UTERINE POLYFIBROMATOSIS (UPF). MEDICAL AND SURGICAL TREATMENT FOR DIFFERENT ANATOMO-CLINICAL AND HISTOPATHOLOGICAL FORMS IN WOMEN UNDER 40 YEARS OF AGE

SUMMARY:
Uterine polyfibromatosis (UPF) is the most common benign tumoral pathology in women. Fortunately UPF malignant transformation is extremely rare, both in our cases (none of the cases studied showed malignant transformation), as well as in both romanian and foreign literature. Unfortunately, the numerous anatomical and histopathological forms of UPF lead to various clinical and biological events which in turn lead to the patients seeking medical attention: more or less abundant menometrorrhagias, with or without secondary anemia, ureteral, bladder and bowel compression phenomena, sterility, and infertility by triggering abortions or premature births.

Undoubtedly, both the medical and surgical therapeutic means have diversified in recent decades. Depending on conditions, indications and contraindications, we studied both the implications of medical hormonal therapy (progesterone derivatives, LRH analogs) and the traditional surgical treatment: conservative (anteroposterior sagittal myomectomy – Aburel technique, supraisthmic hysterectomy with uterine cavity reconstruction – Rebedea technique), and radical (total hysterectomy). More recently, in UPF, laparoscopic treatment, hysteroscopy and embolization are considered.

In our cases, we insisted mostly on the classic surgical treatment, both conservative and radical, the two conservative methods mentioned and analyzed in our study being put into practice by two Romanian academics, especially in women under 40, whose main desire was motherhood, and then retaining the menstrual function, a normal pelvic static and sexual function.

Keywords:
uterine polyfibromatosis, menometrorrhagia, ureterohydrenephrosis, anemia, progestatives, LRH analogs, hysterectomy, myomectomy, laparoscopy, hysteroscopy, embolization, sterility, infertility.

1. - Department of Obstetrics and Gynecology, University of Medicine and Pharmacy of Craiova
2. - Department of Anatomy, University of Medicine and Pharmacy of Craiova, Clinical Emergency County Hospital, Craiova
3. - Department of Pathology, University of Medicine and Pharmacy of Craiova, Clinical Emergency County Hospital Craiova

INTRODUCTION
Our research aimed to review and highlight the UPF incidence, the importance of two traditional conservative surgical treatment methods in women under 40 years with sterility/infertility developed and introduced by two Romanian surgeons, which we also applied the our clinic. These techniques can not be performed laparosopically or by surgical embolization, but ny classical surgery alone. In the vast majority of cases we found that UPF, besides its increased frequency in the woman’s genital pathology, is also a study and treatment objective for many other specialties except Obstetrics and Gynecology (General Surgery, Endocrinology, Nutrition and Diabetes, Interventional Imaging, Oncology, Pathology, Clinical Laboratory, Plastic and

Correspondence to: Prof. Mihai B. Brâila, MD, PhD, University of Medicine and Pharmacy of Craiova, Head of the Second Clinic of Obstetrics and Gynecology, Emergency County Hospital of Craiova, Tabaci Street 1, Craiova, Dolj County

In our research work the hardest problems were those related to the young age of patients, especially those under 40 years where various medical treatments, mostly hormonal, have failed, and in whom we attempted to avoid mutilating total hysterectomy, the most appropriate in such cases being the classic conservative surgical treatment (Iverson RE Jr, Chelmow D, Strohbehn K, et al, 1996; Brosens J, Campo R, Gordts S, et al., 2003). In these categories of patients it is essential to meet the conditions, indications and contraindications (a clean cervix, without lesions, both clinically and paraclinically, the absence of various endometrial hyperplasias, adenomyosis, more or less severe hematological diseases, benign or malignant ovarian tumors, endocervical or endometrial cancer) (Anastasiadis PG, Koutlaki NG, Skaphida PG, et. al, 2000; Bereceanu Sabina, Bădulescu Adriana, Goergescu MB, Bădulescu F, 2000; American College of Obstetricians and Ginecologists Committee on Gynecology practice: Obstet. Gynecol, 2004).

Even in some large forms of UPF in women with sterility/infertility under 40 years, without any associated pathology, we have avoided performing radical surgery (total hysterectomy), practicing one of two conservative methods mentioned above, either for maintaining the gestational function, or at least the menstrual function. Where the conditions were not met, and especially in the case of large, giant forms, we performed the classical radical techniques (total intracapcular hysterectomy and more frequently, extracapsular hysterectomy with or without adnexal conservation). In many clinics around the world, in UPF cases in women under 40 years medical treatment is attempted (LRH analogues/Zoladex, Enantone, Diphereline, soluble progesterone injections, Surgestone or Lutenny tablets) combined with laparoscopic treatment (myolysis) (Hurst BS, Matthews ML, Marshburn PB, 2005), hysteroscopy (endomyometrectomy) or embolization (Dargent D, 1991; Georgescu MB, Bereceanu Sabina, Georgescu P, 1995; Bânceanu G, Bânceanu Mariana, 1998; Dubuisson JB, Fauconnier A, Fourchotte V, 2001; (Cook JD, Walker CL, 2004). These treatments have a certain efficiency but besides being expensive and requiring proper equipment, they also require rigorous immediate and late follow-up and, in some ineffective cases, traditional surgery.

Another fact worth noting is that very few clinicians know and dare to perform the classical conservative procedures. The vast majority perform either the single or multiple myomectomy, or mutilating radical interventions, such as total hysterectomy.

In the case of UPF, an essentially benign pathology, any total hysterectomy, especially in young patients without other associated genital pathology therapy, may be considered “abusive”.

MATERIAL AND METHODS

We studied women hospitalized and operated in the Second Clinic of Obstetrics and Gynecology of the County Emergency Hospital of Craiova for a period of 11 years (2000-2010).

During the aforementioned period 3859 women with gynecological pathology were admitted of which 959 (24.8%) were operated for different anatomical and clinical forms of UPF.

According to protocols, observation sheets, and histopathology records of all operated cases, the parameters we studied were as follows: age, place of residence, profession, personal obstetrical and gynecological pathological history, reasons for hospitalization, clinical and paraclinical diagnosis, surgical indication and preparation for surgery, anesthesia, types of surgery, postoperative evolution, incidents – accidents, complications, macro- and microscopic histopathological study.

In this study we focused mainly on the type of surgery generally performed on the study groups analyzed, especially conservative surgery on patients under 40 years of age.

The data concerning the other parameters that were analyzed were published in a previous paper.

The following are the two romanian conservative techniques we used in the treatment of UPF.

Antero-posterior sagittal myomectomy, the Eugen Aburel procedure. The principle of the technique is primarily linked to the protection of the tubal ostia from the uterine horns. For this reason an incision on the anterior uterine wall is performed; removal of myometrial fibromatous nodules; myometrial control by palpation after removal of fibromatous nodules; further excision of exuberant myometrium and removal of small fibromatous nodules from the myometrial wall; incision of the posterior wall of the uterus with consequent removal of fibromatous nodules within the myometrial wall if present; suture of the myometrium; reconstruction after minimal transverse excision of the uterine fundus without involving the uterine horns, suture of the uterine fundus. This procedure enables the conservation of all genital functions in particular the reproductive and gestative
one. This procedure preserves the utero-adnexal connections and tubal ostia, excising from the anterior to the posterior aspect all fibromyomas as well as the diffusely hypertrophied adjacent myometrium. The surgical phases are shown in Figure 1 (Aburel E, et al., 1971).

Supraisthmic hysterectomy with uterine cavity reconstruction (SHUCR) – the Traian Rebedea procedure. Supraisthmic hysterectomy and uterine cavity reconstruction was performed and described for the first time by prof. Traian Rebedea in 1977. Subsequently, the process was communicated at various conferences and symposia, published in some monographs and textbooks, approached as topic for PhD theses. The original technique is well known to his disciples from the University Emergency Hospital in Bucharest (Rebedea T, 1981/1982).

This is a conservative surgical procedure indicated in women under 40 who have diffuse uterine fibromatosis and polyfibromatosis, without associated adenomyosis or other cervical, uterine and adnexal lesions who, after informed consent, wish to maintain their menstrual function and pelvic statics. Ever since the beginning of surgery, female genital pathology inspired many and various surgical procedures. The Congress of Surgery in Paris in 1924 supported the mutilating excision surgery. Later the switch was made to conservative surgery, which is most suitable for the female genital tract. In the last decades, at least in our country, there is an increasing incidence of mutilating radical surgery in women under 40 years, sometimes without fully justified indication. The “fear of failure by plasty” in the treatment of polyfibromatosis in a young woman who wants to retain the menstrual function and a normal psycho-sexual life is currently difficult to understand in the context of current diagnostic, intensive care and surgical treatment performances. In the absence of concomitant cervical, uterine and adnexal lesions with risk of malignant transformation, the early surgically induced climax (post-total hysterectomy with or without bilateral adnexectomy) is difficult to bear by a patient under 40 years of age.

According to Malinas (1991), when there are injuries associated with potential neoplastic degeneration “mutilation” should not be “partial”, just as it should not be radical, exaggerated, for a so-called trivial polyfibromatosis, asymptomatic or withs minor hemorrhage without other concomitant lesions of the cervix, endometrium or ovary. Attention should be payed to total “abusive” hysterectomies in uterine polyfibromatosis and diffuse fibromatosis without associated adenomyosis.

Meanwhile, the results from the histopathological examination are ready. In case the morphology is that of a benign lesion, the procedure is terminated (mandatory drainage of the pouch of Douglas for 48 hours using a polyethylene tube externalized through the celiotomy breach), followed by the closure of the wall in anatomic planes, and sterile dressing of the wound.

In case the histopathological examination reveals suspicious lesions with potential for malignant degeneration (adenomatous hyperplasia with or without atypia, borderline lesions), we proceed to total hysterectomy and bilateral adnexectomy.

Antibiotic treatment is mandatory both during and after surgery, as well as thromboembolic disease prophylaxis using low molecular weight heparin.

Functional long-time prognosis is good by conserving menstrual and sexual function as well as pelvic statics. Biological balance is maintained within normal limits, the psychological state of the patient is very good, regular menses occurring with an average flow of 2 to 3 days, in amount of around 20 to 30 ml, without associated dysmenorrhea.
Surgeries were performed according to protocols, after preliminary investigations and anesthetic consultation. Extemporaneous histopathological examination (endometrium, myometrium, ovaries) was performed during all surgeries in order to exclude possible precursor lesions for cancer degeneration.

The postoperative course was not encumbered by major complications (bleeding, intestinal occlusion, peritonitis, uterine stump necrosis and/or parenchymal metritis), patients being supported by treatment with antibiotics (multiple antibiotics) and anticoagulants for about 7 days. Intraperoniteal drainage was mandatory and generally maintained for a minimum of 48 hours.

Long-term functional prognosis (preserving menstrual function, pelvic statics, psycho-sexual function, biological balance, social and family integration) are good and very good, the control revealing a quasinormal genital region with no other obvious pathological changes at clinical and ultrasound examination.

RESULTS

The therapeutic strategy focused on:

- Complete urine examination
- In certain situations, where appropriate, interdisciplinary examinations were required: cardiology, internal medicine, diabetes and nutrition diseases, nephrology, urology, interventional radiology.
- Type of anesthesia:
  - general anesthesia with orotracheal intubation (OTI) or rachianesthesia.
  - general anesthesia with OTI in 728 cases (75.9%),
  - rachianesthesia in 231 cazuri (24.1%).
- Type of surgical procedure
  - Mutilating radical surgery
    - Extracapsular total hysterectomy (Wiart) with bilateral adnexectomy.
    - Intracapsular total hysterectomy (Aldrige – Richardson) with bilateral adnexectomy.
    - Intradnexal total hysterectomy (with adnexal preservation).
Usually classic instead of laparoscopic surgery was performed.

- Classic conservative and rarely laparoscopy surgery
  - Single or multiple myomectomy
  - Myomectomy using the Aburel procedure, especially in women under 40 years of age who wanted to bear a child
  - Supraisthmic hysterectomy with uterine cavity reconstruction (the Rebedea procedure), especially in women who wanted to maintain the menstrual, sexual and urinary function as well as the pelvic statics, often associated with partial ovarian resection and posterior colpoperinorrhaphy and myorrhaphy of the levator ani muscles. This type of procedure was performed even in the case of single or multiple large fibromas, with a clean cervix as the only condition for this procedure as well as in the case of the Aburel myomectomy.
- Interventional imagistics by definitive or temporary embolization of the uterine fibroma was not the object of the present study.

Histopathological aspects from the resected samples are shown in Figures 3-8.

**DISCUSSION**

In this context we must discuss the practical value of the two conservative techniques in women under 40 years, regarding function conservation in the young female, keeping the uterus without any serious injuries or potential risk for subsequent malignancy, the role of target tissue like the endometrium and myometrium in the biology of the young female body taking into account the feedback loops involved in functionality of the female genital system.
An older saying, “mulier toto in utero”, can be reevaluated, the uterus being directly involved via various substances synthesized by it and discharged in the blood stream, in the whole female biology.

Currently genetic, cellular, enzymatic, and vascular factors (deficiencies in enzymes that degrade local estradiol), increased aromatase activity (conversion of androgens into estrogens), the intervention of cell growth factors and/or cofactors at different levels (IGF1, IGF2; EGF, interleukins 1 and 2 which facilitate luteinization and increased levels of testosterone in the stromal compartment, inhibiting the production of progesterone), vector modulator proteins (SHBG), various enzymes (thymidine-kinase, 17-beta-steroid dehydrogenase, cathepsins B and D), the genetically induced synthesis of estrogen and progesterone receptors, the intervention of vascular factors (endothelins, prostaglandins, cytokines and other cybernins), are under investigation. The presence of all these substances influences through reverse circuits the functionality of the female genital system and brain monoaminergic, opioidergic/endorphin system, with direct influence over areas of the hypothalamus and suprahyothalamic neurovegetative cybernetic-informational circuits (limbic system, reticular formation, midbrain, epiphysis, cerebral cortex).

Mutilation of young women by using total hysterectomy when there is no cancer or other lesions with a major risk for malignant transformation is not justified in view of some biological implications (trophic, metabolic, sexual, menstrual, psychological, etc.), the uterus, through its presence in the body, with a multiple role as both gestational target organ, “consumer” of steroid hormones, as well as feedback coordination sublevel for central organs (central knot) through the cytokines and cybernins synthetized and discharged into the systemic circulation.

This is why we have brought into discussion the importance of conservative surgery on the uterus in women under 40 years. It makes no sense to remove a polyfibromatous uterus without adenomyosis out of fear...
that the patient might develop a genital cancer in the next 5 to 10 years. Under certain conditions, indications and contraindications, these procedures are beneficial for the patients operated.

We were able to hysteroscopically and histerografically control some of the cases operated many years ago. Good clinical results were confirmed by laboratory exploration, arguing once again for the undeniable practical value of these two techniques.

CONCLUSIONS

Our present retrospective study focused on anatomical and clinical forms of uterine fibroids operated in the Second Clinic of Obstetrics and Gynecology of Emergency County Hospital of Craiova during 11 years (2000-2010).

During this period 3859 women with gynecologic pathology were operated, including 959 cases with uterine fibroids (24.8%).

The highest incidence of operated uterine fibroids was between 41-50 years (62.4%), followed by the age group between 51-60 years (181 cases, 18.8%) and the 31-40 years age group (165 cases, 16.9%). The total number of patients in these three groups is 941 cases (98.1%). In extreme ages, the incidence of uterine fibroids was extremely low (between 20 to 30 years – 1.2% and 0.7% over 60 years of age). Under the age of 20 and over the age of 70 we found no case. Our data show that over 90% of uterine fibroids were encountered mostly in women aged over 30 years, with no cases under the age of 20 or in the late postmenopause.

The surgical indication was established after team consensus (chief clinical physician, attending physician, ICU specialist) with the approval and signature of the patient. Surgical therapeutic approach, conservative versus radical, was established according to the pathological context, the technological possibilities, and the patient’s desire for maternity or maintenance of the menstrual and psycho-sexual functions.

Out of 959 cases operated, 728 cases of fibromyoma (75.9%) underwent general anesthesia with the OTI, the remaining 231 cases (24.1%) being operated under spinal anesthesia.

Classical radical surgery (total hysterectomy + bilateral adnexectomy) was performed in 706 cases (73.6%). A total of 617 cases (81.7%) were extracapsular total or simple hysterectomies (Wiart procedure), and 89 cases (18.3%) were intracapsular total hysterectomies (Aldrige-Richardson procedure). Our study shows that simple or extracapsular total hysterectomy is 7 times more common than intracapsular total hysterectomy. This technique is 15 to 20 minutes faster and is preferred by most practitioners in the clinic. In chronic situations such as uterine fibroids and not obstetric and gynecological emergencies, intracapsular hysterectomy might be performed, even though it is a more laborious technique. This type of intervention provides a certain confidence for the surgeon regarding the ureters and bladder, ensuring more anatomical genital statics for the hysterectomised female by maintaining the capsule, compared to patients whose capsule and uterine supporting ligaments were cut, which means genital-pelvic, urinary and psycho-sexual comfort for the patient with great social importance.

Classical conservative surgery is unfortunately poorly represented in our study group (115 cases from a total of 959 fibroids operated). Only 1/10 of all women with uterine fibromyoma underwent conventional conservative surgery (single or multiple myomectomy – 45 cases, 4.6%; sagittal anterior-posterior myometrectomy using he Aburel procedure – 39 cases, 4.1%; Supraisthmic hysterectomy with uterine cavity reconstruction (the Rebedea-Mihai Georgescu Brăila procedure) – 31 cases, 3.2%). This low incidence of classical conservative uterine surgery, compared with the high incidence of radical mutilating surgery in uterine fibroids was in fact the main objective of my PhD thesis. Patients with large, almost giant uterine fibromyomas, after the age of 40, with severe cervical dysplastic lesions, associated ovarian tumors, endometrial hyperplasia, are characterized by ignorance, lack of regular gynecological control, poor addressability to the specialist, no concrete forms of psycho-sexual and genital education especially of young women by family planning doctors, deliberately giving up contraception and the annual Babeş-Papanicolau cervical cytology.

Very few surgeons or gynecologists have the knowledge and experience in conservative surgical treatment of uterine fibromyoma (mostly they perform myomectomy, do not know the myometrectomy types and especially the Aburel technique, the only one that preserves the reproductive function, or the supraisthmic hysterectomy with uterine cavity reconstruction). Gynecologists’ and surgeons’ current practice is limited to mutilating radical interventions such as total hysterectomy, either intra- or extracapsular, most of them performing simple total hysterectomy.

Laparoscopy can be performed for a total hysterectomy or myomectomy. However, it can not solve the myometrectomy or the supraisthmic with uterine cavity reconstruction.
Hormonal treatments administered in a series of cases of uterine operated fibromyomas, no matter how sophisticated (progesterone, particularly LRH analogs), are expensive and do not solve the problem of the circumscribed tumor while having unwanted side effects by triggering a “chemical menopause” at a young age.

Uterine fibroids, benign tumors with an extremely low rate of malignancy (0.001%), can be resolved in time using conservative methods, and not radical mutilation especially when it comes to young women who desire maternity or at least the maintenance of menstrual and normal sexual functions. This is the biological and clinical reality worldwide and efforts that are made aim for individual, family and social benefits, with maximum efficiency at the lowest possible price.

References:
1. ABUREL E. (și colab.). Obstetrica și Ginecologi, Editura didactică și pedagogica, București, 1971
12. HURST BS, MATTHEWS ML, MARSHBURN PB: Laparoscopic myomectomy for symptomatic uterine myomas. Fertil Steril 83:1, 2005