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Complications in modern hysteroscopic myomectomy

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ABSTRACT

Uterine fibroids (UFs) are common benign tumors of the female genital tract, diagnosed in almost one-quarter of women of reproductive age. UFs may cause numerous clinical symptoms, including prolonged or heavy menstrual bleeding, pelvic pressure symptoms, pain, infertility and others. Submucous fibroids arise from the muscular part of the uterus and penetrate into the uterine cavity. They are mostly managed with the use of hysteroscopic myomectomy (HM), which provides direct visualization from the transcervical approach. The sheer number of HM standards and techniques is reason enough to review the available literature about HM-related complications.

HM is a safe and effective treatment in patients with the normal size of the uterus and with no more than a few UFs. The procedure should not be initiated without adequate preparation and diagnosis, using the best methods available.

Key words: hysteroscopy, myomectomy, uterine fibroid, leiomyoma, complication

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INTRODUCTION

Uterine fibroids (UFs) are common benign tumors of the female genital tract. They are diagnosed in almost one-quarter of women of reproductive age [1]. UFs may cause numerous clinical symptoms, including prolonged or heavy menstrual bleeding, pelvic pressure symptoms or pain, infertility and obstetric complications, but are mostly asymptomatic [1].

Typically, UFs were divided into three groups (submucous, intramural and subserosal), but nowadays the International Federation of Gynecology and Obstetrics (FIGO) fibroid classification, where fibroid location is determined in relation to the uterine cavity (with submucosal fibroids named class 0, 1 or 2) is more commonly used [2]. In 2017, Laughlin-Tommaso et al., published a study about clinical limitations of the FIGO classification, signaling the need for its additional validation [3]. STEPW, which is an acronym of size, topography, extension of the base, penetration and wall, is a less popular classification for submucous UFs by Lasmar et al. [4]. STEPW allows for a greater correlation with complete or incomplete removal of the uterine fibroid by hysteroscopic myomectomy (HM) [5]. Clinically symptomatic intramural and subserosal fibroids are usually treated with laparoscopy or open surgery. Attempts to remove intramural UFs with the use of HM have been reported but, so far, the effects have been questionable [6]. Submucous fibroids arise from the muscular part of the uterus and penetrate into the uterine cavity, which is why they can be managed with the use of hysteroscopy, the current 'gold standard'. Hysteroscopy provides direct visualization of the endometrial cavity and submucous fibroids. In general, only symptomatic tumors are operated upon but HM has sometimes been advised in asymptomatic women, especially if they wish to conceive in the future [7].

In order to achieve optimal conditions during HM, the uterine cavity needs to be distended by a medium. New fiber optic technologies and surgical accessories have improved visual resolution and hysteroscopy in general [8]. Also, multiple hysteroscopic techniques to excise UFs are currently available [9]. Hysteroscopic resection with a monopolar loop electrode is the most prevalent method. Some UFs, especially those located deeper in the myometrial wall, require advanced skills and better instrumentation [9]. Prior to UF removal, most patients are diagnosed with the use of an ultrasound, and some also undergo a diagnostic office hysteroscopy, which can help to determine patient eligibility [10].

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Some gynecologists use sonography-guided hysteroscopy as a method of choice in more complicated cases [9]. In difficult cases, pre-treatment is also advisable [11]. A study by Ferrero et al., showed that a ulipristal acetate preoperative treatment increased the complete resection rate and decreased the operative time in difficult HMs [12]. However, the European Medicines Agency (EMA) has recently issued a warning about the risk of liver failure after ulipristal acetate use [13].

HM might be very easy or extremely difficult, depending on various patient- or equipment-related factors. Only proper diagnosis and surgeon expertise may produce good results and prevent complications.

The availability of a hysteroscopic resectoscope no longer presents a problem and the number of centers which treat advanced cases of UFs continues to grow. That is why, the authors of this manuscript decided to present a review of the main complications which can occur during HM. Advice on how to prevent complications or tackle them has also been included.

MATERIAL AND METHODS

This article presents an up-to-date review of the publications about HM-related intra- and peri-operative complications. A literature search for this review was conducted in PubMed of the National Library of Medicine from January 2000 to November 2017 using the following key words: "hysteroscopy", "myomectomy", "hysteroscopic myomectomy", "morcellation", "uterine perforation', "excessive bleeding", "incomplete resection", "infection", "intravascular absorption syndrome", "venous intravasation", and "venous air embolism". During the search, the key words were combined into pairs, which resulted in: "hysteroscopy" and "myomectomy — 259; "hysteroscopy" and "surgical complications" — 1207; "hysteroscopy " and "morcellation" — 41; "hysteroscopy" and "uterine perforation" — 179; "hysteroscopy" and "excessive bleeding" — 37; "hysteroscopy" and "incomplete resection" — 38; "hysteroscopy" and "infection" — 140; "hysteroscopy" and "intravascular absorption syndrome" — 5; "hysteroscopy" and "venous intravasation" — 5; and "hysteroscopy venous air embolism" — 14 results. The search for "hysteroscopic myomectomy" alone presented 286 results. Additional important articles and reviews from other databases (e.g. Cochrane, Web of Science and Scopus) were considered, when relevant. Articles published in languages other than English were excluded. The emphasis of the review was to critically review data about HMs, the safety of the procedure, and possible adverse outcomes.

DISCUSSION

Complications during hysteroscopy are rare and depend mostly on the difficulty of the surgery. Uterine perforation, infection, excessive bleeding, venous intravasation, and long-term complications like intrauterine adhesions account for the most common surgery-related problems [14].

Uterine perforation

Uterine perforation is the most common HM-related complication [15–17]. However, in a multicenter study by Aydeniz et al., in nearly 22,000 patients, it was reported only in 0.15% of the cases [16]. The causes of uterine perforation vary, with the too deep resection of the uterine fibroid in unfavorable conditions or a perforation during cervical dilatation among the most frequent ones.

A conservative approach and observation are sufficient in most cases of uterine perforation. However, thorough diagnosis in the case of hot loop, damage or morbidity cannot be omitted [8]. In the middle line perforation, serious complications are seldom reported but in the case of lateral damage or damage to the cervix, hemorrhage or retroperitoneal hematoma may occur more often. Laparoscopy or laparotomy are recommended to fully assess the damage to the uterus and the surrounding structures such as the bowel or the urinary bladder [18]. Thermal damage to these structures can also be postponed and appear 5 days to even 2 weeks postoperatively [18]. Still, even if there is no typical injury, the patient should always be advised to report for emergency control in case of symptoms like fever, abdominal pain, nausea or vomiting [18].

According to Mazzon et al., thin free myometrial margin (FMM) is the major risk factor for this kind of complication [15]. The value of 10 mm in the myometrial margin allows the surgeon to consider hysteroscopy as a safe procedure [15]. According to other sources, it can even be as low as 5 mm [8]. Mazzon et al., described the cold loop technique which in their opinion is much safer than the electric loop due to the lower risk of injury to the adjacent organs [15]. These authors also pointed out that the cold loop technique (mechanical loops of Mazzon; Karl Storz, Tuttlingen, Germany) using the blunt dissections constitutes a lower risk for the subsequent pregnancies in those women [15]. It is known that an extremely hot electric loop can damage the surrounding structures e.g. blood vessels, bladder or bowel, even in indirect contact (without uterine perforation). During difficult HMs, the surgeons do not always remember that the loop may cause delayed damage. In cases where FMM is very thin, it is important to consider using a cold loop [15], intraoperative ultrasound [9], or a two-port operation (with a direct laparoscopic supervision), in order to track the exact position of the surgeon. The two-port surgery might be more invasive than the ultrasound-guided one, but no other technique offers such control in the operative field. It is sometimes worth considering if patient outcome will not be more favorable after laparoscopic myomectomy, especially

in case of larger UFs. The use of cold loops should be considered due to the exceptionally good results [15], and to prevent the abovementioned complications.

Some centers have dramatically reduced their complication rate by using intraoperative ultrasonography [9], which has considerable advantage over the ordinary pre-operative ultrasound as FMM is not a stable parameter [19]. Also, transrectal ultrasonography can be an interesting alternative to the transabdominal scanning [20]. Apart from the size, the precise measurement of the UF volume is of paramount importance [8, 9]. According to Emanuel, 3D ultrasonography is a great tool for proper preoperative evaluation, with good reproducibility [8]. The complication rate is also decreasing due to better operator skills, which is yet another proof that it is necessary to constantly train personnel [9, 15, 21].

A thorough gynecological ultrasound scan, with the measurement of the fibroid volume and the residual uterine wall thickness, is the key point in safe HM. The volume of the removed tissue should be assessed during the procedure. If the volume is assessed pre-operatively and is assumed to be high, the surgeon should proceed with greater caution. It should be emphasized that a person undertaking high-risk hysteroscopy needs to have good laparoscopic skills (or be experienced in open surgery) to repair any possible damage. During laparoscopy, if the operator has the skills to suture the uterine muscle, the injury can be repaired in a very short time. Of course, laparotomy may always be performed, but for the patient who has already decided to have a minimally invasive hysteroscopy, laparoscopy will be better tolerated, due to better cosmetic effect, which in turn will provide greater overall satisfaction.

Bleeding

Bleeding can be associated with the perforation but can also occur due to other causes (bleeding may occur from the endometrium, myometrium, or the surrounding vessels [17, 18, 22]. According to Munro and Christianson, anemic patients who require HM can be rendered amenorrheic before the surgery using hormonal treatment (GnRH analogs or SPRMs), and then supplied with adequate iron supplementation to increase their blood morphology and iron stores [18]. Preoperative blood transfusion can be considered in cases when surgical delay could be dangerous [18].

Bleeding may have different severity — from scant to severe hemorrhage. The depth of the resection should be limited in the lateral wall and the isthmus area, where the risk for injuring the large myometrial branches of the uterine artery is elevated [18]. In case of small bleeding, it is sometimes necessary to temporarily increase the fluid pressure to gain more visualization and attempt coagulation, e.g. with the ball electrode [18], although in case of severe bleeding the surgeons should also use some uterotonics. According to Emanuel, small bleeding might be arrested by spontaneous uterine contraction [8, 23]. Some types of bleeding may respond to the administration of vasopressin injection (dilute vasopressin solution (0.05 U mL^{-1}) [18, 22], or uterotonics, e.g. oxytocin (e.g. 5 to 10 IU intravenously) [22] or misoprostol (600–1000 µg). The use of oxytocin was tested in hysteroscopic endometrial resection [24], but there is still not enough data about its use in HM. In cases where the effect of uterotonics is insufficient, an intracavitary balloon tamponade might be used, e.g. a Foley catheter filled with 30–50 mL of fluid, which is consistent with the literature reports [18]. In difficult cases, laparoscopic or open surgery suturing or hysterectomy remain the available alternatives. In general, adequate preparation is vital, especially before the excision of large UFs. It is also advised to remember that the risk for bleeding increases with the depth of the excision. Type 2 fibroids > 6 cm in diameter constitute the limits of this endoscopic technique [9]. Attempts to tackle type 3 UFs using HMs have been reported but in such cases highly experienced surgeons are necessary due to the risk for intrauterine adhesions and other complications.

Incomplete resection

According to the available literature, complete UF removal accounts for almost 90% and 60–80% of surgical interventions in G1 UFs and G2 UFs, respectively [25]. In a study by Cammani et al., complete resection of large (< 5 cm in diameter) fibroids was achieved in 81.8% of the patients. Interestingly, in a study by Korkmazer et al., no remnants were observed in patients after hysteroscopy with the use of perioperative transabdominal ultrasound surveillance [9].

Some authors treat incomplete removal as a severe complication [9]. However, it cannot be strictly treated as a complication. Sometimes incomplete removal signifies well-understood caution, which aims to reduce the risk for complications, e.g. in case of difficult operating conditions, suspected operative hysteroscopy intravascular absorption (OHIA) syndrome, or technical deficiencies. It should be emphasized that a two-step procedure can sometimes reduce the overall risk and result in the same outcome [25]. It is also possible that in case of the inhibition of the UF-derived symptoms (especially when the indication was abnormal uterine bleeding), the remaining part of the UF may become devascularized and undergo spontaneous resorption [8, 25]. However, this procedure does not apply in case of infertility, where the two-step procedure should be proposed [8].

Morcellation

During HM of the larger UFs, the resected fragments often disturb visualization, and these parts have to be removed from the uterine cavity. A hysteroscopic morcellator was

developed precisely for that task. It allows for a fast and automatic tissue removal and reduces the time of surgery [8, 26]. However, morcellation is not free from complications [27].

The fibrotic tissue which has been deformed must be removed from the uterine cavity. This is done most often by holding the tissue remnant using the hysteroscope loop and part by part extraction – this provides the best accuracy [8]. Due to the fact that such a procedure must be repeated several times in case of multiple or large UFs, it raises the risk for complications, e.g. venous air embolism (VAE) [18, 28]. Recently, a hysteroscopic morcellation system, somewhat similar to that used in laparoscopy, has been invented [8, 23, 27]. In a sample TRUCLEAR® system, the tissue is sucked into a special window, excised and extracted without additional coagulation. In those cases, standard saline medium is used for distension and irrigation. Studies about hysteroscopic morcellation are ongoing, but their results have been most encouraging due to low complication rates. It might even be a breakthrough in the field of HM [27]. Good results, e.g. in case of subsequent pregnancies after HM with morcellation using the MyoSure® device, were confirmed by Chen et al., as most subjects became pregnant after the surgical intervention [29].

The limitations to the use of hysteroscopic morcellators remain to be fully elucidated. According to Noventa et al., the operative time depends on volume, density and type of tissue. These authors advise caution in case of large volume UFs which present with high density on ultrasound scan [30].

After the alarm raised by the US Food and Drug Administration (FDA) in 2014 about power morcellation during laparoscopy and the related consequences, the debate among the experts continues. FDA stated that morcellation is a dangerous technique, causing abnormal spreading of cells within the abdominal cavity [31]. According to the current data, the risk for malignancy spread by morcellation is extremely low (around 0.06%) [32, 33]. There is also a study about the risk of malignant cells intraabdominal spread in women with endometrial cancer only during hysteroscopy [34].

Infection

Kerkvoorde et al., reported extremely low risk for infection during office hysteroscopy [14]. Agostini et al., assessed the risk for infection during hysteroscopy to be 1.42% [35], while according to other authors the risk was even smaller [14, 16, 18]. It should be emphasized that the risk for infection increases with manipulation of the cervix, such as dilatation for example [14]. The problem of HM-related infection is so rare that there is no consensus about the prophylactic antibiotics [18]. Nappi et al., found no differences in the risk for infection between groups of patients receiving prophylaxis and controls [36]. Antibiotic prophylaxis should be considered in case of all patients, especially if their medical history is unclear or the patient has a history of recurrent inflammatory conditions of the reproductive tract.

Venous intravasation/operative hysteroscopy intravascular absorption (OHIA) syndrome

OHIA syndrome is such a rare complication that some surgeons do not remember it might occur.

Fluid media are used for operative procedures to allow the use of electrosurgery. Also, continuous irrigation results in more clear vision. Ringer's solution or 0.9% saline solution are the most common fluids used as distension media in modern HM [8]. These media are isotonic and are applicable to bipolar methods, and they are also considered to be much safer than hypotonic media [8, 18, 22, 28]. Gas media (e.g. carbon dioxide) are not applicable in operational hysteroscopies. There are various mechanisms by which the fluid enters the circulatory system — through the endometrium, fallopian tubes or by vessels opened during UF resection. The problem with these media is that large volumes can be absorbed into the circulatory system when the myometrial vessels are opened, which may cause fluid overload, electrolyte imbalance, and serious complications, e.g. pulmonary edema or cardiac failure. Patients who develop fluid overload will experience headache or drowsiness, convulsions or apnea, or vomiting [8, 18]. The occurrence of such symptoms, even without reaching the fluid limits, requires additional diagnostic tests and should be treated as a complication [37].

In general, the best approach to prevent the OHIA syndrome is a scrupulous fluid balance in real life surgery. There are different systems which determine the volume of the fluid and fluid that has drained, but these are always merely the estimated values. It is important to remember about the possibility of complications of excessive venous absorption. In the long-term, it is important to monitor the amount of fluids used in relation to that which has returned (bucket, floor, system etc.) [18].

The use of isotonic distention media reduces the risk for complications as they are safer than hypotonic solutions [27]. In a work by Jansen et al., the rate of complications associated with the medium was assessed as 0.2% [17]. A low complication rate was also proven in a study by Aydeniz et al. [16]. The risk for fluid absorption is even greater during HMs, when large vessels are opened, facilitating the absorption of fluid under high pressure [37]. Prolonged HM is another high-risk procedure [37].

In case of isotonic media, the upper limit of the absorbed fluid has been set at 2,500 mL [38]. Minor OHIA, caused by isotonic media, can be successfully treated with standard diuretics, e.g. furosemide. The limit for hypotonic media is lower and has been reported at 1000 mL [26, 37]. This value has been based on the fact that when the patient absorbs

about 1,000 mL of a 1.5% glycine solution, the sodium concentration drops by about 8–10 mmol/L [22, 37].

As mentioned above, large volumes of hypotonic media used in monopolar techniques (5% mannitol, 1.5% glycine) constitute the problem. The risk for complications is very high and might present as water poisoning, lung or brain edema, and hyponatremia [8, 18, 38]. In such cases, the treatment usually involves co-operation with anesthesiologists and incorporating high-percentage sodium chloride boluses to initially compensate sodium deficiency. Importantly, clinicians should not quickly compensate for hyponatremia due to the threat of additional complications, such as pons myelinolysis. Determination of the amount of fluid intake presents an additional challenge. Different amounts will be acceptable for a young healthy woman than older woman with chronic kidney or heart disease [37]. In high-risk women, the maximum amounts of the absorbed fluid have been estimated at 1500 mL and 750 mL for isotonic and hypotonic media, respectively [38].

Venous air embolism

A venous air embolism (VAE) is one more type of complication which might occur during HM. The available literature describes the seriousness of the problem, allowing surgeons to learn how to deal with such cases [18, 28]. An interesting study on VAE was published in Norway on the basis of three cases from their center [28].

VAE is a rare complication and the gas embolus may come from the medium used to expand the uterus during electrocoagulation or directly from the air in the operating room. The gas entering the cardiovascular system can cause arrhythmia, pulmonary hypertension, gas exchange disorders, and, in the worst-case scenario, can lead to death [28, 39]. A patient who develops VAE will report chest pain, breathing disturbances, shortness of breath, or may cough [39]. Some authors may find it unlikely, but asymptomatic gas in the right heart atrium after hysteroscopy is not a rare phenomenon [28, 40]. More commonly used bipolar systems, which are less likely to cause OHIA, produce more air bubbles and increase the risk for VAE. Echocardiography is a good way to monitor a patient for VAE (although it is a problematic matter to always have a continuous echocardiography during HM). The second most common method is the monitoring of carbon dioxide concentration (end-tidal CO_2 – $EtCO_2$). Even small air bubbles will affect the $EtCO_2$ reduction, so the problem will be quickly noticed. According to Storm et al., the $EtCO_2$ alarm should be set at about 4 mm Hg below the patient baseline, with high frequency (e.g. every minute), less frequent measurements may cause delays in the diagnosis of complications [28]. If an alarm is triggered, the procedure is immediately interrupted until the $EtCO_2$ level returns to baseline [28].

In case of a suspicion or diagnosis of VAE, HM should be immediately terminated. An attempt to locate the gas inlay location and the removal of the hysteroscope should be performed as well. According to Munro et al., 100% oxygen should be applied, the cervical canal should be closed instrumentally, and the patient should be placed in the Trendelenburg position on the left side — Durant maneuver [18]. Another course of action may involve administration of inotropic positive agents, and even cardiocentesis. The size of the complication may be changed with the use of the hyperbaric chamber, as this will reduce the volume of gas; even postponed hyperbaric therapy gives a good effect [28].

Prevention is the key issue as far as HM-related complications are concerned, which sometimes requires redefinition of the usual approach to hysteroscopy, as was done in Norway [28]. The basic task is to train the staff regarding the probability of such complications, and to design a local procedure plan [18]. Proper monitoring has already been described above. The important thing is to consider the choice of the correct position - slightly inverted Trendelenburg position is the best. The medium delivery systems should pump the fluid up to the maximum of 60 mmHg and the outflow should be passive. The surgeon should limit the insertion of the hysteroscope to the necessary minimum [28].

CONCLUSIONS

HM for the removal of submucous UFs is a safe and effective treatment in patients with normal size of the uterus and with no more than a few UFs. The procedure should be preceded by careful preparation, especially adequate diagnosis with the best methods available. 3D ultrasound is both, inexpensive and effective, but the test must be performed by a well-trained sonographer. In such scans, FMM can be properly checked e.g. using the tomography like sequence. The second important point is the adequate qualification for the procedure and the choice of the proper method. In case of HM, where there is a high risk for complications, the procedure should be performed by expert staff. At present, no technique has proven to be superior over others, but the method should reduce the potential risk in very difficult cases, e.g. cold loop or direct laparoscopic supervision. Staff should also be trained in laparoscopic skills in case of complications which could be treated with the use of this method. It should also be considered whether the patient will benefit from laparoscopic myomectomy. It is important to have proper operational protocol which will ensure minimum risk of OHIA or VAE. Severe media-related complications occur more frequently with hypotonic solutions and in women with associated illnesses, which is why caution is advised.

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