Treatment of uterine fibroids with A.Uterina embolisation in Latvia and Lithuania

Diana Uljanionok Zilovic¹, Raimonda Bykovaite², Karolina Eva Romeikienė², Andrius Romeika², Danguole Vildaite¹, Audrius Sirvinskas¹, Algimantas Simkaitis¹, Andrius Pranculis³, Rytis Stasys Kaupas⁵, Inga Nalivaiko⁶, Maija Kokare⁶, Karlis Kupcs⁶, Melita Lagzdina¹, Sanita Ponamorjova⁸, Nellija Lietuviete⁸, Lelde Kulmane⁹, Inga Vevere⁹

¹ Vilnius University, faculty of Medicine
² Lithuanian University of Health Sciences, faculty of Medicine
³ Republican Vilnius University hospital
⁴ Klaipeda University, Klaipeda University Hospital
⁵ Lithuanian University of Health Sciences Hospital Kaunas Clinics
⁶ Pauls Stradins Clinical University hospital
⁷ Latvia Children's Clinical University hospital
⁸ Eastern Clinical University hospital
⁹ LiepAjas Regional Hospital

ABSTRACT

Aim: to evaluate the frequency and results of applying uterine artery embolization for uterine fibroids treating.

Research material and methods: The research retrospectively analyses the medical history of women (n=180), who were treated in 7 hospitals of Latvia and Lithuania. Uterine artery embolization (UAE) was applied for these women to treat symptomatic uterine fibroids. The diagnosis of uterine fibroids (TLK 10 D25.0, D25.1, D25.2, D25.9) was confirmed by ultrasound or magnetic resonance and gynaecologic exam. After the procedure, women were asked to fill out a questionnaire, which had to determine if they were content with the undertaken procedure and to evaluate the dynamics of the symptoms caused by uterine myomas.

Results: Main age of the patients was 43.5 ± 4.6 years, all of them had symptomatic uterine fibroids. For the majority of the patients UAE was the first treatment. According to the follow up results of the Latvian patients, the size of the uterine fibroids reduced 67.3 percent for the women versus Lithuanian - 100 percent. It takes 72.2 percent of the patient's all together. None of the patients experienced early UAE complications. The average duration of hospitalization was 1.85±1.56 days. Three patients became pregnant after the UAE and delivered healthy babies.

Conclusions: UAE is mini¬mally invasive, safe, efficacious, and cost-effective alternative to traditional surgical fibroids treatment. UAE helps to reduce symptoms of fibroids and is associated with rapid recovery with most women. It is suitable for women, who desire future childbearing. Appropriate patient evaluation and selection for a procedure are vital and critical for patient satisfaction.

Keywords: embolization, intervention.

INTRODUCTION

Uterine fibroids (myomas, leiomyomas) are one of the most common non-malignant uterine tumours. According to various literature, their frequency is up to 20-40% among fertile women age [1, 2]. Mostly uterine fibroids have no symptoms, but about 20% of women have symptomatic uterine myomas [3, 4]. The main symptoms are long and heavy menstrual bleeding, acyclic bleeding, pains of lower part of the stomach, painful intercourse [5]. Uterine myomas can be a reason of infertility among these women and it can impact their quality of life. Due to longer menstruation, women are prone to anaemia as well as fatigue, irritability and weakness [6]. To determine the best treatment strategy for women diagnosed with uterine myoma it is important to evaluate the most concerning complaints as well as the age of the patient, the size of the myomas, type and location. For a long time the standard treatment of uterine fibroids was
surgical – abdominal, vaginal or laparoscopic hysterectomy or myomectomy. However, more women request for an alternative to the surgical treatment [7, 8]. There are some other options for the uterine fibroids treatment: pharmaceutical treatment, magnetic resonance-guided high-intensity focused ultrasound (MRgFUS), transvaginal route for radiofrequency ablation, and uterine artery embolization (9). In 2015 pharmaceutical treatment of fibroids with ulipristal acetate (a selective modulator of the receptors of progesterone) began in Lithuania and in Latvia. Since 2017 this medication became compensated in Lithuania. Still, our treatment goals for uterine fibroids are long-term in reduction of fibroids size and numbers, which leads to reduction or elimination of fibroids symptoms. One of the alternatives is uterine artery embolization (UAE). It is the least invasive medical treatment which allows preserving the uterus. Also UAE effectively downsizes the uterine fibroids as well as their symptoms. According to literature overview, fibroids size decreases by 40-70% after UAE. In the course of one year, symptoms of fibroid disappear in 80-90% of women [9]. The main contraindications of UAE are pregnancy, infection of the genitourinary tract, malignant tumours and immunosuppression. Large myomas and submucosal location are not contraindications to not perform UAE. For the first time UAE embolization for treating fibroids was applied in 1991 and in 1995 it was described for the first time by a French gynaecologist J. Ravina [11]. Uterine artery embolization is performed by interventional radiologists in X-Ray operating rooms. Premedication with analgesics and nonsteroidal anti-inflammatory drugs (NSAIDs) are given prior the procedure. Usually, only local anaesthesia or mild sedation is applied. In the case of local anaesthesia, mostly the right common femoral artery is punctuated percutaneously. An introducer is inserted in the artery and through it along with a micro catheter, using an X-Ray, both uterine arteries are reached consecutively. The localisation of the catheter is approved by infusing radiocontrast medication. Usually, microspheres of 700 μm diameter or 500 μm particles are used for embolization, which are infused until the circulation slows down and the distal artery branches stop filling. It is necessary that embolization is performed on both sides. Later, the catheter and introducer are taken out and the artery puncture site is compressed and sealed. After the procedure, the patients must lay in bed up to 2 hours, to ease the post-embolization (PES) symptoms analgesics and anti-inflammatory medicine are prescribed. The following day, the physical activity of the patients is not limited and they undergo a treatment to decrease the symptoms of post-embolization syndrome. During the UAE, a therapeutic tissue infarction is created. This procedure does not require a long period of hospitalization, the recovery after UAE is fast. A retrospective cohort research revealed that uterine artery embolization has less difficult side effects then hysterectomy (the chance ratio 0.25), however, the level of contentment is similar. After uterine artery embolization, 86% of the women would recommend the procedure to a friend [12, 13]. Possible UAE side effects are: PES (pain in the lower part of the stomach, nausea, vomiting, fever and moderately increased inflammatory indicators), infection, a hysterectomy or a second UAE might be necessary after the first procedure. In one year after UAE, the need for hysterectomy and/or second UAE can be up to 10% while in five years in can grow up to 20-25%. Another side effect of UAE might be early insufficiency of the ovary function which develops to 1-2% of the patients. It was noticed that the side effects of UAE are more frequent if the fibroids are submucosal or they are bigger than 10 centimetres [7].
Fig.1 Patient with uterine fibroid visible on digital subtraction angiography (DSA) before uterine artery embolization and after. (IUD marked with arrow.)

Fig.2 The view of uterine fibroid on DSA after contrast media injection pictures showing the vascularization of fibroid from both uterine arteries.
Fig. 3 On picture there can see uterine fibroid sized approximately 8 cm on digital subtraction angiography (DSA) before uterine artery embolization and after it.

AIM

To evaluate the frequency of UAE applying for fibroids treatment and to assess results of this procedure.

METHODS

The research retrospectively analyses the medical history of women (n=180) treated in 3 hospitals of Latvia (Pauls Stradins Clinical University hospital, East Clinical University hospital and Liepajas Regional hospital) and 4 hospitals of Lithuania (Lithuanian University of Health Sciences hospital Kaunas Clinics, Klaipėda University hospital, Vilnius Republican hospital and Panevėžys hospital). Uterine artery embolization (UAE) was applied to these women when treating symptomatic uterine myomas from January of 2008 to December of 2016. The diagnosis of uterine fibroid (TLK 10 D25.0, D25.1, D25.2, D25.9) was confirmed by ultrasound or magnetic resonance, and gynaecologic exam. Exclusion criteria were: pregnancy, active inflammatory disease, pelvic malignancy. An original questionnaire was conducted aiming to evaluate if the women were content with the procedure and to evaluate the dynamics of the symptomatic uterine fibroids after the procedure. Our questionnaire comprised assessment of changes in fibroid-related symptoms (general condition, heavy menstruation, pain, anaemia), satisfaction with the procedure, and recommendation to a friend. Changes in myoma-related symptoms were classified as follows: heavy menstrual bleeding became lighter, menstrual period became less painful, haemoglobin levels have reached the normal levels in patients with previous anaemia, pain in lower abdomen has decreased. Patient satisfaction with the procedure and its outcomes were classified as follows: were satisfied with the procedure, would recommend this procedure to a friend, were unsatisfied with the procedure.

The data was transferred into an Excel 2010 spreadsheet and analysed using the Statistical Package for the Social Sciences software (SPSS) version 17.0 for Windows. For the quantitative variables (age, uterine volume, number of fibroids, size of fibroids), data was expressed as means, medians, standard deviations, minimum, and maximum and percent's. Differences were analysed using Student’s t-test and were considered statistically significant when P < 0.05 and between groups, when P < 0.01.
RESULTS

180 women who underwent uterine artery embolization while treating uterine myomas, took part in the research. There were 155 patients from Latvia (Pauls Stradins Clinical University hospital, East Clinical university hospital and Liepajas Regional hospital) and 25 patients from Lithuania (Lithuanian University of Health Sciences hospital Kaunas Clinics, Klaipeda University hospital, Vilnius Republican hospital and Panevezys hospital). UAE procedure was technically successful on all patients and had no early post-procedural complications. The average age of the women was 43.5 ± 4.6 (27 to 52 years). 91.67% of the patients chose UAE as their first procedure for uterine fibroid treatment. Only 6.1% of the patients (n=11) had the uterine fibroids removed surgically (myomectomy was performed) prior to uterine artery embolization, however, they experienced regrowth of the fibroids. The time period from myomectomy and UAE varies between 5 to 6 years mostly. For patients who underwent UAE twice (n=3, 1.67%), the time period between two procedures was 1 month, 1 year and 3 years, respectively. One patient (0.56%) received abrasion of myoma.

For the majority of the patients UAE was the first treatment. None of the patients were taking any analogues of the gonadotropin-releasing hormone (GnRH) prior to the procedure. Before the procedure, most of the women had menorrhagia and painful menstruation (n=120, 66.7%). Some of the patients (n=17, 9.5%) had a feeling of pressure in the stomach area and neurological symptoms, such as: symptomatic of buttock nerve clenching or newly emerged urination disorders. 36.7% (n=66) of the women were diagnosed with anaemia before UAE. The diameter of the fibroids varied from 1.7 centimetres to 32 centimetres size (similarly to 24 weeks of pregnancy). The average amount of fibroids was 1.74 ± 1.29 (1 to 6 fibroids). The most frequent types of fibroids were intramural (n=118, 65.6%), also subserosal (n=48, 26.7%) and submucosal (n=12, 6.7%), in some cases type of the fibroids was unknown (n=2, 1.1%). Not every patient was followed-up, only 44.4% of all patients: 55 patients from Latvia and 15 patients from Lithuania. During the first month after UAE, size of the fibroids decreased by 3.72 cm (p<0.05) on average. For Latvian followed-up patients, uterine fibroids reduced in size for 67.3% (n=37) of patients. For Lithuanian patients the success rate was 100% (n=15) of the followed-up patients. It takes up 72.2% of the followed-up patients in total.

In Latvia, 10 patients underwent surgical treatment after the procedure: 6 of them had hysterectomy performed, 3 of them received myomectomy and another one had repeated uterine artery embolization procedure. The patient who received repeated UAE, was 46 years old at the moment of the first procedure. Because of minimal decrease in size of myoma and new myomas appearance 4 years later, second UAE was performed. 6 patients, who underwent hysterectomy after UAE, had their operation performed approximately 1 to 2 years after UAE, because there was no reduction in fibroids size or fibroids were even increasing in size. To sum up, 14.3% (n=10) out of 70 patients underwent surgical procedure after the UAE.

The average duration of hospitalization was 1.85±1.56 days. The main duration of hospitalization was 3.68 days in Lithuania and 1.58 days in Latvia (P<0.001). All of the patients evaluated the procedure positively. None of the patients experienced early UAE complications. All patients experienced less painful and less heavy menstruation after the procedure, moreover, they did not experience such intense pressure in the stomach area anymore. Only 11 (6.1%) out of 180 women still had anaemia after UAE. Post procedural premature menopause occurred in 2.9% (n=5) of the patients.

Three patients became pregnant after the UAE. One patient who received UAE six months after this procedure there was also myomectomy performed. 5 years after the UAE procedure and myomectomy she delivered a healthy baby at the age of 32 years. Another 2 patients gave birth after 2-3 years after UAE procedure.
DISCUSSION

The main UAE indication is symptomatic uterine leiomyoma. The procedure is more suitable and safer for patients with prior pelvic surgery, including myomectomy and other interventions [10]. Key factors for performing UAE are: GnRH cannot be prescribed two months before UAE, the patient without a genital infection, the diagnosis of leiomyoma must be approved by a gynaecologist and an ultrasound and/or MRI. For leiomyomas diagnosing MRI sensitivity and its specificity is much better than ultrasound. Also, during imaging examination it is important to consider the type of the fibroid. That treatment tactic changes in 22% after applying MRI [17]. None of the patients from Latvia had MRI performed prior to UAE and only 2 patients from Lithuanian cohort which makes in general only 1.1%. This shows that it is still difficult for patients in Lithuania and Latvia to get an MRI despite its evident clinical benefit. Another group of women, for whom UAE might not be as effective, is infertile patients, who are wishing for pregnancy. UAE might increase miscarriages although there is not enough data to support this. There is not enough evidence based literature about how UAE and a combination of UAE and laparoscopic or laparotomy myomectomy treatment impacts fertility and the chances to get pregnant [16]. According to our research, 1 woman who was diagnosed with infertility, successfully conceived after UAE and gave birth to a healthy child, 2 more patients gave birth after the UAE procedure, but diagnosis of infertility was not confirmed, and that makes 4.3% of followed-up patients gave birth after the procedure. According to our findings it became evident that uterine artery embolization is not a common treatment for uterine fibroids, because as uterine fibroid is most common benign tumour, it should be treated only if symptomatic [21] but still during year 2008 and 2016 there were 180 uterine artery embolization performed in Latvia and Lithuania together. In our research most of women choose UAE as the first uterine fibroids treatment method and it accounted 91.67 % of patients and only 6.1% of the patients had surgical intervention prior to UAE (myomectomy was performed), however, they experienced regrowth.

Tab. 1 Basic characteristic table

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>Total (n=180)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, median (range)</td>
<td>43.5 (27-57)</td>
</tr>
<tr>
<td><strong>Presenting symptoms</strong></td>
<td></td>
</tr>
<tr>
<td>Heavy menstrual bleeding, n(%)</td>
<td>120 (67.2%)</td>
</tr>
<tr>
<td>Painful menstruations, n(%)</td>
<td>120 (67.2%)</td>
</tr>
<tr>
<td>Feeling of pressure in the stomach area and neurological symptoms</td>
<td>17 (9.5%)</td>
</tr>
<tr>
<td>Anemia, n(%)</td>
<td>66 (36.7%)</td>
</tr>
<tr>
<td><strong>Number of fibroids</strong></td>
<td></td>
</tr>
<tr>
<td>1, n(%)</td>
<td>88 (48.9%)</td>
</tr>
<tr>
<td>&gt;1, n(%)</td>
<td>92 (51.1%)</td>
</tr>
<tr>
<td><strong>Dominant fibroid location</strong></td>
<td></td>
</tr>
<tr>
<td>Intramural, n(%)</td>
<td>118 (65.6%)</td>
</tr>
<tr>
<td>Submucosal, n(%)</td>
<td>12 (6.7%)</td>
</tr>
<tr>
<td>Subserosal, n(%)</td>
<td>48 (26.7%)</td>
</tr>
<tr>
<td>Type of fibroid is unknown, n(%)</td>
<td>2 (1.1%)</td>
</tr>
<tr>
<td>Dominant fibroid maximum diameter (cm), median (range)</td>
<td>7.6 (1.7-32)</td>
</tr>
<tr>
<td><strong>Previous treatment</strong></td>
<td></td>
</tr>
<tr>
<td>Myomectomy, n(%)</td>
<td>11 (6.1%)</td>
</tr>
<tr>
<td>UAE, n(%)</td>
<td>3 (1.67%)</td>
</tr>
</tbody>
</table>
of the fibroids. According to the literature, treating uterine fibroids with UAE is effective: there is a decrease in heavy menstruation and pain, the size of the fibroids decreases. [14, 15] We found out that before the procedure, most of the women had menorrhagia and painful menstruation (n=120, 66.7%), but after the procedure all patients experienced less painful and less heavy menstruation, as well as uterine fibroids reduced in size after the procedure in 74% of followed-up patients. The literature data of long-term observation (5 years) shows that there is a significantly smaller chance of complications after UAE than after a hysterectomy [14, 15]. Talking about complications of UAE procedure, they are classified as post embolization syndrome, early post procedural complications and late UAE complications. Post embolization syndrome occurs in up to 52% of patients and constitutes a general malaise with mild pyrexia and flu-like symptoms, which is self-limiting and usually lasts for 7 to 10 days [16]. Early complications are rare and may be described as prolonged pain episodes or liquefaction of the fibroid, which may cause a cramping pain by cervical dilation and passage of the tissue, by infection from ascending bacteria and infrequently heavy bleeding [19]. Rate of the lack of long term patency is high (28%–32%) because of re-intervention – including re-embolization, myomectomy, or hysterectomy – at 5 years post procedure [16, 17, 18, 20] and during 3 years follow up by 15% of re-intervention rate: 10% hysterectomy, 3% myomectomy and 2% repeated UAE [21]. In our study re-interventional rate was pretty similar as mentioned in the last source: 14.3 % (n=10) in general from follow-up patients, 8.6% of them hysterectomies, 4.3% myomectomies and 1.4% repeated UAE. Late complication as early menopause after uterine artery embolization occurred in 2.9% (n=2) of followed-up patients. Induction of amenorrhea after UAE procedures is uncommon and most frequently seen among patients who are older than 45 years and/or perimenopausal [22].

CONCLUSIONS

UAE is a minimally invasive and a safe procedure with a rapid recovery time - women can return to daily activities without restrictions very soon after the procedure. Mostly women chose this procedure because of psychological aspects, wanting to preserve their uterus. Our study shows that this procedure is a good alternative to surgery – the uterine fibroids in most of the cases reduce in size after the uterine artery embolization, symptoms improve, nevertheless, the rate of post procedural re-intervention is rather high but complication rate is low. Also, for patients who have symptomatic uterine fibroids but want to have children after the treatment, this is the most suitable choice. Although the procedure is not that new anymore, further studies are still required about the selection of patients for uterine artery embolization and fertility after UAE. It is also important to note that it is necessary to pursue a pre and post procedural MRI in Lithuania and Latvia in order to obtain better results. This research is merely an overview of the current situation presenting the differences and similarities. The research shows that UAE is still not used as much as it should despite all the good outcomes which are known for a long time. The data obtained during the research is compared to other authors.
REFERENCES


