

Doctor of Philosophy (PhD) thesis

Minimally invasive techniques in certain gynaecological diseases

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Introduction, objectives

More than 120 years ago, the indication of the first hysteroscopic examination was bleeding disorder. After its initial ontological application, hysteroscopy was more often introduced in the investigation of the causes of sterility and those of the disturbances of the development of the uterus. Later on attention was once again focused on the diagnosis of uterine bleedings. The appropriate distending techniques (the application of dextran, “continuous flow”, and that of liquids of low viscosity) made examinations possible in cases in which they could not have been carried out in the presence of carbon-dioxid because of bleeding.

Owing to the development of hysteroscopic techniques, its fields of application have been widely expanded. In Hungary hysteroscopy was introduced in 1984 as a routine. Today the outlines of the two main fields of indication in operative hysteroscopy have become clear: the treatment of bleeding disorders that cannot be controlled by conservative methods (the removal of endometrial polyp, submucous myoma, etc.), and the solution of morphological lesions (adhaesio, septum) causing sterility. One of the most successful fields of application in operative hysteroscopy is the removal of submucous myomas causing bleeding disorders, sterility or habitual abortions. In 82-95% of cases it offers a final solution.

Collaterally, the absolute and relative contraindications of hysteroscopic treatment were drawn up in the cases of diagnosed tumors of the cervix, the acute inflammation of the cervix, the uterus or that of the adnexa, suspected pregnancy, or ample bleeding. In case of subacute or chronic inflammation of the internal genitalia, there is relative contraindication. Taking all these into consideration we can improve the efficiency of treatment, and reduce the number of complications.

Although hysteroscopy is a minimally invasive operative technique, it is not without dangers. We can reduce the number of complications by the appropriate choice of indication and by adequate experience. There are three main types of complications: one during the operation

(perforation, injury of the cervix, transurethral resection-syndrome, anafilactic shock, bleeding), one after the operation (infection, afterbleeding, haematometra), and later complications may also occur (adhaesio, the dispersion of endometrium cells in the abdominal cavity).

Endoscopic surgery can only achieve its goal if it is carried out by well trained experts in a well equipped operation theatre. Today it is a priority that those in charge of financing health care should value the demands of investment into endoscopic surgery and its medical and economic advantages realistically.

Diagnostic hysteroscopy is the most reliable technique for the diagnosis of the internal surface of the uteral and cervical channel, but its application is limited by the cost of equipments and the invasive, although minimally invasive, nature of intervention. By the application of operative methods several lesions can be solved. It is a recent effort to make endoscopic technique accessible for ambulant patients, too, by reducing the cross-section of the instrument and by abandoning anaesthesia.

I did not intend to deal with all the minimally invasive techniques in my thesis, since owing to the use of laparoscopy the diagnoses of several diseases (e.g. extrauterine pregnancy, endometriosis, cysts, the solution of adhesions) are well resolved parts and parcels of our everyday practice. I wanted to focus my attention on less developed techniques.

Objectives:

I tried to seek answers for the following questions in my thesis:

1.: What possibilities does hysteroscopy offer in the diagnosis and therapy of repeated abortions?

- 2.: What are the results of organ preserving endoscopic surgery of submucosus myomas in the long term treatment of patients?
- 3.: What possibilities does laparoscopy offer in the diagnosis and treatment of chronic pain in the lesser pelvis, with special respect to the cutting of sacrouterin bands?
- 4.: To what extent does the diagnosis set up by the subjective evaluation of the endometrium image comply with the results of histological examination?
- 5.: How efficient ultrasound examination is in the diagnosis of intrauterinal focal lesions in comparison with the results of hysteroscopic and histological processing?
- 6.: To what extent does the information about the uterinal cavity gained during hysterosalpingography comply with the clinical images with respect to hysteroscopy carried out later?

Patient, method

1.: Hysteroscopy

We carried out diagnostic and operative hysteroscopy in intravenous narcosis, or sometimes but rarely in paracervical Lidocain blockade, and we timed the operations for the early proliferation period, often after one or two days after menstruation. It is easier to carry out the operation in this period because of better visual conditions. A few days after the operation the regenerating faculty of the endometrium is better owing to the heightened level of oestrogen. We carried out diagnostic hysteroscopy with a 4 mm cross-section, 6 mm outer cross-section hysteroscope equipped with a 30 degree Hopkins II optic (Storz), with a physiological distending medium of 0,9% NaCl solution or carbon-dioxid (single flow). For the insufflation of carbon-dioxid we used a Metromat 2021 (Wolf) insufflator with a maximum intrauterine pressure of 120 mmHg and a maximum flow of 50 ml/min. During diagnostic hysteroscopy

we processed the NaCl solution like infusion with gravitation into the uterinal cavity, from a height of 2 mm “continuous flow” through double capsule, or with 80-100 Mrmm overpressure. During operative hysteroscopy, we used a 27 FrCh cross-section Hamou-type resectoscope (Storz) equipped with a 4 mm and 30 degree optic, and a 0 degree electrode for septotomy, and a 90 degree electrode for myoma resection, for aimed biopsy in 1,5% glicin medium. Then we insured continuous flow with a Hamou Endomat (Storz) roller pump, with a maximum intrauterinal pressure of 100-110 Mrmm. For cutting the septum we used a monopolar cutting electricity of 60-80 Ws, without coagulation. For myoma resection and biopsy we used 100-120W cutting and 50W monopolar coagulating electricity. We projected the image onto an endovideo monitor using a 250W cold light source. The material we obtained during the operation we invariably sent for histological analysis. We recorded the diagnoses on data sheets and U-matic video.

2.: Laparoscopy

We carry out laparoscopic operations in general anesthesia and intubational narcosis. The patient is given some mild laxative or enema a day before the operation for cleaning the gastric-intestinal tract. After washing herself in the evening, her operational area must be epilated if necessary. On the day of the operation she does not eat anything per os and empties her bladder. She reclines in lithotomic, Trendelenburg position on the operating-table. After taking a section of the skin on the lower pole of the umbilical ring, we place a Veress-needle into the abdominal cavity, then we take a security check. The purpose of the check is to make sure that we are really in the abdominal cavity and not in the lumen of the bowel adhered to the abdominal wall. After the previous insufflation of CO₂ we run a 11mm trocar into the abdominal cavity, then introduce a 10 mm 0 degree optic for the examination of the lesser pelvis. We introduce the instruments implemental in the section of the sacrouterin bands from

5 mm, suprapubically. For denervation we use two methods. During the first of these two, we cut the coagulated and thus desiccated bands with scissors at their roots in the uterus, in the second case, we are doing this with the help of a monopolar hook electrode in one step, using 100W cutting electricity. It is a great relief, if during the operation, in order to tighten the bands, we bring it into strong anteflexion with the help of a manipulator introduced into the uterus. For the disconnection of intersecting nerve-fibres on the peritoneum between the sacrouterin bands that have been cut, we make a 1-2 mm deep transversal section with monopolar electrocauter.

3.: U-sound examination

Vaginal U-sound examination was carried out with an ATL-3000 HDI instrument (5-9 MHz vaginal transducer, Bothell, Washington, USA). During the examination the patient lay in dorsal position with empty bladder, in the case of regular cycles of menstruation in the first half of the cycle. In real-time grey-scale projection the double layer thickness of the endometrium was recorded on sagittal level. Then the U-sound morphology of the endometrium was drawn up, panning the endometrium in anterior-posterior and horizontal levels between the entrance of the fallopian tubes, with special attention paid to polypoid spherical structures or those reminiscent of myoma, intrauterine liquid accumulation, uneven echogenicity, hyperechogenicity, cystic rarefaction, premenopausal condition, or, in the case of premenopausal condition or cyclic hormone substitution treatment to the painting convenient to the cycle. In menopause the endometrium we found negative was the one with a normal and well delineated subendometrial hypoechogenicity. In coloured Doppler operation after recording the grey-scale U-sound status, we examined the veining of the endometrium by way of delineating the endometrial and subendometrial venous system (aa. spirales) on the above mentioned levels. We raised the possibility of endometrium polypus, insofar as we illustrated

a singular vein seeming to be an artery judging from its Doppler-spectrum, originating in the venous system of the endometrium, and perhaps ramifying in the projection of the endometrium. In the case of submucosus myoma the vein originating from the endometrium, ramified into branches at the borderline of the myometrium and the endometrium, right after its point of origin, embracing the intrauterine structure supposed to exist by grey-scale representation. We reported all other uterinal and ovarian lesions.

4.: Hysterosalpingography (HSG)

We carried out hysterosalpingography five days after menstruation, having excluded colpitis, cervicitis and the inflammation of the lesser pelvis by gynaecological and laboratorial examinations in the possession of negative oncocytological results not older than a year. After vaginal inspection and desinfection we fixed the Schultze instrument in the cervix, and poured 5-10 ml soluble, ionic contrast material (Isteropac) into the uterinal cavity manually, without pressure control. The anterior-posterior picture we had taken of the lesser pelvis, was evaluated by a radiologist. Analysing the four details (shape, contour, insufficiencies of saturation, cervicography) of the hystero-graphic diagnosis one by one, we used the following notions for the security of scores in HSG:

- sensitivity (S) [$\text{real positive}/(\text{real positive}+\text{pseudonegative})$],
- specificity (SP) [$\text{real negative}/(\text{real negative}+\text{pseudopositive})$],
- negative predictive value (NPV) [$\text{real negative}/(\text{real negative}+\text{pseudonegative})$]
- positive predictive value (PPV) [$\text{real positive}/(\text{real positive}+\text{pseudopositive})$]

We carried out the histological examination with hematoxilin-eozin painting, and with the help a microscope of 40-400 enlargement. We arranged and processed the data with a

Microsoft Access 97 database program. For tracing the patients we used the database of the clinic and questionnaires sent to them by post.

In convenience with the questions asked in the objectives we examined the following groups of patients:

ad 1.: In our retrospective study we surveyed the condition of 66 patients who had had septotomy at our institute between January 1993 and December 1999. In the obstetrical case history of our patients there were repeated spontaneous abortions or primary sterility. In order to keep trace of them we used the computerized database of our clinic, and sent letters to those 26 patients of whom we could not obtain data. 14 did not give an answer, so we excluded them from further survey.

ad 2.: At our clinic we had 2197 cases of diagnostic hysteroscopy between October 1989 and December 31 1999. In 192 of these cases we found myoma. The position and the size of the myoma made transcervical resection of myoma (TCRM) possible in the case of 61 patients. We applied TCRM 66 times on the whole. Repeated operation was necessary because of technical reasons twice and because of the appearance of renewed myoma in the case of three patients. The ages of 61 patients were between 21 and 76. 75% of patients undergoing TCRM were women between the ages of 30 and 50. This lesion was far less frequent under the age of 30, and after menopause. In patients undergoing TCRM the position of the myoma was, by the scale of European Society of Hysteroscopy, ESH "0" in 25 cases, ESH "I" in 27 cases, and ESH "II" in 6 cases. The myoma originated three times from the cervix, and other times from the uterus. In the case of the ESH "II", since more than 50% of it is intramural, the probability of perforation or other operational complications is much higher, so in these cases we chose other operational solutions (e.g. myoma enucleation with laparoscopy or laparotomy). TCRM was always preceded by diagnostic hysteroscopy.

ad 3.: At our institute we have been carrying out sacrouterin band sections by laparoscopy under the above mentioned suggestions for ten years now. In our survey we processed the data pertaining to 20 of our patients who had undergone laparoscopic uterine nerve ablation (LUNA) between December 1994 and March 2000. The ages of the patients were between 23 and 55 (36 years in average, + 19 years, -13 years). 70 % of the patients are between 21 and 40, so our most frequent patients were women in the age of reproduction. The patients visited their doctors because of unceasing abdominal pain. The several months long medical or other treatment of all the patients was unsuccessful. Before operation we applied psychological analysis and therapy as well. Discovering the disturbances of sexuality was an important part of the exploration. Having excluded these, we decided for the operation. We called our patients back 6 weeks after the operation. Those who failed to turn up were sent letters. From the 20 patients who had gone through the operation we reached 16 for further survey.

ad 4.: We evaluated the results of those 835 hysteroscopic examinations carried out by the endoscopic team of our clinic, that included biopsy and histological examination. The examinations were carried out by 3 experts between October 1989 and December 31 2002. The average age of patients were 45 years. The indications of the examinations were bleeding disorders and sterility. In the case of patients without symptoms, if hysterosalpingography, physical or U-sound examinations provided the indication, it was disorder in the uterus. "Bleeding disorders" are cases when bleeding disorder returned within a year after negative preliminary histological results, or cases in which conservative therapy was of no avail.

ad 5.: During visual control or in the course of "directed curettage" or that of operative hysteroscopy we processed the preoperative documentation, the histological results and the epidemiological data (age, gynaecological case history, medical treatment, present complaints, with special respect to incidental bleeding disorders) of our patients in 124 cases of removed and histologically justified, prescribed growth in the uterus, endometrium polypus

and submucosus myoma. By the preoperative U-sound analysis of 124 patients we made only traditional transvaginal grey-scale rendering (TVS group), while in 45 cases we made colour Doppler examination (TVCD group). The average age of the 124 patients that took part in the examination was 51,6 years (21-79), 103 of them were over 40 (83%). We would like to emphasize that in 62 cases bleeding disorder was one of the complaints indicating U-sound examination. The other half of our patients had no complaints, or had eu- or amenorrhoea. 12 of the fertile age patients under 40 with eumenorrhoea (18 cases) had to be examined because of infertility. 12 of the patients above 40 with no complaints (44 cases) went through adjuvant tamoxifen therapy because of carcinoma in the breast. The sensitivity of our methods were defined by comparing the results of histological analysis with those of the grey-scale U-sound and the colour Doppler U-sound examinations and the opinions about hysteroscopic judgement. We analysed the differences in the sensitivity of these procedures by applying the χ^2 test. We applied the two-patterned t-test in comparing the average age of the groups under examination and the thickness of the endometrium.

ad 6.: We surveyed the documentation of hysteroscopic examinations carried out between December 1 1989 and December 31 1998. We analysed the results of patients who had undergone HSG at our institute within a year, according to their examination sheets. We chose 104 examinations for analysis, comparing the radiological and endoscopic findings, taking four aspects into consideration:

- the shape of the uterus
- unevenness of contours
- insufficiency of filling
- lesions in the cervix uteri

The indication of examinations was sterility or infertility, the average age of the patients was 28,9 years (20-42).

Results

ad 1.: As we could not gather data about 14 patients, we chose 52 of 66 for final evaluation. There were 36 successful pregnancies after septotomy. 3 patients did not want to be pregnant, and one of the patients had to be operated on with cervix carcinoma several years after hysteroscopy. After unsuccessful attempts we enrolled 12 patients for the in vitro fertilisation-embryo transfer (IVF-ET) program (23,8%) at our institute. Judging from anamnestic data, there were 29 successful pregnancies after repeated spontaneous abortions (38 patients), while in the case of primary sterility (14 patients) we achieved 7 successful pregnancies. There was spontaneous delivery in 28 cases (77,78%), and abdominal delivery in 8 cases (22,22%). Septotomy carried out previously did not feature among the indications of Caesarean section, the operation had to be carried out because of fetal reasons. 12 patients participated in the IVF program after septotomy. Success was achieved in the case of one patient, where pregnancy resulted in spontaneous delivery. There was no pregnancy in the case of 11 patients.

ad 2.: Out of the 61 patients who had been operated on, we could only trace 51 with the help of the database in our institute and the questionnaires sent to them by post. 30 patients out of the 51 had no complaints, we found 14 cases of renewed myoma, and there were other gynaecological complaints in 7 cases. Out of the 30 patients with no complaints two women are pregnant now, one patient has already delivered, and there was missed abortion and artificial abortion in 3-3 cases. 1-1 patient is under treatment for secondary sterility and amenorrhoea.

In 8 out of 14 cases there was no repeated intervention in the case of reoccurring centres, there was hysterectomy in 3 cases, twice within a year, for the third time after 2 years. We repeated TCRM in the case of 3 patients.

ad 3.: Laparoscopic sacrouterin band sections were carried out 20 times. 12 patients indicated their complaints to be 10 on the visual-analogue scale before operation, 2 patients indicated them to be 8, and another 2 patients to be 5. We could survey the results of the operations in 16 patients, again by applying the visual-analogue scale. We found full recovery in 9, partial recovery in 2, unchanged condition in 5 cases.

ad 4.: In the possession of histological results, we evaluated the particular lesions separately, and arrived at the following data:

polyp: sensitivity, specificity, negative predictive value, positive predictive value

myoma: sensitivity, specificity, negative predictive value, positive predictive value

hyperplasia: sensitivity, specificity, negative predictive value, positive predictive value

endometrial carcinoma: sensitivity, specificity, negative predictive value, positive predictive value

atrophy: sensitivity: 0,95, specificity 0, 96, negative predictive value: 0,99, positive predictive value: 0, 28.

ad 5.: During the histological processing of intrauterine growths we found polypus endometrii 114 times, leiomyoma 10 times, endometrium carcinoma in 3 cases of polypus, and endometrium hyperplasia in 15 cases.

In the TVS group 59 out of 79 patients were diagnosed with focal intrauterine lesion during U-sound examination, in 48 cases we could trace its histological origin, too. In 14 cases we reported the pathological thickness of the endometrium, in 6 cases the findings were erroneously negative.

In the TVCD group we discovered the growth in 42 out of 45 patients, in 41 cases its histological origin was properly described. An endometrium polypus was erroneously taken for a myoma, and 3 times only thick endometrium was reported.

Out of the 124 growths found during hysteroscopy in 120 cases the presumed diagnosis on the basis of the macroscopic image complied with justified diagnosis of histological processing. In 4 cases, in which the abnormality had been presumed to be a polypus, proved to be a myoma in its histological diagnosis. It was 0,74, 0,93 and 1,00 with respect to traditional vaginal grey-scale U-sound examinations, a the colour Doppler U-sound examination, the sensitivity of hysteroscopy and the discovery of intrauterine growths, while the proportion of scores, taking the origin of the abnormality into consideration, was 0,61, 0,91 and 0,97. There is a statistically significant difference between the sensitivity of traditional grey-scale U-sound examinations and colour Doppler examinations with respect to the discovery of intrauterine growths ($p<0,01$) and the judgement of histological origins ($p<0,01$).

ad 6.:

- the shape of the uterus

In the case of the 104 patients who underwent examination, normal anatomic conditions were justified (real negative) comparing the findings during HSG and later hysteroscopy. In 37 cases the morphological difference was easy to be discovered even with HSG (real positive), it was pseudonegative in 10 and pseudopositive in 17 cases.

- contour

In 80 out of 104 patients we achieved real negative results by HSG, real positive in 7 cases, and pseudopositive results in 17 cases. There were no pseudonegative findings.

- filling

In 63 cases we achieved real negative results with HSG, in 13 cases real positive results, in 5 cases pseudonegative results, and in 23 cases pseudopositive results.

- cervix

We gained 86 real negative, 17 pseudopositive results, and there was 1 pseudonegative finding. During cervicography we obtained no real positive results.

Statements:

ad 1.: Septum uteri taking shape as a result of unification disorders in the Müller tubes is a frequent reason of infertility and repeated spontaneous abortions. For the solution of developmental disorders, as opposed to traditional abdominal metroplastic, the best solution today is hysteroscopic transcervical septotomy. In our operational experience we found transcervical septotomy safe, simple and efficient, a procedure by which we can save costs for both the patient and the institution, and it greatly reduces the proportion of abdominal deliveries.

ad 2.: Our results comply with literary data. 59% of our patients have no complaints, 14% had other complaints not pertaining to the myoma, renewal is 27%. TCRM is an efficient and safe method for the minimal invasive treatment of submucosus myomas.

ad 3.: Relying on our results we can claim that LUNA provides us with promising alternatives for the reduction of complaints of patients suffering from pains in the lesser pelvis. Intervention seems to an effective solution in the case of patients with chronic pelvic pain (CPP) not reacting to medical and other conservative treatments. Their pain limits their sphere of activity in several fields of life. Owing to the development of the methods and instruments of microsurgery and laparoscopy we can cut sacrouterin bands with good therapeutical efficiency, relatively safely, with few postoperative complications, and short terms of treatment.

ad 4.: Hysteroscopy does not replace histological examination, it has a different objective. Its aims at the finding of lesions, their possibly isolated removal for histological examination.

ad 5.: In our material, the sensitivity of the vaginal colour Doppler U-sound examination carried out according to aspects mentioned above, significantly surpassed the sensitivity of the traditional grey-scale U-sound examinations in case of focal lesions in the uterinal cavity, and approached that of hysteroscopy in discovery and in the definition of origin. The experienced proportions of discovery comply with the best results in sonohysterography. In cases of infertility and repeated bleeding disorder we can reckon with more frequent focal lesions of the endometrium in patients suffering from carcinoma of the breast exposed to tamoxifen for a longer period, and in menopause, in cases of pathologically thick endometrium. On the basis of our examinations we suggest that a primary examination of venuousness in the endometrium should be taken with vaginal colour Doppler U-sound in addition to the simple U-sound examination.

ad 6.: The efficiency of HSG in judging the shape and the contour of the uterus is reliable, less acceptable in the abnormalities taking place in the uterinal cavity and causing shadow drop-outs (polypus, myoma, adhesion), and is almost useless in judging the cervix. The rather favourable NPV shows at every component of the hysteroqram, that there is no need for another diagnostic procedure for the morphological examination of the uterus within a year. Because of all these reasons we must go on applying the advantages offered by HSG in the diagnosis of genital morphological lesions, knowing the assets as well as the liabilities of this method.

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