology (e.g. adnexal masses) and the dimensions of the largest fibroid were measured.

Patients were enrolled and information recorded onto a specifically designed data sheet for the clinic.

Informed consent was taken, pre-procedural bloods including a haemoglobin and platelet value, urea and creatinine value as well as an international normalised ratio were drawn and the patient was given a date to return for UAE by the radiology department. A week after the procedure the patient was instructed to return to the UAE clinic.

If the patient suffered from any complications post-procedure, she was admitted to the gynaecology ward for observation and treatment.

The protocol as per the UAE clinic involved follow-up at the following periods: between 2 to11 weeks, 3 to 5 months, 6 to 11 months, 12 to 23 months and finally at 24 months or more.

4.8 DATA ANALYSIS

Data was collected on a data sheet specifically designed for this study. It was entered onto a Microsoft Excel spread sheet and then cleaned. The values were exported into a statistical software package (STATA 11). Continuous variables were described using means and

standard deviations and medians with ranges. Analytical statistics were used. The Wilcoxon signed-rank test for paired non-parametric numeric variables, was used specifically the height of fundus and the paired t-test was used for the uterine size. Statistical significance was accepted where $p<0.05$.

4.9 ETHICS

Patient confidentiality was maintained. Each patient was assigned a study number and no identifiers were recorded on the data sheet.

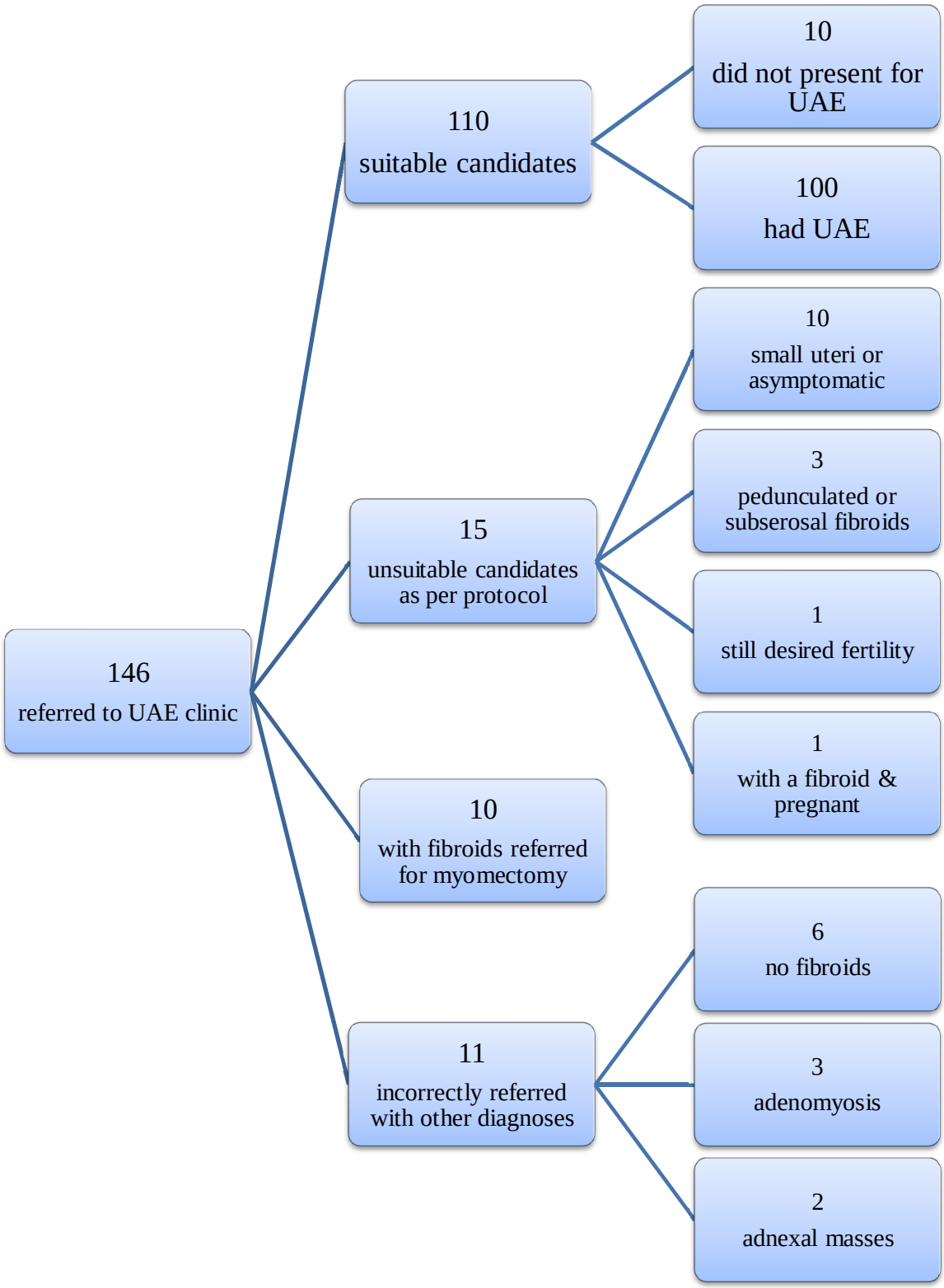
An application was submitted to the Human Research Ethic Committee (Medical) and to the hospital authorities for permission to do the study. Permission was obtained from the relevant hospital authorities and unconditionally approval was given by the Human Research Ethic Committee (Medical). Clearance certificate number is M140213.

4.10 FUNDING

The cost of this study was self-funded.

5. RESULTS

5.1 DESCRIPTION OF RESULTS



Women who were assessed and had UAE done but whose follow up fell beyond the study period were not included and amounted to 6 patients.

Table 1: Age distribution of women in the study

Age	Number n	Percentage %
20 ï 24	5	5.4
25 - 29	17	18.3
30 ï 34	24	25.8
35 ï 39	30	32.3
40 ï 44	12	12.9
45 ï 50	5	5.0
Total	93	100

The mean age of women in the study was 34.5 years (SD ± 6.0), with the maximum number of affected patients falling into the 35-39 year age group. There were 17 women (18.3%) between the ages of 25 to 29 who underwent UAE. The youngest patient was 20 years old and the oldest was 50 years old. There were 7 women in whom the age was not known.

Table 2: Parity of women in the study

Parity	Number n	Percentage %
0	57	70.4
1	14	17.3
2	8	9.9
3	1	1.2
4	1	1.2
Total	81	100

Women who were ever pregnant constituted 40 women (54%) and the remaining 34 women (46%) had never conceived. A total of 19 miscarriages had occurred, 4 women (6.4%) had 1 miscarriage, 3 women (4.8%) had 2 miscarriages and 3 women (4.8%) had 3 miscarriages. Twenty women (27%) had conceived once, with one woman having had 5 pregnancies (1.4%) and 1 woman having had 4 pregnancies (1.4%). The mean gravidity was 1. In my study 57 (70.4%) women were nulliparous and 14 (17.3%) women had one child. However one woman (1.2%) had the highest parity which was 4 and one woman (1.2%) had a parity of 3. There were nineteen women in whom the parity was not known.

Table 3: Number and percentage of common presenting symptoms in women participating in the study

Symptom	Number n	Percentage %
Menorrhagia	78	85.7
Pain	77	90.6
Dyspareunia	22	55.0
Frequency	17	29.5
Constipation	8	21.1

Pain was the most common symptom experienced by women in my study, occurring in 90.6% of patients, which was 78 women out of 91, followed by menorrhagia in 85.7%, which was 77 women out of 85. Pressure symptoms occurred less commonly, with 17 (29.5%) women experiencing urinary frequency and 8 (21.1%) women experiencing constipation.

Table 4: Sites where fibroids most commonly occurred on ultrasound diagnosis

Location	Number n	Percentage %
Submucosal	1	3.0
Intramural	31	93.9
Serosal	1	3.0
Total	33	100

On ultrasound, fibroids were located most frequently intramurally in the women in my study. In women with more than one fibroid on ultrasound, only the dominant fibroid was measured in this study.

Table 5: Haemoglobin (Hb) levels in study participants prior to UAE procedure

Hb (g/dL) pre-procedure	Number n	Percentage %
6 - 6.9	1	1.1
7 - 7.9	7	7.6
8 - 8.9	7	7.6
9 - 9.9	12	13.0
10 - 10.9	17	18.5
11 - 11.9	15	16.3
12 - 12.9	13	14.1
13 - 13.9	16	17.4
14 - 14.9	3	3.3
15 - 15.9	1	1.1
Total	92	100

The mean pre-procedural haemoglobin level in women participating in my study was 11.1g/dL (SD ±2.0). The lowest haemoglobin level was 6.5g/dL and the highest 15.8g/dL. Eight women had no pre-procedural haemoglobin level taken according to laboratory records.

Table 6: Haemoglobin (Hb) levels in study participants subsequent to UAE procedure

Hb (g/dL) post-procedure	Number n	Percentage %
4 - 4.9	1	3.3
5 - 5.9	0	0
6 - 6.9	0	0
7 - 7.9	2	6.7
8 - 8.9	5	16.7
9 - 9.9	4	13.3
10 - 10.9	3	10.0
11 - 11.9	5	16.7
12 - 12.9	3	10.0
13 - 13.9	5	16.7
14 - 14.9	1	3.3
15 - 15.9	1	3.3
Total	30	100

The mean post-procedural haemoglobin level in women participating in my study was 10.7g/dL (SD ±2.5). The lowest haemoglobin level was 4.3g/dL and the highest 15.3g/dL. Seventy women had no post-procedural haemoglobin level taken according to laboratory records.

Table 7: Use of single puncture compared to double puncture during UAE procedure

Puncture	Number n	Percentage %
Single	45	83.3
Double	9	16.7
Total	54	100

Of note nine (16.7%) patients needed a double puncture of the femoral artery during UAE. There were 46 patients whose puncture sites were not recorded.

Table 8: Rate of success compared to failure of UAE procedure

Procedure	Number n	Percentage %
Success	50	89.3
Failure	6	10.7
Total	56	100

In the 56 patients where success or failure was specified, 89.3% were deemed successful and 10.7% failed. Although the UAE procedure failed in 6 patients, these women were still included in the study because even though the procedure may not have been successful it was still performed, and it had to be acknowledged that some patients do undergo UAE and it

may be unsuccessful. In such cases UAE can be attempted at a later stage. Technical failure is a possibility thus it must be accounted for.

Table 9: Duration of vaginal bleeding experienced by study participants in days

Days	Initial visit before UAE		Follow-up 1 2 to 11 weeks		Follow-up 2 3 to 5 months		Follow-up 3 6 to 11 months		Follow-up 4 12 to 23 months		Follow-up 5 Ó24 months	
	N	%	n	%	n	%	n	%	n	%	n	%
0 ï 9	73	86.9	15	88.3	19	95	20	100	18	100	1	100
>10	11	13.1	2	11.7	1	5	0	0	0	0	0	0
Total	84	100	17	100	20	100	20	100	18	100	1	100

On initial presentation 73 women (86.9%) bled between 0 ï 9 days and 11 women (13.1%) bled more than 10 days. After the UAE procedure was done, at the 1st follow-up visit 17 women presented of which 2 (11.7%) women reported to bleed more than 10 days. At the 2nd follow-up visit 20 women presented of which only 1 reported to bleed more than 10 days. At the 3rd, 4th and 5th visit, there were 20, 18 and 1 woman who came for follow-up visits respectively, of those women none of them bled more than 10 days.

On initial presentation 43 women (51.2%) had vaginal bleeding between 5 and 9 days, with 11 women (13.1%) bleeding for 10 or more days. One woman bled for more than 30 days.

At the 1st follow-up visit post-UAE, 9 women (53%) continued to bleed for between 5 to 9 days. No women bled beyond 15 days.

At the 2nd follow-up visit post-UAE, there was a reduction in the duration of bleeding; 12 women (60%) bled for 4 days or less and the women who bled for 5 to 9 days decreased by 18%. The percentage of women who bled for 10 to 14 days had also decreased to 5%.

At the 3rd, 4th and 5th follow-up, no women in this study bled beyond 9 days.

Table 10: Overall symptom relief experienced by participants at each follow-up visit

Symptom Relief	Follow-up 1 2 to 11 weeks		Follow-up 2 3 to 5 months		Follow-up 3 6 to 11 months		Follow-up 4 12 to 23 months		Follow-up 5 Ó24 months	
	n	%	n	%	n	%	n	%	n	%
Overall relief from symptoms	26	86.7	28	80	22	78.6	20	90.9	4	80
No relief	4	13.3	7	20	6	21.4	2	9.1	1	20
Total	30	100	35	100	28	100	22	100	5	100

Patients were asked at each follow-up visit if there was any relief of the main symptom they experienced at initial presentation, referring to menorrhagia, pain, dyspareunia, urinary frequency and constipation.

The number of patients assessed at each follow-up visit was different, because although at each follow-up visit symptomatic relief was meant to be assessed it was not always specified by the patient at each visit, even if the patient had presented for a follow up visit, therefore symptomatic relief specifically was assessed in fewer than 35 patients at each follow-up visit. Overall symptomatic relief was predominantly experienced by most patients at follow-up, as demonstrated in Table 10 above, with the lowest percentage of overall symptom relief being 78.6% at the 3rd follow up visit and the maximum percentage of overall symptom relief being 90.9% at the 4th follow up visit.

Table 11: Complications experienced by participants after UAE procedure

Complication	Immediate		Follow-up 1 2 to 11 weeks		Follow-up 2 3 to 5 months		Follow-up 3 6 to 11 months		Follow-up 4 12 to 23 months		Follow-up 5 Ó24 months	
	n	%	n	%	n	%	n	%	n	%	n	%
Nil	20	27.8	2	6.1	-	-	1	12.5	-	-	1	100
Pain	21	29.2	9	27.3	1	25	2	25	-	-	-	-
Bleeding	1	1.4	7	21.2	1	25	2	25	2	40	-	-
PV Discharge	2	2.8	12	36.4	-	-	2	25	2	40	-	-
Post-Embolisation Syndrome	17	23.6	-	-	-	-	-	-	-	-	-	-
Sepsis	1	1.4	-	-	-	-	1	12.5	-	-	-	-
Wound Haematoma / Infection	7	9.7	1	3.0	-	-	-	-	-	-	-	-
Other	3	4.2	2	6.1	2	50	-	-	1	20	-	-
Total	72	100	33	100	4	100	8	100	5	100	1	100

0 = (-) in each cell where no numeric value present

When assessing complications, immediately after the procedure 20 women out of the 72 that were seen reported no complications; at the first follow-up visit 33 women presented and 2 had no complication; at the second follow-up visit 4 women presented but all 4 reported complications; at the third follow-up visit 8 women presented and 1 reported no complications; at the fourth follow-up visit 5 women presented and they all reported

complications; at the fifth follow-up visit only 1 women presented and she had no complications. So a total of 24 patients over the follow up period specifically responded having no complications to the procedure.

An assessment of pain post procedure was made on 33 patients over the entire follow up period. Immediately after the procedure 72 women were seen and 21 women reported pain; at the first follow-up visit 33 women presented and 9 women reported pain; at the second follow-up visit 4 women presented and 1 reported to have pain; at the third follow-up visit 8 women presented and 2 reported pain; at the fourth and fifth follow-up visits 6 women presented but reported complications apart from pain.

An assessment of bleeding post procedure was made on 13 patients over the entire follow up period. Immediately after the procedure 72 women were seen and 1 women reported bleeding; at the first follow-up visit 33 women presented and 7 women reported bleeding; at the second follow-up visit 4 women presented and 1 reported to have bleeding; at the third follow-up visit 8 women presented and 2 reported bleeding; at the fourth follow-up visit 5 women presented and 2 reported bleeding.

An assessment of per vaginal discharge post procedure was made on 18 patients over the entire follow up period. Immediately after the procedure 72 women were seen and 2 women reported per vaginal discharge; at the first follow-up visit 33 women presented and 12 women reported per vaginal discharge; at the second follow-up visit 4 women presented and none reported per vaginal discharge; at the third follow-up visit 8 women presented and 2 reported per vaginal bleeding; at the fourth follow-up visit 5 women presented and 2 reported per vaginal discharge.

Post embolisation syndrome was assessed immediately post procedure and reported in 17 of the 72 women who were assessed. It was not reported by any other women at any subsequent follow-up visit.

Sepsis was reported 2 patients over the entire follow-up period. One women had sepsis immediately post procedure out of the 72 that were assessed and 1 woman out of the 8 women that presented at the third follow-up visit.

Wound haematoma/infection was reported in 8 women over the entire follow-up period. Of the 72 women assessed immediately post procedure 7 women had a wound haematoma/infection; 1 women reported a wound haematoma/infection at the first follow-up visit.

Eight women were assessed to have ñotherò complications over the entire follow up period presenting at different follow-up visits.

The commonest complication immediately post-UAE was pain. Notably 27.8% of patients had no complications immediately post-UAE. Post-embolisation syndrome occurred in 23.6% of women, requiring admission after the procedure. The least common complications were bleeding and sepsis.

At the 1st follow-up visit PV discharge was highest complication. Approximately twenty-seven percent of women complained of persistent pain.

At the 2nd follow-up visit pain and bleeding were equally prevalent. Two woman experienced complications unrelated to UAE or fibroids, however they reported these unrelated symptoms at follow-up. For example one woman had hip and thigh swelling probably related to lymph node damage after radiation for cervical cancer. This woman had been treated for cervical

cancer stage IIa and received radiation therapy, she was in remission when she presented with symptomatic fibroids the following year.

At the 3rd follow-up visit 8 patients were assessed: 2 women had pain, 2 had bleeding and 2 complained of vaginal discharge.

At the 4th follow-up visit 5 patients were assessed: 2 had bleeding, 2 had vaginal discharge and 1 had ñotherò complication, this was the passing of ñfleshò which was found to be necrotic fibroid material on histology.

At the 5th follow-up visit, 1 patient was assessed and she had no complications.

At each follow-up visit a different number of patients presented, but within the number of patients that presented, only certain patients responded to some of the questions, not necessarily all questions. Thus the number of patients at each follow up visit differed but the number that responded to each specific question also differed. The table included the patients who presented and responded directly to that question. This table specifically refers to those women that responded to questions regarding complications.

These are complications not ongoing symptoms, because symptom relief was separately assessed.

Table 12: Outcomes in participants after UAE procedure

Outcomes	Follow-up 1 2 to 11 weeks	Follow-up 2 3 to 5 months	Follow-up 3 6 to 11 months	Follow-up 4 12 to 23 months	Follow-up 5 Ó24 months
	Number	Number	Number	Number	Number
Vaginal Discharge	-	-	-	1	1
Amenorrhoea	-	1	3	3	1
Pregnancy	-	-	1	3	1
Hysterectomy	2	-	-	-	1
Myomectomy	-	1	2	2	-
Re-intervention	-	-	-	-	-
Other	1	-	-	1	-

0 = (-) in each cell where no numeric value present.

Outcomes were assessed post-UAE procedure in a total of 24 patients over the 5 follow-up visits. Two patients were discharged. Eight patients became amenorrhoeic. Five patients became pregnant. Three patients were referred for hysterectomy and 5 patients were referred for myomectomy. No patients had re-intervention. Two patients had ñotherò outcomes.

From the ñotherò outcomes, one patient was referred for infertility treatment and the second patient required a blood transfusion after expulsion of a submucosal fibroid that caused her to bleed to an Hb of 4.3g/dL.

At each follow-up visit a different number of patients presented, but within the number of patients that presented, only certain patients responded to some of the questions, not necessarily all questions. Thus the number of patients at each follow up visit differed but the number that responded to each specific question also differed. The table included the patients who presented and responded to specific questions regarding outcomes. The outcomes I defined were some of the adverse effects of the procedure, such as vaginal discharge, amenorrhoea, pregnancy, patients requiring further surgical interventions such as hysterectomy or myomectomy and re-intervention or any ñotherò adverse effect.

5.2 ANALYSIS OF RESULTS

Analytical statistical tests were employed to analyse the results of the data collected. The Wilcoxon rank-sum test for paired non-parametric numeric variables and the paired t test was used. Statistical significance was accepted where $p<0.05$.

Table 13: Comparison of the mean height of fundus (HOF) & transverse area of dominant fibroid on ultrasound at presentation and at final visit and respective P values

	Height of Fundus (cm)	Area (cm^2)
At initial presentation	17.8	109.8
At final visit	12.5	71.9
P value	<0.01	<0.01

The mean HOF at presentation of women in this study was 17.8cm (SD ± 3.8) after UAE the final mean HOF was 12.5cm (SD ± 6.4). This was a 5.3cm difference in the mean height of fundus after treatment. P value<0.01 resulting in statistical significance.

The formula used to calculate the transverse area of the dominant fibroid on ultrasound was

$$\frac{\text{[illegible]} + \text{[illegible]}}{2}$$

The mean area of the dominant fibroid at initial presentation was $109.8cm^2$ (SD ± 49.4) and at final visit was $71.9cm^2$ (SD ± 35.4). There was a mean area difference of $40.0cm^2$ (SD ± 47.9). This result is statistically significant with a P value<0.01. This reduction in area indicates the substantial effect of UAE on fibroid shrinkage.

Ninety three women had their HOF measured at presentation and 85 women had their HOF measured at their final follow up visit.

Ninety women had the transverse uterine area of the dominant fibroid measured on ultrasound at presentation and 53 women had the transverse uterine area measured on their last follow up visit.

Table 14: Comparison of height of fundus (HOF) at presentation and area at presentation in patients with follow-up visits and those who did not follow-up with the respective P values

	HOF at presentation (cm)	Area at presentation (cm^2)
Follow-up	18.3	113.2
No follow-up	16.3	105.6
P value	0.0048	0.47

The mean difference in HOF of patients who did follow-up compared to those who did not follow-up was 2.06cm. This was statistically significant ($P < 0.05$).

The area on initial presentation of patients who did follow-up was 113.2 cm^2 (SD ± 47.4) and in the patients that did not follow-up was 105.6cm^2 (SD ± 52.0). The P value was not statistically significantly.

6. DISCUSSION

Age distribution

The mean age of the women in this study was 34.5 years, over a decade less than women in other studies reviewed. In the African population symptoms present at a younger age, with more severe symptoms and larger fibroids.[20,25]Since the study population was African in the present study, this could account for why the mean age was lower in my study.

Study by author (year published)	Women with fibroids	
	Age Range	Mean Age
Ravina et al (1995)	34 ï 49 years	44 years
Spies et al (2001)	30 ï 52 years	43 years
Pron et al (2006)	19 ï 56 years	43 years
Walker et al (2006)	30 ï 44 years	44 years
Sasa et al (2011)	-	41.7 years
Present study(2014)	30 ï 38 years (IQR)	34.5 years

Previous pregnancy outcomes:

In this study, 70.4% of women were nulliparous and 45.6% of women in the study had never conceived. Whether the relationship between nulliparity and fibroids are causal or vice versa the association between the two variables was incidental in my study.

Contraceptive use

In my study adequate data was not collected on contraceptive use, only 8 women had information on contraceptive use so I was unable to establish an association between contraceptive use and the occurrence of fibroids.

Presenting symptoms

In most of the literature reviewed, menorrhagia is the most common presenting symptom in women with fibroids and is also the major indication for UAE.[14,26]However in my study, pain was the most frequent symptom (90.6%) followed by menorrhagia (85.7%).

Passing of clots during menstruation was included as a symptom of menorrhagia in my study. Menorrhagia occurred between 30 to 85% in other studies[17,20,22,25], correlating with the rate in my study. Menorrhagia is not only the most common presenting symptom but it results in iron deficiency anaemia.[6,12,20]Dysmenorrhoea is associated with menorrhagia in most cases, with 62% to 83% of women reporting this symptom.[20,22,25]Pelvic pain and pressure symptoms depend on the area of fibroid growth.[17]Dyspareunia was recorded in 41% of women in the Ontario trial.[20]Pressure symptoms were found to be the least frequent presenting symptom in my study but results were variable, in other studies ranging up to 73%.

In the Black Womenôs Health Study, 55% of women were diagnosed with fibroids after seeking treatment for fibroid related symptoms.[9]Five percent of women had a combination of symptoms, this rate was higher in my study, with 76% of women having more than one symptom. In the Ontario Uterine Fibroid Trial black women and younger women were more likely to report pain and bleeding.[20]This was similar to my study where the mean age of black women was younger (34.5 years) and the two commonest symptoms were abdominal pain and menorrhagia.

Fibroid Locations

Fibroids were located intramurally in 93.9% of women in my study in keeping with the Ontario trial where the largest fibroid was predominantly located intramurally on ultrasound or MRI imaging.[14]

According to the records kept, only 33% of women had the location of the fibroids noted. This lack of record keeping may have been due to difficulty in determining where the fibroid was located or whether to classify the fibroid as intramural, submucosal or subserosal depending on how much of the fibroid was in which area.

Pedunculated fibroids are a contraindication to UAE as embolisation of these fibroids can lead to stalk necrosis and potential detachment of the fibroid from the uterus either into the abdominal cavity or into the endometrial cavity and lead to complications.

Submucosal fibroids were also excluded from my study as per the protocol at CHBAH, due to the risk of intracavity necrotic debris that may obstruct the cervix or become infected and require further intervention. However one patient with a submucosal fibroid did have UAE performed but this patient was an exception. She was discussed with the radiologist, as she had menorrhagia that had required a blood transfusion on two previous occasions and still had prolonged bleeding of 18 days per month. She showed no response to medical management and refused surgery, so UAE was attempted as another measure to treat her.

Haemoglobin levels

According to the WHO classification anaemia is defined as a haemoglobin (Hb) level under 12g/dL in a non-pregnant woman over the age of 15 years. In my study the pre-procedural mean Hb was 11.1g/dL suggesting that the average woman in the study was mildly anaemic.

A post-procedural Hb level was not done routinely at the same interval on all patients. In fact less than a third of patients had Hb levels performed, on occasion up to two years after the procedure, and were only taken if the patient presented for a complication of UAE or of fibroids or even an unrelated problem. Thus this result is not an accurate reflection of Hb levels post-UAE.

Further, the patient in my study with an Hb of 4.3g/dL, experienced a complication post-UAE, with persistent vaginal bleeding caused by expulsion of the fibroid and on first follow-up visit, the patient needed a blood transfusion.

In a study in Japan with a one year follow-up, anaemia significantly decreased in just two months after the procedure with the mean Hb improving from 8.5 g/dL to 11.5 g/dL.[23]

Although haemoglobin levels would be a good marker of response in patients with a history of menorrhagia and is not subjective, surprisingly only one study in the literature reviewed included this variable in their data collection as an indicator of reduced bleeding in the women studied.

UAE procedure

The femoral puncture site was not mentioned in the patient's notes unless double puncture was done. We assumed that 91% of patients required only a single skin puncture to gain access. In a study by Spies et al in 2002 the rate of women who had bilateral femoral puncture was 1%.[24]

Duration of vaginal bleeding

The duration of bleeding per menstrual cycle ranged mostly between 5 to 9 days in my study. A normal menstrual period may be between 2 to 7 days but this varies among women. By the second follow-up visit and every visit thereafter there was reduction in the duration of

bleeding, showing a response in the majority of women to UAE. Of interest, only 16 of the 84 women had menses for 8 or more days, however menorrhagia was a complaint among 78 out of 91 women, so the number of days did not necessarily relate to perception of menorrhagia. Rather it seems the menstrual flow was more distressing to patients. Perhaps if the blood loss had been quantified, this link would be more meaningful.

In the REST trial, the mean duration of menstrual flow decreased significantly from baseline to 12 months with a reduction in number of days of bleeding by 1.7 days but no statistically significant change in mean cycle length.[16]In the Ontario trial, the mean menstrual duration significantly reduced from 7.6 to 5.4 days. The number of women who reported a menstrual duration of more than 7 days decreased from 30% to 9% subsequent to UAE.

Symptomatic relief

Symptomatic relief after UAE, was found to be improved in the majority of women in my study. The women were questioned on each follow-up visit whether symptomatic relief had occurred referring to their main presenting symptom. Reflecting on all follow-up visits, a minimum of 78.6% and a maximum of 90.9% women responded positively to having symptomatic relief. The results of my study were slightly more encouraging than a case series of 400 women in which 73% to 90% reported symptomatic improvement within six months.[15]Although this was a ñyes/noò response, it reflected the womanôs feeling of whether UAE was effective in relieving their symptoms and indirectly indicating satisfaction with the procedure.

Apart from symptomatic relief, other studies assessed quality of life (QOL).That parameter was not addressed in my study.

Complications

Pain

Pain was reported as a complication in 33 out of the 100 women in my study. Twenty one women experienced this, not unexpectedly as an immediate complication post-procedure. Only 3 women experienced pain beyond 12 weeks. As compared to other studies pain was the commonest complication after UAE, however isolated pain control that required readmission did not occur, and pain was managed routinely but without opioids.

Vaginal discharge

In my study 18 patients complained of vaginal discharge in the 2 years of the study. This rate is unusually low compared to the literature reviewed. Vaginal discharge is a common gynaecological complaint for which women may access help at a primary health care clinic. This could account for the low rate in my study. Also patients with submucosal fibroids were excluded from my study so there should be less expulsion of fibroids experienced by my patients.

Post-Embolisation Syndrome

PES was reported in fewer than 25% of women in my study. Recommended treatment was administered routinely post-procedure and on discharge possibly accounting for why the rate was lower than in other studies. Patients were questioned about these immediate symptoms on their initial follow-up 2 to 11weeks after UAE so it is unlikely that this rate is due to underreporting. If a patient had only one suggestive symptom of PES it was included as a complication.

Sepsis

Sepsis occurred in 2 patients in my study, but it was not overwhelming sepsis and they were treated successfully with antibiotics only.

In an Iranian study (2013) unspecified immune compromise was a contra-indication to UAE. Perhaps the concern that prompted this was a potential for higher sepsis rates after UAE in these individuals.[26] The retroviral status of patients in my study was not tested, but with a low rate of sepsis in my study, I do not think retroviral status would have impacted on sepsis rates post-UAE. This could be investigated further.

Wound haematoma/infection

This a minor complication of the procedure. In my study wound haematomas occurred in 8 out of the 100 patients, predominantly as an immediate complication post-procedure in 7 of the 8 cases. Treatment was instituted and symptoms resolved subsequently. There was no trauma to the femoral artery in any of the patients who underwent UAE in my study and pulses were checked routinely post-procedure to ensure this.

Other complications

A variety of minor complications of <1% incidence have arisen from other studies but not in mine, such as urinary tract infections or urinary retention, drug reactions, phlebitis or thrush.

There were no fatal or major complications in my study. As with prospective data collected from two studies, one by Spies et al with 400 patients with follow-up up for a year where there were no deaths or permanent disabilities, and the other from the FIBROID registry with 3160 patients where there were no deaths.[24,30]

Outcomes

Amenorrhoea

In my study 8% of women became amenorrhoeic. Of the ages of women whose menses ceased, 6 were between 40 to 45 years and the other 2 women were both 33 years old. These results were similar to those of women in the under 40 year age group referred to in the literature, however I would have expected the amenorrhoeic women to be in the over 45 year age group.[21,27] Thus I cannot attribute the amenorrhoea to a perimenopausal state, or related to UAE. Furthermore the cause of amenorrhoea cannot be ascertained as it was not investigated for.

Pregnancy

The consensus from literature is that women must be cautious about fertility after UAE and that even though pregnancy is a possibility, fertility preservation and improvement cannot be guaranteed. Possible complications of pregnancy are not predictable.[26]

In my study, 5 women who followed up within the 2 year period conceived, however the success of those pregnancies was not pursued in 2 of the cases. Two women carried to term and 1 experienced a miscarriage. This conception rate is higher than rates mentioned in the literature. Interestingly, patients in my study were excluded if they were trying to conceive, however the conception rate was still higher than other studies previously mentioned.

Re-intervention

No patients had a repeat UAE in my study. If there was no improvement in symptoms or size reduction then the patient was referred for surgical intervention. Hysterectomies were performed in 3% of women and 5% of women had myomectomies. The rate of any re-intervention was much lower in my study, compared to studies discussed earlier, however the

follow-up period in my study was not as long as others in the literature, which may account for the lower rate of intervention. Further the only alternative offered to my patients, in the event of failure of UAE or recurrence of symptoms was surgery. In women who initially refused surgery and opted for UAE, this may be why the intervention rate was lower because these patients may have opted to tolerate symptoms instead. Also in terms of surgical re-intervention, dilatation and curettage with hysteroscopic resection was not offered as an alternative in my study.

Mean Height of Fundus (HOF) & Transverse area of dominant fibroid on Ultrasound at presentation and at final visit

The measurement of fundal height is less scientifically accurate and less objective than diameters measured on imaging, thus both assessments were made. UAE proved to be effective in fibroid reduction in my study both by HOF assessment which decreased by an average of 5.3cm as well as area on ultrasound which decreased by 40cm^2. A statistically significant reduction correlates with all studies reviewed in the literature, confirming the efficacy of UAE. Specific to my study compared to most other studies, area was used instead of volume.

Height of fundus (HOF) at presentation and area at presentation in patients with follow-up visits and those who did not follow-up

The mean difference in HOF of patients who did follow-up compared to those who did not was statistically significantly. Thus the reason for loss of follow-up must be considered. It is likely that the patients who did follow-up had larger fibroids and were more symptomatic and

thus were more inclined to monitor their response. Conversely the patients who did not follow-up had smaller fibroids at presentation and perhaps there was a positive response after initial UAE so the patient felt follow-up was not necessary.

The area on initial presentation of patients who did follow-up and those that did not, was not statistically significantly. This also reflects that the initial area of the fibroid did not impact on whether or not the women followed up or not.

I speculated as to the reasons for loss to follow-up:

- Patients may have had unresolved or worsening symptoms and decided to seek treatment elsewhere;
- Patients may have had a negative experience with the actual UAE procedure and decided against returning for fear of a repeat procedure
- Patients may have moved from the area or demised or
- They may have experienced adequate symptom relief not requiring further treatment

Patient information and counselling at initial consultation was extensive, so lack of knowledge should not have been a reason as to why patients defaulted follow-up.

Each study reviewed had different patient selection criteria and contraindications for UAE, most were in keeping with the inclusion and exclusion criteria in my study, apart from the following criteria. In my study patients who wanted to retain fertility were not offered UAE, in keeping with ACOG and RCOG guidelines, however some studies have offered UAE after thorough counselling and informed consent allowed for UAE in patients who wished to conceive. Useful information has been gathered from these studies, such as the Ontario trial, creating a broader applicability.[14]

Large fibroid size was also a contraindication in some studies, such as a uterus larger than 20 weeks in a Japanese study or larger than 24 weeks in Spies et al study, however in studies such as mine, where initial fibroid size or height of fundus was not an exclusion criteria, positive results were noted.[14,23,24]

Although number of days admitted would have been a useful indicator of immediate complications and recovery time in my study, it could not be determined due to lack of details in patient records. Patients were also not asked about the number of days of absenteeism from work or return to normal activities. These variables could have been used as indicators for recovery.

Failure in symptomatic relief occurs between 4 to 21%, this could be due to misdiagnosis. In our study only ultrasound was performed, whereas MRI would have been more beneficial to identify other benign conditions like adenomyosis or rarely leiomyosarcoma in less than 1%.

Despite favourable outcomes of UAE it is still not routinely offered and used widely both locally and internationally. Perhaps if people had more awareness of this procedure and it had more publicity it would attract wider use.

A study in Netherlands, involving patients, radiologists and gynaecologists, identified factors which either facilitate or restrict the implementation of UAE. Restricting factors and recommendations were assessed, from perspectives of each group. Obstacles identified were the lack of knowledge about UAE, the absence of a multidisciplinary protocol and the absence of UAE as a treatment option in the Dutch National guideline on the management of menorrhagia.

7. LIMITATIONS

In my study comparisons were not made to other treatment modalities.

The study may have been prone to selection bias because referrals to the UAE clinic were by specialist gynaecologists and registrars from the general gynaecology out-patients departments. If the criteria for referral was not known or if registrars rotating through CHBAH during the course of their training, did not know about the clinic then eligible women would not have been referred.

Although follow-up monitoring was standardised and done by the same specialist gynaecologist, the actual UAE procedure was done by radiology registrars with different levels of experience and training, therefore the same level of success may not be achieved in each case.

No data was collected on whether the women were smokers or not. BMI was not ascertained.

A minimal account of patientôs contraception history was obtained.

A detailed menstrual history, beyond duration of bleeding and menorrhagia, was not sought.

In my study, only ultrasound measurements of the dominant fibroid were used, as MRI was not a feasible option. This could have resulted in less accurate measurements of the fibroids or even misdiagnosis in certain cases, which may account for treatment failure.

My study did not address the patient satisfaction and impact on quality of life. Time taken off work for fibroid-related reasons was as high as 40% in a year where often women were absent from work around the time of their menstrual period.[20]Should symptoms be resolved then functionality in the workplace would also be improved.

Follow-up in terms of fertility beyond the study period was not assessed. Also patients who wanted to retain fertility were excluded from the study. If a patient did conceive post-UAE the outcome of pregnancy was not established, thus success of pregnancies was uncertain.

FSH and AMH levels prior to and post-procedure were not taken, thus premature ovarian failure could not definitively be diagnosed.

Many patients defaulted follow-up visits. Data obtained on symptom relief in some patients is not detailed as to which symptom was relieved. Information was often missing regarding the actual UAE procedure. Thus there are many gaps in the data due to lack of information obtained or documented at each visit. As a result of missing information accurate assessment of certain results could not be made.

Follow up visits were variable among the patients and not maintained consistently from the first visit till the last/5th follow-up visit. At each follow-up visit there were a different number of patients that presented but also within the number of patients that presented, not all women responded to every question, so some may have details regarding their symptoms at follow up but may not have elaborated if there were any complications for example.

Loss to follow is one of the difficulties with studies conducted in an operational setting. The difference in the HOF in the group that was followed up compared to those lost to follow up make it difficult to extrapolate my results to the general population.

8. CONCLUSION

With symptomatic fibroids that occur more commonly in younger African women with more severe symptoms that impact on quality of life and have a high disease burden, treatment is sought that is an alternative to invasive surgery and conserves the uterus, yet is effective and safe. Despite the discomfort and inconvenience women experience preserving their uteri, they are still seeking alternatives to hysterectomy.[20]The benefits aside from fibroid size reduction, are that it is potentially an outpatient procedure with a quick recovery time and a less complications.[13,20,28]Published data is indicative that it is effective in controlling symptoms caused by fibroids.[17,20]It is a low risk procedure with little variability in short term outcome based on either demographics or practice settings.

There were only minor complications, no major complications or fatalities. However due to loss of follow up long term outcomes cannot be commented on. There should be ongoing surveillance of women who have undergone the procedure.

In appreciation of the results found in my study, the subsequent step would be for these results to have an impact on patients, gynaecologists and interventional radiologists so that UAE can be better implemented and more patients can be referred to the UAE clinic at CHBAH. Similar strategies as found in the Netherlands study could assist in publicising UAE and its efficacy so that there is more awareness of the procedure and thus more implementation of it for the treatment of symptomatic fibroids in suitable candidates.

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APPENDIX A - DATA SHEET

Study no:

Demographics

Age :

Parity :

Gravidity :

Miscarriages :

Presenting Symptoms and History

Contraception (yes / no / unknown)

Bleeding

Flow (days) :

Clots: (yes / no)

Pain (yes / no)

Dyspareunia (yes / no)

Pressure symptoms

Frequency (yes / no)

Constipation (yes / no)

Examination

Height of fundus (HOF):

Ultrasound: location

Submucosal	1
Intramural	2
Serosal	3
Pedunculated	4

Measurement of largest fibroid

Diameter 1 in cm Diameter 2 in cm

Haemoglobin level

Pre-procedure Post-procedure

Puncture

Single 1 Double 2

UAE procedure

Success 1 Failure 2

No of days admitted in hospital :

Complications (key to be used below)

Nil	0
Persistent pain	1
Bleeding	2
PV discharge	3
Post-Embolisation Syndrome	4
Sepsis	5
Haematoma/Infection at wound site	6
Other	7

Outcomes (key to be used below)

Discharge	0
Amenorrhoea	1
Pregnancy	2
Hysterectomy	3
Myomectomy	4

Re-intervention 5

Other 6

Follow-up at 2 weeks - 11 weeks:

Symptom relief : (yes / no)

Flow (days) :

Complications :

Outcomes :

Follow-up 3 months – 5 months:

Symptom relief : (yes / no)

Flow (days) :

HOF :

Fibroid size : shrinkage / unchanged / enlarged

Diameter 1 in cm : Diameter 2 in cm :

Complications :

Outcomes :

Follow-up at 6 months – 11 months:

Symptom relief : (yes / no)

Flow (days) :

HOF :

Fibroid size : shrinkage / unchanged / enlarged

Diameter 1 in cm : Diameter 2 in cm :

Complications :

Outcomes :

Follow-up at 12 months – 23 months

Symptom relief : (yes / no)

Flow (days) :

HOF :

Fibroid size : shrinkage / unchanged / enlarged

Diameter 1 in cm : Diameter 2 in cm :

Complications :

Outcomes :

Follow-up at 24 months or more

Symptom relief : (yes / no)

Flow (days) :

HOF :

Fibroid size : shrinkage / unchanged / enlarged

Diameter 1 in cm : Diameter 2 in cm :

Complications :

Outcomes :

APPENDIX B - ETHICS CLEARANCE CERTIFICATE

R14/49 Dr Fatima Zahra Surtee

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M140213

NAME: (Principal Investigator)	Dr Fatima Zahra Surtee
DEPARTMENT:	Obstetrics and Gynaecology Chris Hani Baragwanath Academic Hospital
PROJECT TITLE:	A Descriptive Study of Uterine Artery Embolisation for Leiomyoma in an African Population in a Low-Resource Setting
DATE CONSIDERED:	28/02/2014
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Karlyn Frank
APPROVED BY:	Professor PE Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	03/03/2014

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor Senate House, University

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**

Principal Investigator Signature

Date 28 / 3 / 2014

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX C - ñTURNIT INò REPORT

SurteeMmed2015.docx

ORIGINALITY REPORT

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SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Dattakumar Kunde. "Alternatives to hysterectomy for treatment of uterine fibroids", The Obstetrician & Gynaecologist, 10/2004 Publication	1%
2	S Rashid. "The effects of uterine artery embolisation and surgical treatment on ovarian function in women with uterine fibroids : Effects of embolisation and surgery on ovaries", BJOG An International Journal of Obstetrics & Gynaecology, 05/11/2010 Publication	1%
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UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF HEALTH SCIENCES

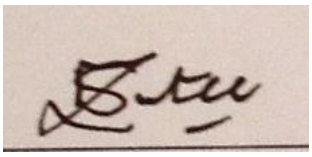
PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY

I, Dr Fatima Zahra Surtee (Student number: 0103876 A) am a student registered for the degree of Master Of Medicine in Obstetrics & Gynaecology in the academic year 2015.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.



Signature: _____ Date: 22 September 2015