VRIJE UNIVERSITEIT

Hysteroscopic Sterilization

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Introduction

Female sterilization, by tubal ligation or tubal occlusion, is the most commonly used method of family planning in the world. Overall, in developed regions 8.1% of women between the ages of 15 and 49 years, married or in a union, currently use female sterilization for contraception, compared with 22.3% of those in less developed regions. More than 180 million couples rely on tubal sterilization for contraception (1). Approximately 75% of these people live in Asia (China and India). The majority of procedures are abdominal, by laparotomy or laparoscopy.

Approximately 50% of all female sterilizations are performed during Caesarean Section or in the puerperal period. The other 50%, which is called "interval sterilization", is performed at least six weeks after the last pregnancy or delivery (2). Pomeroy in the 1930s made tubal sterilization well known but, because a laparotomy was needed, it was still considered a major procedure. The mini-laparotomy, an abdominal incision of 2-3 cm in length, was first described by Uchida and colleagues in 1961, offered a reduced recovery time and a better cosmetic result (3). Colpotomy, a technique that dates back to the early 19th century, began to attract new interest in the 1970s. Through a small in incision in the anterior or posterior vaginal fault a modified Pomeroy technique or fimbriectomy was done. Surprisingly the complication rates in Europe and the US were much higher than those in India and the method was abandoned.

Laparoscopic sterilization

Techniques and settings of sterilization have progressively changed since the 1960s with the introduction of minimally invasive surgery. While in developing countries mini-laparotomy remains the most common approach, in developed countries nearly all interval sterilizationsand an increasing proportion of postpartum sterilizations are performed by laparoscopy (4). Various laparoscopic methods have been introduced since 1936. Unipolar coagulation was the first method of laparoscopic tubal occlusion to achieve widespread use. Although highly effective, it was associated with early reports of thermal injuries, including thermal bowel lesions and deaths. In 1972 bipolar electrocoagulation of the tubal isthmus was first introduced, which eliminates the need for a ground plate and was safer for the patient (5). The first laparoscopic sterilization in the Netherlands was performed in Leiden in 1972 by Prof. van Hall (6). Several alternative laparoscopic techniques were introduced in the early 1970s. The elastic rubber band was developed by Yoon. The band is introduced with a specially designed laparoscopic applicator. The application of the band onto a tubal loop is associated with 2-3% incidence of haemorrhage from stretching the vessels underneath the tube or tearing the tube itself (7).

Approximately 3 cm of constricted tube undergoes necrosis. An advantage of the spring/Hulka clip was that it only compresses 3 mm of the mid-isthmus of the tube. As a result, anastomosis for reversal of sterilization is fairly successful. Another technique, described by Filshie and colleagues, uses a silicone rubber-lined titanium clip that is applied to the mid isthmus and must include the entire circumference of the tube (8). The Filshie Clip has been used around the world for the past 20 years and was approved by the Food and Drug Administration in the United States in 1996.

All methods currently in use are highly effective when performed properly, although pregnancy can occur in spite of optimal application. Such failures are often due to tuboperitoneal fistula formation. When pregnancies do occur they are much more likely to be ectopic than pregnancies during use of other methods or when no method is used. The risk of pregnancy persists during the fecund period and it is therefore important to consider the long-term cumulative probability of pregnancy with any contraceptive method -or methods- over time. Unfortunately there are no controlled trials comparing the different laparoscopic techniques with a follow-up period long enough to provide evidence on long term failure rates (1,9). Pregnancies can and do occur even many years after sterilization, as has been documented by the U.S. Collaborative Review of sterilization (CREST study) (10) in which pregnancies occurred in the 10 years after each of the four methods of laparoscopic sterilization studied (unipolar coagulation, bipolar coagulation, silicone rubber band application, and spring clip application). An analysis of the experience of 10,685 women followed prospectively for up to 8 to 14 years in the CREST study identified 143 sterilization failures (pregnancies other than luteal phase pregnancies) and found that the risk of pregnancy after sterilization varied by age at sterilization and method of tubal occlusion. The 10-year cumulative probability of pregnancy was low for most women aged 34-44 years at sterilization but was as high as 5% for women aged 18-27 years with two methods (bipolar coagulation and spring clip application). Another noteworthy finding from this analysis is that the risk of pregnancy accumulated over time. The timing of sterilization failures varied by method; for example, a high proportion of pregnancies after clip application occurred in the first three years after the procedure, whereas pregnancies after bipolar coagulation occurred at approximately the same rate year after year. A total of 47 (32.9%) of the 143 pregnancies identified were ectopic. The cumulative probability of ectopic pregnancy, like that for pregnancies overall, increased over time and varied by method of occlusion and age at sterilization (11). The findings from this review of sterilization techniques should be interpreted with some precaution, keeping in mind that they were based on procedures performed more than 20 years ago and that a substantial number of the procedures were performed shortly after the introduction of laparoscopic sterilizations in the USA.

A subgroup analysis of women undergoing bipolar tubal coagulation showed that the cumulative failure rate during the period 1978 – 1982 (19.5 per 1,000) was three times higher than during the period 1985 – 1987 (6.3 per 1000). In addition, those women who had three or more sites coagulated had a very low probability of pregnancy (3.2 per 1,000) compared to women with fewer sites coagulated (12.9 per 1000).

The Filshie Clip was not available in the United States until 1996 and was not included in the U.S. Collaborative Review of sterilization. However, published data suggest that the clip is, like the other methods of tubal occlusion, highly effective. Four studies from the Family Health International (FHI) were designated pivotal evaluations: all were prospective, randomised and multicenter investigations of interval sterilizations. A 12-month cumulative pregnancy rate of 0.1-0.2 per 100 women for the Filshie Clip were reported (12). Long-term follow-up data for the Filshie Clip such as those obtained by CREST are limited. A five-year follow-up study from Kovac and Krins involving 30,000 women revealed a failure rate of 73 per 30,000 (2.4 per 1,000) (13).

Hysteroscopic sterilization

The idea of utilising hysteroscopy for tubal occlusion goes back for more than a century. In the last 100 years transcervical approaches were studied and promoted during four separate periods, beginning in the early 1920s. During World War II, in 1942, Clauberg started his criminal research in Auschwitz on thousands of imprisoned Jewish and Gypsy women, looking for a cheap and efficient method to sterilise women. He injected acid liquids in to their uterus without the use of anaesthetics. After the war Lindemann continued sterilization experiments with the Claubergs technique of coagulating the fallopian tubes (14). The fourth period started at the beginning of this century (15). Hysteroscopic sterilization techniques have been sought because they avoid the risks of the laparoscopic route, they allow women a quicker return to normal activities and are especially useful in women for whom laparoscopy is contraindicated. The methods for tubal closures include chemical applications, mechanical devices and thermal methods where electrosurgery, cryocoagulation, radiofrequency and laser are used.

Thermal

In 1934 the first hysteroscopic sterilization with electrocoagulation was performed in two patients. Both procedures were unsuccessful. In the 1970s an overall bilateral tubal occlusion rate of 83% was achieved, but pregnancies including ectopics were reported (16). Finally the method did not prove to be reliable and suffered from serious complications due to bowel injury (17). Other methods with cauterization of the tubal openings have not been developed further (18,19,20).

Chemical

Quinacrine sterilization is used in many developing countries because of good results and low costs. The technique requires two insertions of quinacrine into the uterine cavity. This can be done "blind" or by hysteroscopic guidance and direct tubal instillation by a specially developed catheter (21). The procedure is reported to have a 1-2% failure rate, although the rates for ectopic pregnancy and serious complications are equal to or less than those for transabdominal sterilization (22,23,24). Drawbacks from the procedure include the need for multiple applications and the problem of reliably confirming tubal occlusion. An HSG is not recommended, because of the risk to blow out the delicate occluding scars (25). The need to make this procedure simple, safe, inexpensive and thereby more acceptable, even in countries with limited surgical facilities is well recognized. Use of quinacrine pellets has become the most widely adopted method of non-surgical female sterilization (26). The Family Health International has recently decided not to pursue further research on quinacrine, partly because of the relatively high pregnancy rates after quinacrine compared to other contraceptive methods (27). The 10-year pregnancy probability is approximately four times higher than after laparoscopic tubal sterilization (bipolar coagulation) as reported by CREST.

Mechanical

To avoid the risk of complications many different device were developed and have been tried during the second half of the last century. Most of the devices were unsuccessful (24). Three devices became commercially available and were introduced on the European Market.

Ovabloc Intra-Tubal Device

The concept of blocking the fallopian tubes with silicone was first introduced by Crofman (28). The first studies performed on rabbits, proofed an efficacy of 100% if the silicone material was applied up to the isthmic part of the tubes. Erb developed a technique for hysteroscopic intratubal administration of liquid silicone, mixed with a catalyst and cure-in-place to form rubbery implants, with the aim of producing a non-incisional, non-scarring method for permanent contraception with minimal discomfort for the patient (29).

This Ovabloc method has been in use since 1978. Phase II and III studies were performed in the late 1970s and early 1980s in Belgium and the USA (30). These FDA trials were stopped when the initially assumed reversibility was poor (31,32). In 1985 the Ovabloc procedure became commercially available in the Netherlands (Ovabloc Europe BV, Alphatron Medical Systems, Rotterdam, later Advanced Medical Grade Silicones BV, Beverwijk, the Netherlands), where its use has mainly been confined to a few centers (33). A CE Mark for the European market is achieved in 2001.

The insertion is an outpatient procedure. The procedure involves high pressure injection of viscous silicone into the ostium with a catheter placed in the tubal ostium through a hysteroscope with a 7 French working channel. The silicone conforms to the shape of the ampoule of the tube and solidifies in approximately five minutes. The silicone contains radio-opaque silver powder, which enables a radiological check for correct placement at completion of the procedure. Bilateral placement takes around 30 minutes. The woman is asked to use contraception for three months, at which point a second plain X-ray is performed to exclude migration and expulsion. Published data report a high failure rate, expulsion to the abdominal cavity and complete expulsions. The method never became very popular, probably because it was too complicated. It was stopped in 2009. In 2012 CE approval was obtained for Ovalastic (Urogyn BV, Nijmegen, the Netherlands), which is the result of a technical upgrade of Ovabloc. With this upgrade the manufactory claims a less time consuming, more reliable and safe procedure.

Essure

In November 2002 the Food And Drug Administration approved the Essure sterilization while it has been available on the European market since 2001 (Conceptus Inc. Mountain view, CA, USA). The device is a dynamically expanding insert that consists of a stainless steel innercoil, a nickel titanium (nitinol) expanding outercoil and Polyethylene Teraphtelate (PET) fibres. The device, with a length of 4 cm, is placed into the fallopian tube using a modern standard hysteroscope with a 5 French working channel. After placement the device will be anchored in the tubo-cornual junction by the expanded nitinol coil. The PET fibres induce an inflammatory reaction that causes scarring and occlusion of the tubes. The exact time that it takes for tubal occlusion of the tubes to allow the patient to rely on the devices as permanent contraception is unknown (34). Obliteration of the tubal lumen was demonstrated histologically in four of nine tubes removed within four weeks after device placement and five of five tubes removed within four to eight weeks after placement. Functional occlusion confirmed by hysterosalpingography (HSG) was already confirmed one week after placement (35). Patients are instructed to use alternative contraception until a three months confirmation test has shown adequate bilateral localization and tubal occlusion. In the US a HSG is required for confirmation according to the FDA approval while in other countries, scout X-ray or transvaginal ultrasound is used for confirmation. The ESS205, a modification of the former ESS105 device, with higher insertion rates was introduced in 2004. In 2007 the ESS305 with automatic release mechanism of the introducer catheter and a special introducer was introduced.

Successful placement is achieved in 95-99% of the cases in an office setting (36,37). Worldwide more than 500,000 women rely on Essure sterilization. The cumulative nine years failure rate is 0.2% on the basis of follow-up data from 449 women included in the phase II and pivotal trials (34) More than 700 unintended pregnancies are reported (38). Data analysis of patient files shows that 44% of the pregnancies are attributed to patient non-adherence to the protocol or misreading of the confirmation test. Shavell reported a 12.7% compliance with the three months HSG in a general clinic population in an urban environment, despite both preoperative and postoperative counselling and a follow-up rate of 70% for the one-week postoperative control (39).

Adiana

Adiana's complete transcervical sterilization procedure (Adiana Inc., Redwood City, CA purchased by Hologic, USA) is a two-stage procedure. First, a superficial lesion of the epithelium of the intramural part of the tube is created with bipolar radiofrequency energy. The second step is placement of a 3.5 mm porous, silicone, non-biodegradable implant (matrix) into the tubal lumen. The implant provokes a fibrous reaction that occludes the tube over a period of weeks. Patients must use alternative contraception for three months until an HSG is performed. A CE Mark for the European market was obtained in December 2008 and the FDA approved the application in July 2009. The Evaluation of Adiana System (EASE trial) was completed in 2005 (40). It was stated that 611 women were treated, with a 95% bilateral insertion rate. Almost half of the patients (47%) received conscious sedation with an intravenous agent. The HSG confirmation test after three months showed tubal patency of one or both tubes in 8.8% of the patients. During the first four years of this trial, 15 pregnancies have been reported. Five of the pregnancies occurred while subjects were instructed to rely on an alternate contraceptive: two pregnancies following placement failure, and three pregnancies after successful placement, but during the waiting period (patient non-compliance). Ten pregnancies occurred following successful placement and HSG showing tubal occlusion. Six of these pregnancies occurred in the first year of rely. Retrospective review of HSGs for three of these subjects suggests that the diagnosis of tubal occlusion was in error (misread). The six pregnancies contributed to a one-year failure rate of 1.1%. In March 2012, the manufactory decided Adiana was not generating the expected revenue and the manufacturing of Adiana was stopped. At that moment a long-standing battle over patent infringement between the two companies was going on.

Hysteroscopy

Between the 1970s and 1980s modern hysteroscopy was introduced. Procedures for distending the uterine cavity were introduced, with carbon dioxide and high-molecular weight fluids to allow visualization of the uterine cavity and tubal ostia (15). The Ovabloc ITD procedure was performed with a single flow hysteroscope with an Alberan deflexion bridge, initially with Hyskon (32% Dextran 70 in 10% glucose) or carbon dioxide as distension medium. From 1991, a continuous flow 8.0 mm hysteroscope with a 2.2 mm (7 French) working channel and an Alberan deflexion bridge, fitted with a 4.0 mm 300 fore-oblique telescope was used with sorbitol for uterine distension (33).

At the beginning of the 1990s, scopes were used with operative sheats with a diameter equal or less than 5.5 mm with a working channel of 1.7 mm (5 French) and telescopes with a diameter ranging between 1.2 and 3.0 mm. With the use of these smaller instruments the use of a speculum and tenaculum and dilatation of the cervix was no longer necessary: the vaginal cavity can be distended with a distension medium to facilitate location of the cervical canal. The anatomy can be followed by gentle movements of the hands that correctly drive the hysteroscope into the cervix and through the internal cervical os (41). This method has been defined as the "vaginoscopic approach", the patient discomfort associated with the traditional approach to the uterus has been eliminated (42).

As anesthesia and analgesia are not required for hysteroscopy, women now have the option of permanent contraception while avoiding the risk associated with laparoscopy and general anesthesia. Some physicians are still hesitant to perform the procedure in an office setting, most commonly citing patient discomfort as the major concern, but several studies support high tolerability and satisfaction with an office approach (43).

One study indicates that patients undergoing hysteroscopic sterilization experience significantly less pain than those undergoing laparoscopic sterilization (44).

Paracervical block with 1% lidocaine provides effective pain relief for cervical manipulations during office hysteroscopic sterilization, but does not reduce the pain associated with upper uterine/tubal manipulation when placing the devices (45).

Pain scores were associated with procedural time. A likely explanation for this is that procedural time is a marker for difficulty of the procedure or skills of the hysteroscopist. In general, the more difficult the Essure placement is, the longer it will take to achieve correct placement, and frequently additional manipulations are needed to assist in appropriate placement, the more cramping of the fallopian tubes will be induced. An important finding is that the largest difference in observed pain scores was 2.3 on the VAS. Even though for the purposes of this study a relatively conservative difference of 0.9 on the VAS was used to be clinically relevant to prevent

under powering, some studies indicate that the clinically relevant VAS difference is around 2.5. Therefore, although a difference was observed and found to be statistically significant, this may not represent a clinically relevant difference. When examining the placebo group, we observed that pain was not significantly greater than reported menstrual pain. This is critical when counselling patients regarding the pain from the Essure procedure, as well as likely other office hysteroscopy procedures that require less manipulation than Essure. Because pain is one of the most common patient concerns when choosing to undergo an office procedure, the ability to tell a patient that the pain will be similar or less than a typical menstrual period can be very reassuring for many patients (45).

According to a Cochrane review from 2012 the available literature is insufficient to determine the appropriate pain regimen for outpatient sterilization by hysteroscopy. Neither paracervical block with lidocaine nor conscious sedation significantly reduced overall pain scores during sterilization by hysteroscopy with Essure. Although paracervical block with lidocaine did not reduce overall patient-reported pain, it did reduce pain during some portions of the procedure, particularly with injection into, or manipulation, of the cervix. Since paracervical anesthesia is safe and inexpensive it may be a reasonable option. The provision of intravenous conscious sedation did not reduce the total pain score but did significantly reduce pain at the time of insertion of the second tubal insert; this is one of the most painful parts of the procedure. Thus, it may have some benefit (46).

Confirmation test

In the late 1970s the hysterosalpingography (HSG) was abandoned as a routine follow-up after laparoscopic sterilization because of discordance between tubal patency and pregnancy rate. In a study of 250 women with laparoscopic tubal fulguration the patency rate with HSG was 3.6% while the pregnancy was only 0.62%. A review of additional contemporary studies confirmed discordant patency and pregnancy rates (47).

The results of the CREST review did not change the policy of confirmation of laparoscopic sterilization. The CREST review reported an overall cumulative failure rate of 1.9%. This was more than double what has been accepted as the standard failure rate for tubal sterilization. This failure rate contrasted sharply with previous studies of common tubal occlusion techniques that cited figures lower than 1%. Until then, comparisons of contraceptive failure rates had reported the probability of failure during the first year after sterilization ranging between 0% and 0.4% (48). These failure rates, however, were based on investigations having only one or two years of follow-up. Alternative diagnostic tests for confirmation of laparoscopic sterilization have not been described.

An HSG is also not recommended after transcervical sterilization with quinacrine, because of the risk to blow out the delicate scars (25). No other tests have been evaluated.

For all hysteroscopic techniques initially a HSG was recommended. For the Ovabloc method finally two X-rays images were required to evaluate the effectiveness of the device: one X-ray immediately following instillation to check the integrity and shape of the plug and a second X-ray at three months post-instillation to check the proper location of the Ovabloc devices. This decision that patients could not rely on the sterilization for three months was an arbitrary point in time (49).

In the US, according to the FDA, an HSG is required after hysteroscopic sterilization with Essure, while in Europe and other countries initially X-ray was an accepted alternative. In February 2011 the Conformité Européene Mark approved to use Transvaginal Ultrasound (TVU) to confirm proper placement of the microinsert, three months following the procedure. Available data confirm that proper location of the microinserts correlates very well with tubal occlusion and high effectiveness (50). Evaluation of data from 745 patients with unintended pregnancies showed a high incidence of misreading of the HSGs and patient non-compliance to the HSG confirmation test (38). In an urban clinic population in Michigan the compliance to a protocol with HSG revealed only 12.7%, despite correct counselling and a 70% follow-up rate for the post-operative visit (39). Studies with confirmation tests other than HSG report higher patient compliance (36,37,43, 50).

The first and only study available data for the Adiana method reports 53 of 604 patients with unilateral or bilateral tubal patency with the three months HSG. By six months post-procedure, 26 still showed at least unilateral patency. With TVU, 598/604 subjects had devices visualized bilaterally. There have been a total of 10 pregnancies among 553 women who were told to rely on Adiana for contraception based on the three-months HSG, two pregnancies of which were ectopic. It is unclear how the TVU imaging correlates with these unintended pregnancies. The devices are not radiopaque, therefore pelvic X-ray is not useful for the confirmation (40).

There is a need for other tests to confirm proper position and tubal occlusion after sterilization. HSG is still the gold standard. The procedure is invasive and uncomfortable for the patient. In addition it is associated with infection, vasovagal reaction and anaphylactic shock. Also uterine bleeding and perforation may occur.

Alternative ideas are suggested and are subject of research:

- *Contrast Infusion Sonography (CIS)* or *Saline Infusion Sonography (SIS)*. NaCl infusion in the uterine cavity while inspecting for real time flow within the tube or unequivocal dye spill in the adnexa (51).

- *Hysterosalpingo Contrast Sonography (HyCoSY)* with the use of an ultrasound contrast agent to examine tubal patency.

- *Volume Contrast 3D Ultrasound* produces a 5 mm thick volume image in the C-plane (VCI-C) similar to HSG. The images yield more detail with regard to the relationship of the device to the uterine cavity than conventional (2D) ultrasound or HSG. Like 2D US it gives information about the position of the microinsert but not about the integrity of the fallopian tubes. A Classification has been developed to assess the position of the microinsert. Four positions are described: perfect, proximal, distal and very distal. Only the last one is associated with a higher chance of tubal patency on HSG (52,53).

Tubal occlusion prior to IVF

Hydrosalpinx is associated with poor in-vitro fertilization outcome but the actual mechanism is not yet fully understood. The passage of hydrosalpingeal fluid into the endometrial cavity might create an unfavourable environment for embryo implantation or development (54). Laparoscopic salpingectomy prior to IVF in patients with ultrasound-visible hydrosalpinges is recommended. Hysteroscopic sterilization techniques offer the possibility of an alternative for salpingectomy by proximal tubal occlusion prior to IVF. Previous reports estimated the efficacy of proximal tubal occlusion in patients with hydrosalpinges and shows excellent reproductive outcomes after Artificial Reproduction Techniques (ART). The presence of nickel in the Essure device is cause of concern related to embryologic development, but Nitinol showed no cytotoxic, allergic or genotoxic activity in animal studies (55). Second look hysteroscopy after Essure placement showed that the devices are encapsulated and the devices may therefore be compatible with implantation and successful pregnancies outcomes after IVF (56).

Aims of this thesis

- To review the history and current practice of hysteroscopic sterilization.
- To review placement rates, effectiveness and safety of current hysteroscopic sterilization methods.
- To validate different diagnostic tests for the three months confirmation after hysteroscopic sterilization.
- To evaluate the outcome of unintendend pregnancies and IVF pregnancies after regret or pre-procedure closure of hydrosalpinges.

Outline of the thesis

Chapter 2 determines the placement rate, efficacy and safety of hysteroscopic sterilization methods that are currently available or has been available.

Chapter 3 determines the diagnostic characteristics of X-ray and transvaginal ultrasound to localize Essure microinserts after successful bilateral placement.

Chapter 4 determines the reproducibility and inter-observer agreement of pelvic X-ray 3 months after hysteroscopic sterilization with microinserts.

Chapter 5 describes different types of incorrect position of microinserts after successful bilateral placement.

Chapter 6 estimates the causes of unintended pregnancies after hysteroscopic sterilization and determines whether this can be prevented.

Chapter 7 evaluates the protocol for confirmation of satisfied position of microinserts after hysteroscopic placement based on first-line examination with transvaginal ultrasound.

Chapter 8 determines the success rate of proximal tubal occlusion with microinserts in subfertile women with hydrosalpinges.

Chapter 9 evaluates the obstetrical outcome of intended and unintended pregnancies after Essure hysteroscopic sterilization.

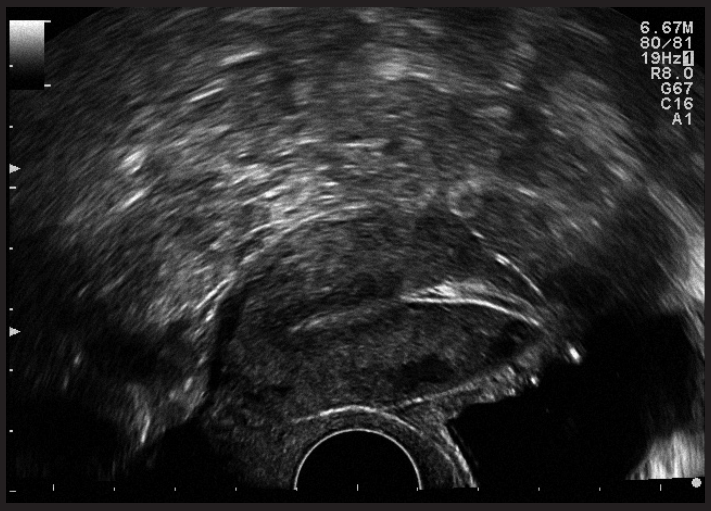
Chapter 10 summarizes the results of the studies presented in this thesis and gives clinical implications and implications for future research.

References

1. Lawrie TA, Nardin JM, Kulier R, Boulvain M. Techniques for the interruption of tubal patency for female sterilization. Cochrane Database Syst Rev. 2011.
2. Contraceptive sterilization: Global Issues and Trends. 2002, New York, Engender Health.
3. Uchida H. Uchida's abdominal sterilization method and its result. Fourth Asian Congress on Obstetrics and Gynecology. Singapore. 1968
4. Westhoff C, Davies A. Tubal sterilization: focus on the U.S. experience. Fertil Steril 2000;73:913-9225
5. Peterson HB, Xia Z, Wilcox LS, Tylor LR, Trussel J. US Collaborative Review of sterilization Working Group. Pregnancy after tubal sterilization with bipolar electrocoagulation. Obstet Gynecol 1999:94:163-167
6. van Hall EV, Schellekens LA. Sterilisatie van de vrouw. Ned T Geneesk. 1973; 117: 625
7. Yoon IB, King TM, Parmley TH. A two-year experience with the Falope ring sterlization procedure. Am. J. Obstet. Gynecol. 1977;127:109
8. Filshie GM, Casey D, Pogmore JR, Dutton AG, Symonds EM, Peake AB. The titanium/silicone rubber clip for female sterilization. Br J Obstet Gynecol. 1981;88:655-62.
9. Nardin, J. M., Kulier, R., and Boulvain, M. 2003.Techniques for the interruption of tubal patency for female sterilization (Cochrane Review).
10. Peterson HB, Xia Z, Hughes JM, Wilcox LS, Tylor LR,Trussell J. The risk of pregnancy after tubal sterilization : findings from the U.S. Collaborative Review of sterilization. Am J Obstet Gynecol 1996;174:1161–8.
11. Peterson HB, Xia Z, Hughes JM, Wilcox LS, Tylor LR, Trussell J. The risk of ectopic pregnancy after tubal sterilization .U.S. Collaborative Review of sterilization Working Group. N Engl J Med 1997;336:762–7.
12. Pollack A. The Contraception report 1996
13. Kovacs GT, Krins AJ, Female sterilizationswith Filshie Clips: what is the risk of failure? A retrospective survey of 30000 applications. J Fam Plann Reprod Health Care 2002;28:34–5.
14. Kaupen Haas H Experimental obstetrics and national socialism: the conceptual basis of reproductive technology today. Reproductive and Genetic Engineering, Vol. 1, No. 2, pp. 127–132, 1988
15. Lindemann HJ. Transuterine tubal sterilization by hysteroscopy. J Reprod Med. 1974;13:21-2.
16. Abbott J. Transcervical sterilization. Best Pract Res Clin Obstet Gynecol 2005:14:1-14
17. Quinones R, Alvarado A, Ley E. Hysteroscopic sterilization .Int J Gynecolo Obstet 1976;14:27-34
18. Hurst BS, Thomson S, Lawes K, Ryan T. Controlled radiofrequency endotubal sterilization. Adv Contracept 1989;14:147-52
19. Brumsted JR, Shirk G, Soderling MJ, Reed T. Attempted transcervical occlusion of the fallopian tube with the Nd: YAG laser. Obstet Gynecol 1991;77:327-8
20. Droegemuller W, Greer BE, Davis JR, Makowski EL, Chvapil M, Pollard A. Cryocoagulation of the endometrium and uterine cornua. Am J Obstet Gynecol 1978;131:1-7
21. Zipper J, Trujillo V. 25 years of quinacrine sterilization experience in Chile: review of 2,592 cases. Int J Gynecol Obstet 2003; 83 (Suppl 2):S23–S29

22. Hieu DT, Luong TT. The rate of ectopic pregnancy for 24,589 quinacrine sterilization (QS) users compared to users of other methods and no method in 4 provinces in Vietnam, 1994-1996. Int J Gynecol Obstet 2003; 83 (Suppl 2):S35-S43.
23. Ferreira CR, Magalhaes DR, Ferreira DC, et al. Quinacrine female nonsurgical sterilization (QS): endometrial assessment by vaginal sonography in 128 women. Int J Gynecol Obstet 2003; 83 (Suppl 2):S59-S66.
24. Brundin J. Transcervical sterilization in the human female by hysteroscopic application of hydrogelic occlusive devices into the intramural parts of the Fallopian tubes: 10 years experience of the P-block. Eur J Obstet Gynecol Reprod Biol 1991; 39:41-49.
25. Hamou J, Gasparri F, Cittadini E. Hysteroscopic placement of nylon intratubal devices for potentially reversible sterilization. In: Seigler A, Ansari A, eds. The fallopian tube: basic studies and clinical considerations. Mount Kisco: Futura; 1986.
26. Kessel E. 100,000 Quinacrine sterilizations. Adv Contracept 1996; 12:69-76.
27. Sokal DC, Trong Hieu D, Dinhloan N, Hubachert D, Nanda K, Weiner DH, Huu Vach T. Contraceptive effectiveness of two insertions of quinacrine: results from 10-year follow-up in Vietnam. Contraception. 2008;78(1)
28. Crofman PA, Obstetric and Gynecology 1966; 27:880-3
29. Erb RA, ReedTP 3rd. Hysteroscopic oviductal blocking with formed-in-place silicone rubber plugs. I. Method and apparatus. J.Reprod. Med. 1979; 23:65-68
30. Reed TP 3rd, Erb R. Hysteroscopic tubal occlusion with silicone rubber. Obstet Gynecol 1983;61:388-92.
31. Cooper JM. Hysteroscopic sterilization. Clin Obstet Gynecol 1993;35:282
32. Loffer FD. Hysteroscopic sterilization with the use of formed-in-place silicone plugs. Am J Obstet Gynecol 1984;148:261
33. De Blok S, Dijkman AB, Wamsteker K. Hysteroscopic tubal occlusion with ovabloc ITD - results of 115 cases. Gynecol Endosc. 1992;1:151-4.
34. Connor VF. Essure: a review six years later. J.Minim Invasive Gynecol. 2009;16:282-290
35. Valle RF, Carignan CS, Wright TC and the STOP Prehysterectomy Investigation Group. Fertil steril. 2001;76:974-980
36. Heredia F, Cos R, Moros S, Torrabadella L, Cayuela E. Radiological control of Essure placements. Gynecol Surg. 2004;1:201-203.
37. Ubeda A, Labastida R, Dexeus S. Essure: A new device for hysteroscopic tubal sterilization in an outpatient setting. Fertil Steril. 2004 Jul;82(1):196-9.
38. Munro MG, Nichols JE, Levy B, Vleugels MP, Veersema S. Hysteroscopic sterilization: Ten-Year Retrospective Analysis of Worldwide Pregnancy Reports. J Minim Invasive Gynecol 2014;21:245-251
39. Shavell VI, Abdallah ME, Diamond MP, Kmak DC, Berman JM. Post-essure hysterosalpingography compliance in a clinic population. J Minim Invasive Gynecol. 2008;15:431-4.
40. Vancaillie TG, Anderson TL, Johns DA. A 12-month prospective evaluation of transcervical sterilization using implantable polymer matrices. Obstet Gynecol.2008;112:1270-7.
41. Bettocchi S, Nappi L, Ceci O, Selvaggi L. Office hysteroscopy. Obstet Gynecol Clin North Am. 2004;31:641-54

42. Bettocchi S, Selvaggi L. A vaginoscopic approach to reduce the pain of office hysteroscopy. 1997;4:255-8.
43. Levie M, Weiss G, Kaiser B, Daif J, Chudnoff SG. Analysis of pain and satisfaction with office-based hysteroscopic sterilization. Fertil Steril. 2010;94:1189-94.
44. Syed R, Levy J, Childers ME. Pain associated with hysteroscopic sterilization. JSLS. 2007;11:63-5
45. Chudnoff SG, Einstein M, Levie M. Paracervical block efficacy in office hysteroscopic sterilization: A randomized controlled trial. Obstet Gynecol. 2010;115:26-34
46. Kaneshiro B, Grimes DA, Lopez LM. Pain management for tubal sterilization by hysteroscopy. Cochrane Database Syst Rev. 2012 Aug 15;8:CD009251
47. Sheikh HH. Hysterosalpingographic follow-up of laparoscopic sterilization. Am J Obstet Gynecol. 1976;126:181-5.
48. Pollack A, ACOG Committee on Practice Bulletins-Gynecology. ACOG practice bulletin. Clinical management guidelines for obstetrician-gynecologists. Number 46, September2003. Obstet Gynecol. 2003;102:647-58.
49. Loffer FD, Loffer PS. Hysteroscopic tubal occlusion with the use of formed-in-place silicone devices: A long-term follow-up. Gynecol Endosc. 1992;1:203-5.
50. Veersema S, Vleugels MP, Timmermans A, Brolmann HA. Follow-up of successful bilateral placement of essure microinserts with ultrasound. Fertil Steril. 2005;84:1733-6.
51. Connor VF. Contrast infusion sonography to assess microinsert placement and tubal occlusion after essure. Fertil Steril. 2006;85:1791-3.
52. Legendre G, Gervaise A, Levaillant JM, Faivre E, Deffieux X, Fernandez H. Assessment of three-dimensional ultrasound examination classification to check the position of the tubal sterilization microinsert. Fertil Steril. 2010;94:2732-5.
53. Legendre G, Levaillant JM, Faivre E, Deffieux X, Gervaise A, Fernandez H. 3D ultrasound to assess the position of tubal sterilization microinserts. Hum Reprod. 2011;26:2683-9.
54. Strandell A, Lindhard A, Waldenström U, Thorburn J, Janson PO, Hamberger L. Hydrosalpinx and IVF outcome: a prospective, randomized multicenter trial in Scandinavia on salpingectomy prior to IVF. Hum Reprod. 1999;14:2762-9.
55. Wever DJ, Veldhuizen AG, Sanser MM, Schakenraad JM, van Horn JR.Cytotoxic, allergic, and genotoxic activity of a nickel-titanium alloy. Biomaterials 1997;18:1115-20.
56. Kerin JF, Munday D, Ritossa M, Rosen D. Tissue encapsulation of the proximal essure microinsert from the uterine cavity following hysteroscopic sterilization. J Minim Invasive Gynecol. 2007;14:202-4.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3 Follow-up of successful bilateral placement of Essure microinserts with ultrasound.

S. Veersema
M.P.H. Vleugels
A. Timmermans
H.A.M. Brölmann

Fertil Steril. 2005;84:1733-6.

Abstract

Objective To evaluate the reliability of pelvic X-ray and transvaginal ultrasound to localize Essure microinserts (Conceptus, San Carlos, California) after successful placement in both fallopian tubes 3 months after placement.

Design Prospective, observational study.

Setting Gynecology departments at two teaching hospitals.

Patient(s) One hundred eighty-two patients who underwent hysteroscopic sterilization by placement of Essure microinserts between August 2002 and August 2004.

Intervention(s) Transvaginal ultrasound, pelvic X-ray, and hysterosalpingography (HSG) 3 months after sterilization with Essure.

Main Outcome Measure(s) Transvaginal ultrasound confirmation of correct localization of microinserts after a 3-month follow-up.

Result(s) In 150 of 182 patients, confirmation of successful bilateral placement of two microinserts (300 devices) was possible. In 9 patients it was not possible to identify both devices with ultrasound, or there was doubt about the extension of the device through the uterotubal junction. The other 291 devices were identified as being in a good position.

Conclusion(s) Hysterosalpingography at the 3-month follow-up after successful placement of Essure microinserts can be replaced by transvaginal ultrasonography. A 3-month follow-up with HSG after the Essure procedure is only required after unsatisfactory placements. In those patients in whom transvaginal ultrasonography cannot confirm satisfactory localization, a complementary pelvic X-ray should be performed.

Key Words Essure, hysteroscopic sterilization , hysterosalpingography, pelvic X-ray, transvaginal ultrasound

Introduction

Essure is a new device for hysteroscopic tubal sterilization. The Essure System (Conceptus, San Carlos, CA) was approved by the European Health Office in November 2001 and by the U.S. Food and Drug Administration in November 2002. It is an expanding spring device made of a nickel–titanium outer coil and a flexible stainless steel inner coil with Dacron fibers. This microinsert is placed in the proximal section of the fallopian tube under hysteroscopic visualization. The Dacron fibers cause localized tissue ingrowth from the surrounding tube, thereby achieving mechanical occlusion of the tube. The tissue response is the result of a chronic inflammatory and fibrotic response to the fibers. Over a 3-month period this ingrowth completely occludes the tubal lumen.

The effectiveness of the Essure microinsert in preventing pregnancy is believed to be due to a combination of the space-filling design of the device and this local, occlusive, benign tissue response to the fibers. This tissue ingrowth in the devices, caused by the fibers, results in both device retention and pregnancy prevention (1).

Initially all patients were scheduled for hysterosalpingography (HSG) 3 months after an Essure microinsert placement procedure (2,3). The HSG was performed to evaluate microinsert location and fallopian tube occlusion. Until the Essure sterilization was completed after 3 months and confirmed by HSG, all patients were advised to use alternative contraception.

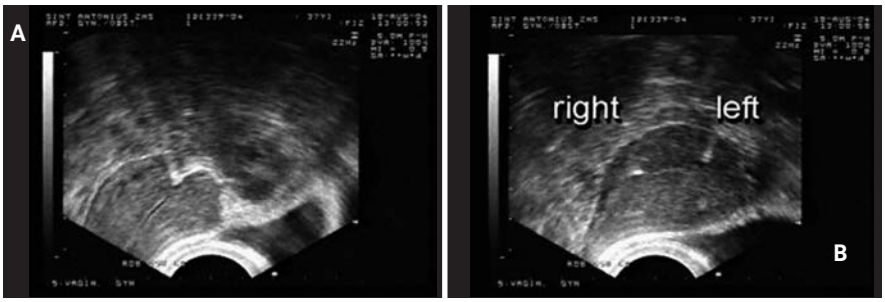
Because of the potential risks, higher cost, inconvenience, and discomfort of the required HSG, clinical data of 700 patients included in a phase II trial were reviewed (4). This included a review of HSGs, radiographs, and videotapes of all the procedures in which the HSG detected a potential problem. On the basis of this review, criteria were developed for identifying the small proportion of patients who might benefit from an HSG evaluation, on the basis of their 3-month pelvic X-ray results. The current recommendation is to check the position and alignment of the microinserts with pelvic X-ray 3 months after a satisfactory bilateral placement. Satisfactory placement involves good visualization of the tubal ostia and microinsert location across the uterotubal junction, with 3–10 visible expanded coils trailing into the uterus. Hysterosalpingography is only requested in cases of no placement, unilateral placement, or incorrect placement (>10 device loops outside the tubal lumen) (4,5). In cases of satisfactory bilateral one-step placement, X-ray showed 100% correct position of both devices (5). In another report (4), only one patient had abnormal X-ray findings (too much distance between the two devices) after satisfactory bilateral placement. Hysterosalpingography revealed tubal occlusion. Therefore, in cases of optimal placement, 100% bilateral occlusion was detected with X-ray only (5).

Although X-ray seems to be a sensitive test in detecting the microinserts, limited information is gained about the soft tissue structures that envelope it. Ultrasound seems to be well suited for microinsert localization. It has many advantages over X-ray. Ultrasound has the ability to locate the device and visualize its relationship with the surrounding tissue. The position of the device within the uterotubal junction can be displayed on ultrasound, whereas it can be merely inferred on plain X-ray films. Ultrasound provides real-time and dynamic imaging information to aid with device location, whereas X-ray provides a single, static image. Importantly, ultrasound is a nonionizing method of imaging that potentially can be performed in the doctor's office without the need for an extra visit to a radiology department, thus shifting and reducing follow-up expenses. An early post-insertion ultrasound can even be used to ensure correct positioning of the device or its eventual malposition. In an earlier study, 5 patients were examined by ultrasound within 4 weeks after insertion. Fourteen pairs of devices were seen. One device was malpositioned, and in 1 patient a device was missing (6).

In this study, we assessed the test characteristics of transvaginal ultrasonographic localization of the microinserts, compared with pelvic X-ray and HSG.

Figure 1

Transvaginal ultrasound at 3 months. (A) Microinsert crossing the cornua of the uterus, with the proximal end in the uterine wall. (B) Transverse section of the uterus demonstrating both microinserts.



Materials and methods

Between August 2002 and August 2004, 182 consecutive patients were included in the clinical evaluation of the Dutch Essure trial in two clinics in the Netherlands (St. Antonius Hospital Nieuwegein and the Rivierenland Hospital Tiel). In both clinics the investigators followed the same study protocol and obtained approval from the clinical and ethics committees. All women gave their written, informed consent in the knowledge that this new method of sterilization is irreversible, and data of a long-term follow-up are not yet available. In 150 women (82.4%), a successful bilateral Essure placement in a one-step procedure was achieved. These patients were advised to continue alternative contraception for the next 3 months and were scheduled for transvaginal ultrasound after 3 months. Transvaginal ultrasound was followed by HSG in that same session. Hysterosalpingography was started with a blank abdominal X-ray. Ultrasound was performed with an Aloka SSD 550 (Biomedic Nederland BV, Almere) or a Toshiba Eccobee (Toshiba Medical Systems Nederland BV, Zoetermeer).

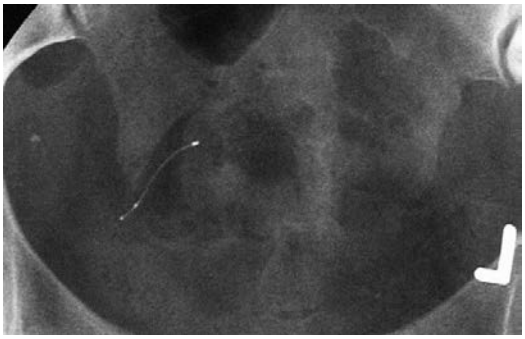
After the microinserts were localized by ultrasound, the position of the reflections of the microinsert in relation to the outer line of the uterus was described. The position of the devices was "satisfactory" when the reflections of the microinsert crossed the outer line of the uterine wall and the proximal ends of both devices were visualized inside the outer line or in the region of the endometrial cavity (Fig. 1). The physician was asked to predict the occlusion of each fallopian tube, which was confirmed by HSG. The criteria used to evaluate the HSG for "satisfactory" placement were [1] both microinserts visible with ≤50% of the length of the inner coil trailing into the cavity, [2] the proximal ends of the inner coils appear to be <30 mm into the tube from where contrast fills the uterine cornua, and [3] no contrast visible in the tubes beyond the microinserts or in the peritoneal cavity (7).

The pelvic X-ray was "satisfactory" when the microinserts appeared to be in the tubal lumen, spanning the uterotubal junction, and relatively symmetrical.

All data were collected with commercial statistical software (SPSS, Chicago, IL). Sensitivity, specificity, positive predictive value, and negative predictive value for transvaginal ultrasound and X-ray were calculated. Hysterosalpingography was considered the "gold standard".

Figure 2

Pelvic X-ray at 3 months, demonstrating expulsion of the left microinsert; only the right microinsert is present.



Results

In 150 patients with successful bilateral placement, 2 microinserts (300 devices) could be examined by transvaginal ultrasound. In 9 patients it was not possible to identify both devices with ultrasound, or there was doubt as to the extension of the device through the uterotubal junction. The other 291 devices were identified and in a good position. In 1 of the 9 patients with unsatisfactory ultrasound results only 1 microinsert was present on pelvic X-ray; this patient seemed to have had an expulsion (Fig. 2). In 149 patients the pelvic X-ray was determined to be satisfactory with both microinserts. One of these 149 women was found to have some evidence of dye passage (patency) past the microinsert into the distal tubal lumen upon HSG (Fig. 3). This patient refused to continue the use of alternative contraception and insisted on sterilization. Forty-nine weeks later she underwent a repeat HSG, and bilateral tubal occlusion was achieved at this time. This patient did not become pregnant despite unprotected sexual intercourse. One hundred forty-eight patients were instructed to discontinue alternative contraception because of bilateral tubal occlusion 3 months after the procedure. In the patient with the expulsion a second microinsert was placed in a new attempt. The patient continued with alternative contraception for 3 more months, and HSG was repeated.

The results of transvaginal ultrasound as compared with the results of HSG as the "reference test" show a sensitivity of 50% and a specificity of 95%. Compared with pelvic X-ray as the reference test these values are 100% and 95%, respectively. The predictive value of a satisfactory transvaginal ultrasound result is 99% and the predictive value of an unsatisfactory result is 11%.

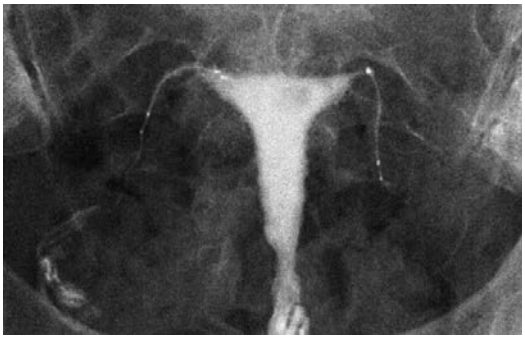
Discussion

The 3-month follow-up period after hysteroscopic sterilization with Essure is based on the time it takes the tissue ingrowth to completely occlude the tubal lumen (1). Because the initial recommendation of an HSG has been changed to pelvic X-ray 3 months after successful bilateral placement, exclusion of tubal patency is no longer a requirement (4). After satisfactory pelvic X-ray results, the patient can rely on the microinserts for sterilization (7). In the present study, ultrasound detection of both devices was satisfactory in 141 of the 150 patients with successful bilateral placement. One patient with an expulsion of a microinsert was recognized with ultrasound as well as with pelvic X-ray. A second patient with tubal patency on HSG had a satisfactory pelvic X-ray, and both devices were in a good position on transvaginal ultrasound. It has been postulated that the absence of absolute physical occlusion of the tubes does not necessarily equate with failure of sterilization. In only 8 patients with satisfactory pelvic X-ray results was it not possible to confirm the satisfactory position of the devices with transvaginal ultrasound. Transvaginal ultrasound has great advantages over pelvic X-ray because it is a non-ionizing method of imaging. It can be done on an outpatient basis in departments of gynecology by the patient's own physician and can be repeated at any time without any risk to the patient.

We conclude that HSG at the 3-month follow-up of hysteroscopic sterilization with Essure can be replaced by transvaginal ultrasound. In those patients for whom transvaginal ultrasound cannot confirm satisfactory localization, a complementary pelvic X-ray should be performed.

Figure 2

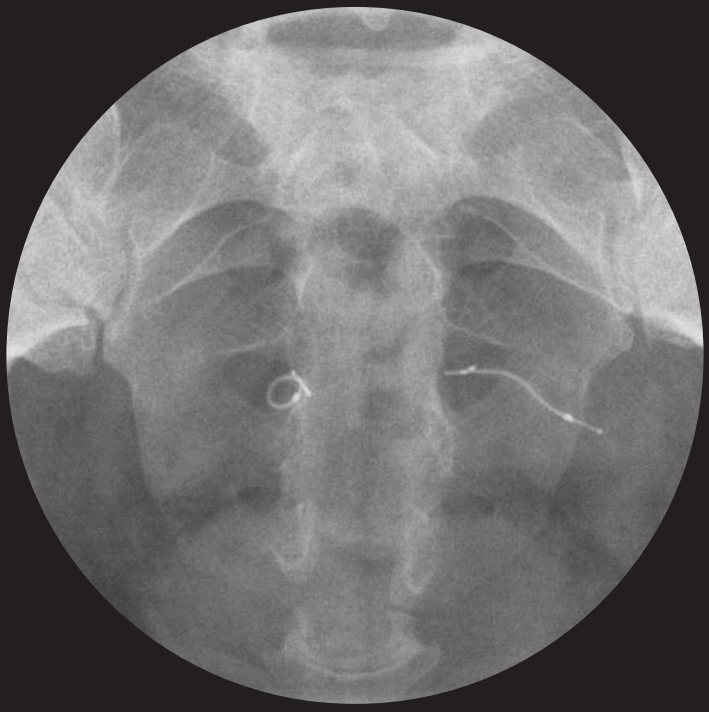
Hysterosalpingogram at 3 months: note correct placement of both devices and patency of the right fallopian tube.



Hysterosalpingography is only required after unsatisfactory placements. The number of HSGs and pelvic X-rays can be minimized, thus reducing costs, inconvenience, and discomfort. In cases of technical difficulties during the procedure or for patients with abnormal bleeding after the insertion, a transvaginal ultrasound can be scheduled 4 weeks after the procedure. This will prevent unnecessary anxiety in these women and offers the possibility of preventing a potential delay in diagnosing expulsion or misplacement of a microinsert.

References

1. Valle RF, Carignan CS, Wright TC, STOP Prehysterectomy Investigation Group. Tissue response to the STOP microcoil transcervical permanent contraceptive device: results from a prehysterectomy study. Fertil Steril 2001;76:974-80.
2. Kerin JF, Cooper JM, Price T, Van Herendael B, Cayuela-Font E, Cher D, et al. Hysteroscopic sterilization using a microinsert device: results of a multicenter phase II study. Hum Reprod 2003;18:1223-30.
3. Cooper JM, Carignan ChS, Cher D, Kerin JF. Microinsert nonincisional hysteroscopic sterilization. Obstet Gynecol 2003;102:59-67.
4. Heredia F, Cos R, Torrabadella L. Radiological control of Essure placements. Gynecol Surg 2004;1:201-3.
5. Ubeda A, Labastida R, Dexeus S. Essure: a new device for hysteroscopic tubal sterilization in an outpatient setting. Fertil Steril 2004;82:196-9.
6. Teoh M, Meagher S, Kovacs G. Ultrasound detection of the Essure permanent birth control device: a case series. Aust N Z J Gynecol 2003;43:378-80.
7. Conceptus. Physician training manual. San Carlos, CA: Conceptus, 2003.



4 Reproducibility of the interpretation of pelvic X-ray 3 months after hysteroscopic sterilization with Essure.

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H.A.M. Brölmann

Fertil Steril. 2009; 91(3): 930-5.

Abstract

Objective To estimate the diagnostic accuracy and the interobserver reproducibility of pelvic X-rays in the diagnosis of successful bilateral sterilization with Essure after a 3-month follow-up period.

Design Interobserver study.

Setting Outpatient department of obstetrics and gynecology in a Dutch teaching hospital.

Patient(s) Patients with successful bilateral Essure placement.

Intervention(s) Hysteroscopic sterilization with Essure and pelvic X-ray and hysterosalpingography after a 3-month follow-up period.

Main Outcome Measure(s): Six observers evaluations of 47 pelvic X-rays from 47 patients 3 months after a technical successful bilateral placement of microinserts to estimate the reliability of the sterilization. Diagnostic accuracy of pelvic X-ray per observer in detecting incorrectly positioned microinserts was expressed in terms of sensitivity and specificity, with hysterosalpingography as the reference strategy. Reproducibility of the interpretation of the pelvic X-ray was expressed as κ-values.

Result(s) The sensitivity and specificity for X-rays read by gynecologists was 0.67 (95% confidence interval [CI], 0.29-0.96) and 0.79 (95% CI: 0.58-1.00) and for radiologists 1.0 and 0.5 (95% CI: 0.36-0.64). The interobserver agreement in reliability of pelvic X-ray of hysteroscopic sterilization assessment with Essure ranged from slight (k-value 0.09) for gynecologists to moderate (κ-value = 0.52) for radiologists.

Conclusion(s) Test characteristics of pelvic X-ray as the imaging technique to assess the position of the Essure microinserts and tubal patency were poor, as was the reproducibility, particularly if gynecologists performed the evaluation. We do not recommend the use of pelvic X-ray for the assessment of the positioning of microinserts after hysteroscopic sterilization. (Fertil Steril 2010;94:1202–7)

Key Words Essure, hysteroscopic sterilization , confirmation test, X-ray, interobserver reproducibility

Introduction

The Essure Permanent Birth Control System (Conceptus Inc, Mountain View, CA) is a new method of proximal tubal occlusion by hysteroscopic placement of a microinsert in the uterotubal junction (1–3). The procedure is gaining popularity because it can be performed under local or no anesthesia in the office. During hysteroscopy, the introduction device is inserted in the fallopian tube, after which the device can expand and the Essure microinsert remains in position. The Essure microinsert consists of a stainless steel inner coil, a nickel titanium alloy outer coil, and polyethylene terephthalate (PET) fibers covering the inner coil. The PET fibers induce a tissue response, which causes fibrous tissue in growth with tubal occlusion (4).

The position of the devices has to be confirmed 3 months after the procedure before the patient can rely on this permanent contraception and cease her alternative contraception. Different imaging techniques are used to document localization of the microinserts and tubal occlusion 3 months after placement. The traditional hysterosalpingography (HSG) is the only imaging method currently approved by the U.S. Food and Drug Administration (FDA). The current recommendation in countries outside the United States is to check the position and the alignment of the devices with pelvic X-ray (5). The limitations of pelvic X-ray are the risk of ionizing radiation and lack of soft tissue and tubal patency information.

Adverse events after the Essure sterilization , such as subsequent pregnancy, expulsion of the microinsert, or perforation, have been described in previous studies and are associated with incorrect placement procedures (1,3).

Earlier phase II and pivotal multicenter trials were started in 1998 and strongly advised patients to use alternative contraception for 3 months after the procedure until tubal occlusion was confirmed by HSG (1,3). Satisfactory bilateral insertion was achieved in 664 of 734 patients (90%). Satisfactory placement implied good visibility of the tubal ostia in hysteroscopy and microinserts location across the uterotubal junction, with three to eight visible expanded coils trailing into the uterine cavity. The 100% bilateral tubal occlusion after an initial satisfactory bilateral placement was confirmed by HSG. To exclude unexpected failures, a less invasive diagnostic test may be sufficient.

Two earlier reports on the results of clinical trials in Spain with hysteroscopic sterilization with Essure and the use of pelvic X-ray 3 months after a satisfactory bilateral placement (6,7) are available.

A recent analysis of 1630 women who underwent an office hysteroscopic tubal sterilization with Essure between January 2003 and June 2006 showed a successful insertion rate of 99% (8). Women were advised to use an alternative contraceptive method until a simple X-ray examination was performed at least 3 months after

the insertion. Hysterosalpingography or ultrasonography was performed when the placement was not satisfactory (more than eight or fewer than three coils remaining visible by hysteroscopy, insertion in only one tube, unclear radiologic results). None of these patients have become pregnant after confirmation at the 3-month follow-up evaluation. These results indicate that pelvic X-ray may be useful to confirm successful bilateral placement in an uncomplicated procedure. However, no data are available about the diagnostic accuracy and the reproducibility of the pelvic X-ray as a confirmation test for Essure sterilization. In cases of poor test characteristics or reproducibility, routine use of pelvic X-ray may be misguided, adding no useful additional information and wasting health-care resources.

Our study was designed to test the accuracy of pelvic X-ray compared with the standard HSG as reference test among radiologists and gynecologists for the diagnosis of successful bilateral sterilization with Essure after a 3-month follow-up period and to estimate the interobserver agreement.

Materials and methods

The study was conducted in the Department of Obstetrics and Gynecology of the St. Antonius Hospital, a teaching hospital in Nieuwegein, the Netherlands. The approval of the institutional review board was not considered necessary as patients were not in any way involved in the study and patient data were anonymous. Moreover, the study is part of large cohort study of 100 consecutive patients (9) that was approved by the institutional review board. All women gave their written informed consent to being part of the cohort, and to knowing that the Essure technique of sterilization is irreversible and that data of a long-term follow-up study were not yet available. Patients were eligible for this study if an adequate plain pelvic X-ray as well as a HSG were digitally available. As the quality of the X-rays was suboptimal in many cases, only 47 cases were included as having digital X-rays of optimal quality.

Hysteroscopic sterilization using the Essure system inserted by use of the standard technique was performed in an outpatient setting. Three months after the procedure, a pelvic X-ray was performed with the patient in supine position, followed by a HSG with a water-soluble contrast medium (Telebrix-Polyvidone; Guerbet SA, Villepinte, France). The contrast medium was instilled into the uterine cavity after the pelvic X-ray was made, using a silicone balloon HSG catheter (Cook Ireland Ltd., Limerick, Ireland). All images were digitally recorded to enable digital demonstration afterward (5). The captured images were evaluated by a radiologist and gynecologist using the algorithm from the HSG protocol in the manufacturer's physician training manual (5). If there was a satisfactory position of both devices

and bilateral tubal occlusion, the sterilization was considered successful, and the patient was advised to cease alternative contraception.

In 2005, all X-rays were evaluated simultaneously by an international panel formed by six observers. The observers were not informed about the clinical data of the hysteroscopic sterilization procedures. The only clinical information available at the time of evaluation was that a bilateral hysteroscopic sterilization had been successfully performed 3 months before the X-ray. The participants were three gynecologist, all specialists in hysteroscopic sterilization with good experience in reading X-rays after Essure sterilization (Gyn 1-3), two radiologists, with good and moderate experience (Rad 1 and 2), and a registrar in radiology with experience in reading HSGs after Essure sterilization (Rad R).

The observers were blinded for the results of the HSG. They were not allowed to discuss the results. The Essure X-ray protocol from the manufacturer's physician training manual (5) was used while evaluating of the pelvic X-rays.

According to the manufacturer's protocol, the observers evaluated the pelvic X-rays with regard to the position of the microinserts, the symmetrical appearance of the devices, and the distance between the two devices. In addition, they had to judge the X-ray as satisfactory, uncertain, or unsatisfactory and determine whether the patient could rely on the sterilization (Table 1).

Table 1
Observer assessment items for 3-month evaluations of Essure placement X-rays.

Evaluation items	Options		
Ability to assess	Good	Acceptable	Nondiagnostic (ND)
Position right device	Correct	Incorrect	ND
Position left device	Correct	Incorrect	ND
Symmetrical appearance	Yes	No	ND
Distance	<4 cm	4-5 cm	>5 cm
Conclusion	Satisfactory	Suspicious	Unsatisfactory
Rely on Essure?	Yes	No	ND

Notes: The observers evaluated the pelvic X-rays on ability to assess the position of the microinserts, symmetrical appearance of the devices, and the distance between the two devices. They also had to grade the X-ray as satisfactory, uncertain, or unsatisfactory and determine whether the patient could rely on the sterilization .

Statistical Analysis

Reproducibility was expressed using Fleiss's κ-statistics (10). Fleiss's kappa (κ) works for any number of raters giving categorical ratings to a fixed number of items. It can be interpreted as expressing the extent to which the observed amount of agreement among raters exceeds what would be expected if all raters made their ratings completely randomly. A κ-value of 0 indicates no agreement beyond chance, a κ-value of 1 indicates perfect agreement between observers. The reproducibility in the case of κ-values between 0 and was regarded as slight, between 0.2 and 0.4 as fair, between 0.4 and 0.6 as moderate, between 0.6 and 0.8 as substantial, and between 0.8 and 1.0 as almost perfect.

The κ-values were calculated for the six observers together and for the three gynecologists and three radiologists separately.

In the assessment of diagnostic accuracy of the X-ray, HSG was considered to be the reference test.

Diagnostic accuracy was calculated for each observer and expressed in terms of sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). An unsatisfactory or uncertain evaluation of an X-ray as of the position of the microinserts was regarded as a positive test result, whereas a satisfactory evaluation was regarded as a negative test result (successful sterilization).

Results

Between December 2003 and July 2004, 47 patients with technically successful bilateral placement of Essure were included in the study. All patients were evaluated by HSG and pelvic X-ray after a 3-month follow-up period. In 44 cases, the HSG confirmed correct position of both implants and bilateral occlusion of the fallopian tubes. There were three cases of an abnormal position of one of the microinserts and a patent tube on HSG: one complete expulsion, one expulsion to the uterine cavity (Fig. 1), and one perforation with the device in the abdominal cavity (Fig. 2).

The diagnostic accuracy for each observer is expressed in terms of sensitivity and specificity. The pooled sensitivity and specificity of both gynecologists and radiologists was 15 out of 18 (83%) and the specificity 170 out of 264 (64%). According to medical specialty, the sensitivity for the three radiologists was 100%, and the specificity was 66 out of 132 (50%). For 27 cases, at least one of the radiologists advised additional HSG to confirm a reliable sterilization (false positive). The sensitivity for the X-ray evaluated by the gynecologists was 6 out of 9 (67%), and the specificity was 79%. Two gynecologists accepted the X-ray from the case with the perforation as satisfactory, and one gynecologist did not recognize the expulsion into the cavity (false negative) (Table 2).

Table 2
Diagnostic performance of X-ray as diagnostic tool for the assessment of reliability of hysteroscopic sterilization with Essure for each observer (gynecologists and radiologists) expressed as sensitivity, specificity, positive predictive value, and negative predictive value.

Observer	Sensitivity%	Specificity%	PPV%	NPV%
Gyn 1	33	100	100	96
Gyn 2	67	70	13	97
Gyn 3	100	66	17	00
Mean (±95% CI)	67 (±38)	79 (±21)	43 (±56)	98 (±3)
Rad 1	100	64	16	100
Rad 2	100	48	12	100
Rad R	100	39	10	100
Mean (±95% CI)	100	50 (±3)	12 (±0.03)	100

Note: Rad R = Radiology Registrar.

The overall interobserver agreement with regard to reliability of the hysteroscopic sterilization with Essure ranged from slight (κ=0.09) for gynecologists to moderate (κ=0.52) for radiologists (Table 3).

There was agreement between all observers that the sterilization was satisfactory in 11 cases, with advice to the patients that they could rely on the sterilization. Only for the case with one patent microinsert (due to expulsion of the other) was there agreement between all six observers that the sterilization was unsatisfactory. The agreement between the observers on the visibility of both devices was perfect, while the agreement on the position of the devices (0.28 to 0.30), the symmetrical appearance of both devices (0.37), and the distance between the two devices (0.27) was fair. The agreement on the final conclusion of the X-ray was slight (0.17) (Table 3).

The patient with the perforation underwent a laparoscopic sterilization with Filshie Clips (Femcare-Nikomed Limited, Hampshire, UK.). During the same procedure, the microinsert was released from the omentum. The two other patients with incorrect position of the microinsert underwent a second successful hysteroscopic sterilization confirmed by HSG after 3 months. None of the patients has become pregnant.

Table 3
Interobserver agreement kappa values.

		All		Radiologist		Gynecologists	
		κ 95% CI		κ 95% CI		κ 95% CI	
Right device	Visible	1.0		1.0		1.0	
	Optimal position	0.28	0.25–0.31	0.45*	0.30–0.59	0.15	0.3–0.28
Left device	Visible	1.0		1.0		1.0	
	Optimal position	0.30*	0.27–0.33	0.54*	0.39–0.69	0.08*	-0.05–0.21
Accessibility		0.14*	0.11–0.18	1.0		0.27	0.12–0.42
Symmetrical		0.37*	0.34–0.41	0.77*	0.61–0.94	0.05	-0.10–0.19
Distance		0.27*	0.24–0.30	0.44*	0.32–0.58	0.07	-0.05–0.19
Conclusion		0.17*	0.14–0.20	0.25*	0.13–0.37	0.14	0.01–0.27
Rely on		0.24*	0.21–0.28	0.52*	0.35–0.68	0..9	-0.05–0.25

Notes: Agreement between the three radiologists and three gynecologists about visibility, optimal position of the device, accessibility of the X-ray, symmetrical appearance, and distance between the two devices, the final conclusion for the X-ray, and the reliability of the sterilization. The reproducibility in the case of κ-values between 0 and 0.2 was regarded as slight, between 0.2 and 0.4 as fair, between 0.4 and 0.6 as moderate, between 0.6 and 0.8 as substantial, and between 0.8 and 1.0 as almost perfect. (*P< .0001.)

Discussion

In this study, six observers evaluated 47 X-rays, including three cases of incorrect position of a device. The test characteristics of the X-rays were better in the hands of radiologists (sensitivity 100%, specificity 50%) than in the hands of gynecologists (sensitivity 67%, specificity 79%). The interobserver agreement (κ) in visualizing the microinsert was 100% in both radiologists and gynecologists; however, in scoring reliability of the Essure sterilization there was a large difference in the agreement between radiologists (52%) and gynecologists (9%).

In the United States, hysterosalpingography (HSG) is the only imaging method currently approved by the FDA for the diagnosis of tubal occlusion after the Essure sterilization procedure. In other countries, other diagnostic tools are used for confirmation. In Europe, pelvic X-ray is recommended by CE Mark guidelines.

To the best of our knowledge, ours is the first report on the diagnostic accuracy of pelvic X-ray in the assessment of the correct placement of the Essure microinserts using HSG as a reference test. Hysterosalpingography is the best available diagnostic test to assess the efficacy of the Essure sterilization in terms of position of the microinserts and blockage of the tubes. However, the combination of position and patency is crucial, as blocked tubes alone do not guarantee an effective sterilization.

As to the different performance of gynecologists and radiologists in favor of the latter, any explanation is speculative. The pelvis X-rays as evaluated by the gynecologists gave a low sensitivity and evaluated by the radiologists gave insufficient specificity.

Figure 1

Pelvic X-ray and hysterosalpingography of patient with partial expulsion of right device into the uterine cavity.

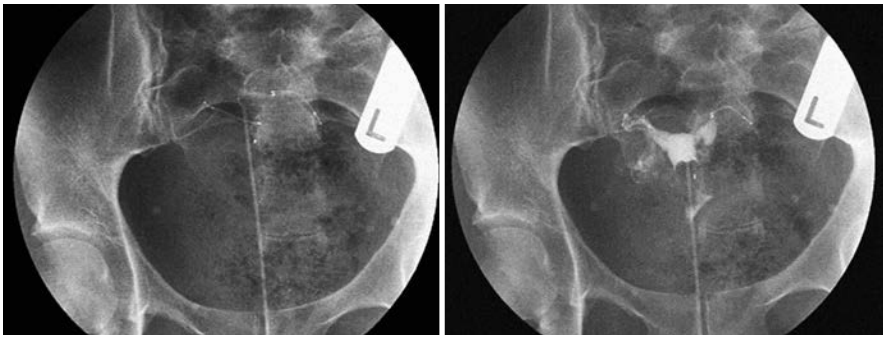
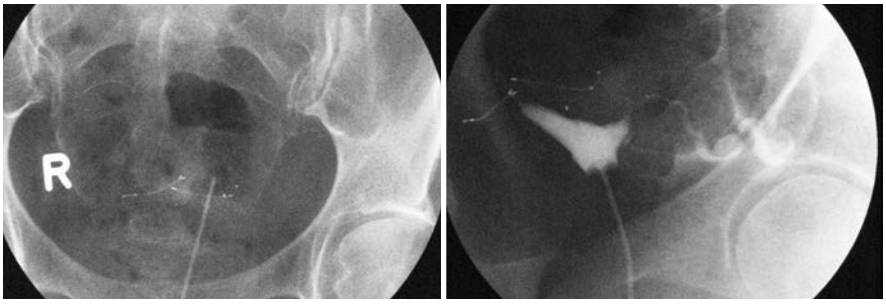


Figure 2

Pelvic X-ray and hysterosalpingography of patient with perforation of the left device to the abdominal cavity.



In other words, not one radiologist confirmed an adequate sterilization for the three patients with a failure, but they advised additional HSGs to perform, whereas the gynecologists accepted more X-rays as reliable sterilization s, but two gynecologists did not recognize the perforation, and one of them did not recognize the expulsion to the uterine cavity.

Radiologists are used to evaluating images with little or no clinical data, and they are aware of the clinical consequences if they miss an important abnormality. As imaging specialists, they may be more inclined to adhere to given instructions on diagnostic criteria than doctors in other specialties. All the observers were instructed on the criteria of failed position of the microinserts according to the protocol (see Table 1).

Unfortunately, the alignment of the fourth marker, which is considered to be an important criterion nowadays, was not included in the criterion list. As the frequency of failed insertion of the Essure device is low, so is the experience of the observers.

In our case series, in three out of 47 X-rays the displacement of the microinsert was reported. This low frequency is in line with former publications (1,3,8,11). In the phase II study (1) of 226 patients evaluated with HSG after a three-month follow-up period, six perforations of the uterine wall or tubal lumen and one expulsion were reported. In the published European series with X-ray as the confirmation test, there was a 100% success rate after bilateral placement, with no unsatisfactory device locations (12, 13). In the most recent study by Arjona et al. (8), three pregnancies occurred during the first 3 months after 1650 procedures.

The issue of better instruction and training of the X-ray reviewers was also addressed by van der Leij et al. (12), who reported in 1997 on the interobserver and intraobserver agreement in the evaluation of radiographic images after hysteroscopic sterilization with Ovabloc (formed-in-place intratubal silicone devices; European Medical Contract Manufacturing B.V., CH Nijmegen, the Netherlands). A group of eight gynecologists had only poor interobserver agreement on the reliability of the sterilization. The investigators concluded that this underlined the need for training in standardized interpretation of X-rays concerning the reliability of sterilization (12).

Another reason for the poor diagnostic performance and agreement among gynecologists in particular may be the lack of clinical data, such as information on any difficulties during experienced the Essure insertion procedure. In daily practice, these data may alert the X-ray observer that there may be cause for an underestimation of the accuracy of the X-rays.

In a recent study in the United Kingdom to determine patient satisfaction of outpatient female sterilization , the majority of women (96%; 95% CI: 88-99%) reported satisfaction with their overall experience of the Essure hysteroscopic sterilization procedure and follow-up evaluations. Two patients declined to have their scheduled HSG, and only 72% of the patients reported the HSG as an ''acceptable test.''

The use of pelvic X-ray, which is less invasive and causes less inconvenience, demonstrates intra-abdominal localization of the microinserts. Because of the lack of soft tissue detail and no filling of the uterine cavity with contrast dye, no information is available regarding the relationship of the microinsert to the uterine cornua.

Our study shows that a correct position of the microinserts in the fallopian tube is difficult to assess by plain X-ray alone. Pelvic X-ray was a perfect diagnostic tool to confirm a complete expulsion of a microinsert, but it missed discrete dislocation where the dislocated microinsert was still attached to the uterine wall. The lack of additional clinical information and history of the patient, and possibly the insufficient training of the observers may be associated with the poor test characteristics and reproducibility of pelvic X-rays after Essure sterilization. The results of our study do not justify the routine use of this radiographic tool in clinical practice.

Recently, it was shown (13-17) that transvaginal ultrasound assessment may be as reliable as HSG for uterotubal localization of the microinserts. The use of ultrasound obviates the need for ionizing radiation in the majority of patients. Future studies on other imaging techniques such as ultrasound are necessary to optimize imaging after Essure placement.

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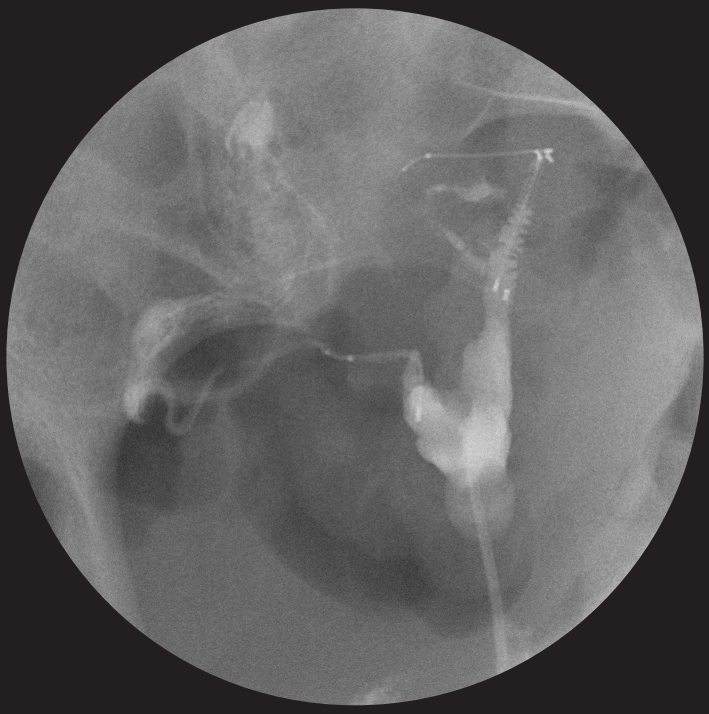
References

1. Kerin JF, Cooper JM, Price T, Van Herendael BJ, Cayuela-Font E, Cher D, Carignan CS. Hysteroscopic sterilization using a microinsert device: results of a multicenter phase II study. Hum Reprod 2003;18: 1223-30.
2. Kerin JF, Munday DN, Ritossa MG, Pesce A, Rosen D. Essure hysteroscopic sterilization: results based on utilizing a new coil catheter delivery system. J Am Assoc Gynecol Laparosc 2004;11:388-93.
3. Cooper JM, Carignan CS, Cher D, Kerin JF. Microinsert nonincisional hysteroscopic sterilization. Obstet Gynecol 2003;102:59-67.
4. Valle RF, Carignan CS, Wright TC. Tissue response to the STOP microcoil transcervical permanent contraceptive device: results from a prehysterectomy study. Fertil Steril 2001;76:974-80.
5. Conceptus. Physician training manual. San Carlos, CA: Conceptus, 2003.
6. Ubeda A, Labastida R, Dexeus S. Essure: a new device for hysteroscopic tubal sterilization in an outpatient setting. Fertil Steril 2004;82:196-9.
7. Heredia F, Cos R, Moros S, Torrabadella L, Cayuela E. Radiological control of Essure placements. Gynecol Surg 2004;1:201-3.
8. Arjona JE, Mi˜no M, Cordon J, Povedano B, Pelegrin B, Castelo-Branco C. Satisfaction and tolerance with office hysteroscopic tubal steilization. Fertil Steril 2008;90:1182-6.
9. Gerritse MB, Veersema S, Timmermans A, Brolmann HAM. Incorrect position of Essure microinserts, 3 months after successful bilateral placement. Fertil Steril 2009;91:930-4.
11. Fleiss JL, Levin B, Paik MC. Statistical methods for rates and proportions. 3rd ed. New York: Wiley, 2003.
12 Litta P, Cosmi E, Sacco G, Saccardi C, Ciavattini A, Ambrosini G. Hysteroscopic permanent tubal sterilization using a nitinol-Dacron intratubal device without anesthesia in the outpatient setting: procedure feasibility and effectiveness. Hum Reprod 2005;20:3419-22.
13. van der Leij G, Lammes FB. Radiographic aspects of office hysteroscopic tubal occlusion with siloxane intratubal devices (the Ovabloc method). Int J Gynecol Obstet 1997;59:123-31.
14. Kerin JF, Levy BS. Ultrasound: an effective method for localization of the echogenic Essure sterilization microinsert: correlation with radiologic evaluations. J Minim Invasive Gynecol 2005;12:50-4.
15. Teoh M, Meagher S, Kovacs G. Ultrasound detection of the Essure permanent birth control device: a case series. Aus NZ J Obstet 2003;43: 378-80.
16. Veersema S, Vleugels MP, Timmermans A, Brolmann HA. Follow-up of successful bilateral placement of Essure microinserts with ultrasound. Fertil Steril 2005;84:1733-6.
17. Weston G, Bowditch J. Office ultrasound should be the first-line investigation for confirmation of correct Essure placement. Aus NZ J Obstet Gynecol 2005;45:312-5.
18. Thiel JA, Suchet IB, Lortie K. Confirmation of Essure microinsert tubal coil placement with conventional and volume-contrast imaging threedimensional ultrasound. Fertil Steril 2005;84:504-8.



5 Incorrect position of Essure microinserts 3 months after successful bilateral placement.

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Abstract

Objective To describe incorrect positions of Essure microinserts detected at 3 months' follow-up.

Design Case series report.

Setting Outpatient department of obstetrics and gynecology in a Dutch teaching hospital.

Patient(s) Initial series of 100 patients who underwent hysteroscopic sterilization using Essure between December 2003 and June 2004.

Intervention(s) Hysteroscopic placement of the Essure System, follow-up at 3 months with transvaginal ultrasound (TVU), and hysterosalpingograp (HSG).

Main Outcome Measure(s) Bilateral placement rate, tubal obstruction, and detection of incorrect Essure microinsert localization at follow-up after apparent successful bilateral placement.

Result(s) Bilateral placement of Essure microinserts in one session was successful in 93 women (93%). In 90 of these women (96.8%), tubal obstruction was proven at follow-up 3 months later. Three incorrect positions of an Essure insert were seen: two expulsions and one perforation into the abdominal cavity.

Conclusion(s) Incorrect position of Essure microinserts was seen only when the initial placement procedure was difficult. When a placement procedure was difficult or other suboptimal conditions are present during the procedure, we advise performing a TVU or pelvic X-ray in these women 4 weeks after the procedure or after the first vaginal bleeding, instead of waiting for follow-up after 3 months.

Key Words Essure, Hysteroscopic sterilization , Transcervical sterilization , Perforation, Expulsion

Introduction

Transcervical sterilization using the Essure System (Conceptus, Mountain View, CA) is becoming increasingly popular as a means of permanent birth control. Worldwide, more than 100,000 women have been sterilized with this method. It is a patient-friendly procedure that does not require general anesthesia and surgical incisions (1,2).

During office hysteroscopy the uterine cavity is inspected and the tubal openings identified. The introduction device is inserted in the fallopian tube, after which the device can be deployed and the Essure microinsert remains in position (2). After insertion and deployment, ideally 3-8 coils of the insert are visible outside the tubal opening (2).

An Essure microinsert consists of a stainless steel inner coil, a nickel titanium alloy outer coil, and polyethylene terephthalate (PET) fibres covering the inner coil (1,3). The PET fibres induce a tissue response, which causes fibrous tissue ingrowth and thus tubal occlusion (3, 4). Patients have to use additional contraception until at 3 months' follow-up correct placement of the inserts and/or tubal obstruction is proven.

Transvaginal ultrasound (TVU) examination has proved to be an adequate method to confirm the microinsert position at follow-up (5-8). When ultrasound examination is inconclusive or an undesirable position of an insert is suspected, a hysterosalpingography (HSG) can be performed (8).

Bilateral placement rate in one session ranges from 86% to 91.3% (2,6,11,12). Perforation, expulsion, and inability to place the inserts bilaterally are known undesirable events of the Essure placement procedure. Most of these events described in earlier studies have been detected during the procedure itself and were attributed either to a design problem of the material that was subsequently improved or to incorrect placement procedures (3,4). Malformations or abnormalities of the uterine cavity and the fallopian tubes are associated with placement failure (1,2, 9,10). Other factors, such as tubal spasms, are also suspected to have a negative influence on Essure placement procedures (1,10,12). More recently, a case has been described in which there was no tissue ingrowth with a correctly positioned device 3 months postpartum (13).

Between December 2003 and June 2004 an initial series of one hundred women were sterilized with the Essure System in our teaching hospital. At three months follow-up three patients were diagnosed with an incorrect position of one of the inserts; we report those cases here.

Materials and methods

This was a prospective cohort study set in a university-affiliated teaching hospital with outpatient hysteroscopy facilities, where 500 outpatient hysteroscopic procedures are performed annually. Institutional Review Board approval was not necessary for this study. Placement of Essure devices started in December 2003, and the first 100 procedures were recorded. One gynecologist (S.V.) specialized in hysteroscopy performed all the procedures. The procedure was scheduled in the proliferative phase of the cycle or shortly after a withdrawal bleeding if patients were using oral contraceptives. Women were advised to take a non-steroidal anti-inflammatory drug (NSAID) the evening before and 1 h before the placement of the Essure microinserts.

The procedure was performed using a 5.5-mm continuous flow rigid hysteroscope with a 30° lens (Olympus; Winter and Ibe, Hamburg, Germany) and a 5-French working channel. Uterine distension was obtained using pumped saline solution with a pressure of 100 mm Hg. The hysteroscope was introduced using a vaginoscopic approach without speculum, tenaculum, or local anaesthetics. If bilateral placement was unsuccessful in the first session, a second attempt was offered.

Patients' characteristics and procedure characteristics were recorded in a database. All procedures were recorded on VHS video.

After surgery, patients were instructed about possible complications and when they should contact the hospital. They were scheduled for a 3-month follow-up, which included TVU and HSG. After proven correct position of microinserts at follow-up, patients were given the advice to stop other methods of contraception.

Outcome was defined as successful bilateral placement and tubal obstruction. Incorrect localizations detected at 3 months' follow-up were analyzed. Findings at TVU and HSG were also recorded in the database.

Results

From December 2003 to June 2004, 100 women underwent an Essure procedure. Mean operating time was 10 min (range 4-34 min). Patients were 29-47 years old with a mean age of 38 years, and parity ranged from zero to six with a median of two births (Table 1). Before the procedure, most women (47%) used oral contraception. All of the patients left the hospital within 2 h after the procedure and were able to return to normal activity within 24 hours.

Table 1
Patients' characteristics.

	Mean	Median	Range
Age (yrs)	38	38	29 – 47
Parity	2	2	0 – 6
Operating time (min)	10	8	4 – 34

Bilateral microinsert placement in one session was successfully performed in 93 patients (93%); in seven patients (7%) the procedure failed. A second attempt was performed in three of these seven patients, and in all three cases the second procedure was also unsuccessful.

At 3 months' follow-up, correct cornual localization of both devices was confirmed by ultrasound in 84 (90.3%) of the 93 cases with successful bilateral placement. In 90 patients (96.8%), HSG showed bilateral occlusion of the fallopian tubes. In three patients an incorrect localization of one of the microinserts with patency of the ipsilateral fallopian tube was seen on HSG: one perforation, an expulsion into the uterine cavity, and one complete expulsion. The latter two patients were successfully sterilized in a second Essure placement procedure. We present here the three cases with failure of the Essure system detected at follow-up.

Case Descriptions

Patient A was a 42-year-old multiparous woman. No abnormalities were seen during hysteroscopy. During insertion of the microinsert in the left fallopian tube, a resistance occurred and was eventually over won. This was thought to be a tubal spasm. When bilateral placement was completed, three coils were visible on the right side and six coils on the left side. Procedure time was 10 min.

At TVU follow-up after 3 months, both inserts were not clearly visible. On pelvic X-ray an abnormal configuration of the left microinsert was seen. In evaluating microinsert position with X-ray or HSG, it is very important to note the ''markers'' for the proximal and distal ends of the inner and outer coil.

The inner coil can be recognized very easily as a thin line structure with two landmarks: the distal end, most lateral (first marker), and the proximal end (third marker). The distal end of the outer coil (second marker) is next to the first marker, and the platinum band at the proximal end of the outer coil is visible as the fourth marker. In a normal configuration, the fourth marker is in line with the other three

markers. In this case, the fourth marker was not in line with the other three markers and too close to the second marker. The HSG showed patency of the left tube (Fig. 1).

Retrospectively, the patient had experienced abdominal pain for several weeks after placement of the Essure System. Perforation of the left device into the abdominal cavity was suspected, and a laparoscopy was performed. The Essure microinsert was detected in the omentum. No signs of inflammation or adhesions were seen. During laparoscopy, the insert was removed, and tubal ligation of the left tube was performed using a Filshie Clip.

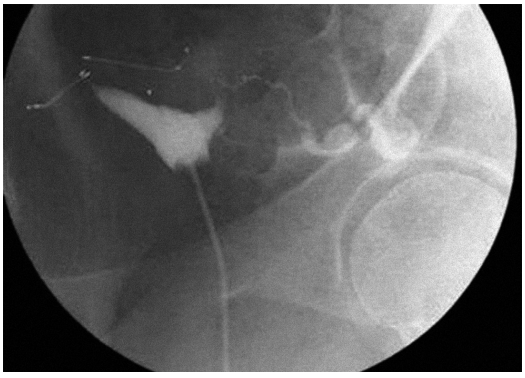
Patient B was a 42-year-old multiparous woman. During hysteroscopy, a normal uterine cavity was seen with some small endometrial polyps. Insertion of both Essure microinserts was difficult. After insertion, one coil extended from the right tubal ostium. The number of coils extending from the left tubal opening was not clearly visible. At the time of the procedure, it was speculated that this was attributable to thickened endometrium. Procedure time was 17 min.

The TVU 3 months later detected only the right microinsert in a cornual position; no insert was seen on the left side. Pelvic X-ray showed one device present in the pelvis. On HSG, the right microinsert was seen with tubal occlusion, whereas the left tube was patent (Fig. 2). The patient had not noticed an expulsion. In a second procedure, another microinsert was placed in the left fallopian tube. After another 3 months, obstruction of both fallopian tubes was proved by HSG.

Patient C was a 43-year-old multiparous woman with a history of two caesarean sections. During the procedure, a levonorgestrel intrauterine device was removed.

Figure 1

The microinsert on the right side shows a normal configuration of the four markers. The left-side insert has an abnormal configuration and an abnormal position in the pelvis; on HSG the left tube is patent.



Intrauterine adhesions were seen in the left tubal corner. Insertion of the left device was very difficult but successful, although it took longer than usual. Owing to the formation of edema caused by the extended procedure time, the placement on the right side became unexpectedly difficult, too. Three coils were visible on the left side and two coils on the right side; total procedure time was 31 min.

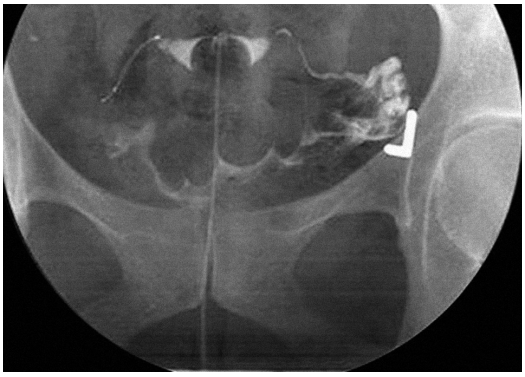
On follow-up TVU, the left insert was visible in a correct position, but the insert on the right side could not be made clearly visible. On pelvic X-ray, the right device was seen in an abnormal position, proximal of the right tube. The HSG showed a patent right fallopian tube (Fig. 3). During hysteroscopy, the right microinsert was floating in the uterine cavity. After removal, another Essure microinsert was placed in the right tube with three coils visible. Control HSG after 3 months showed tubal obstruction on both sides.

Discussion

Perforation rate in our initial series of 100 patients was 1%, which is in accordance with the literature. Through the years, the perforation rate has decreased from 3-7% (2,4) to 1-2,6% (1,9). In 2% of our patients, we observed an expulsion after an initially apparent successful placement procedure. Expulsion from the fallopian tube is reported in 1.3-3.6% and is due to incorrect insertion of the microinsert, mostly concerning placement too proximal in the tube (1,2).

Figure 2

Only the right insert is visible, and the left tube is patent for contrast fluid.

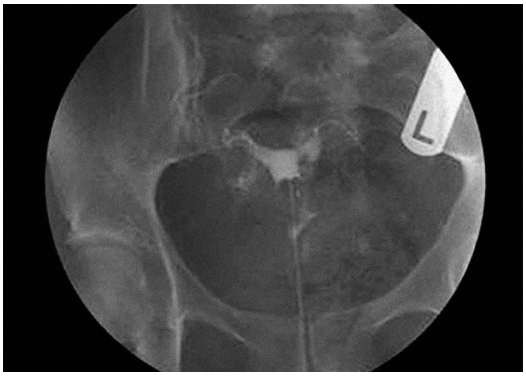


Every procedure has its period of training, and the learning curve for this particular intervention has been shown in other studies to be short, about five completed procedures (1,2). When accustomed to performing a hysteroscopy, physicians rate the Essure placement procedure as simple or moderately simple (1). It is unlikely that the learning curve contributes much to misplacement rates. However, even in the hands of experts, placement procedures can result in an incorrect position of microinserts.

When we review our own cases, we see that in case A, in which the left insert perforated into the abdominal cavity, a resistance thought to be a tubal spasm was over won. In retrospect, this was probably the moment of perforation. The insert migrated to the abdominal cavity in the weeks after the procedure, causing the patient abdominal pain. Why the patient did not contact the hospital with this complaint is unknown. Patient education and staff education are very important to recognize symptoms associated with complications. Tubal spasms can occur during a hysteroscopic procedure, but perforation and thus making a false route with the Essure placement device can mimic a tubal spasm, as we have seen here. Tubal spasms have been reported to have an adverse effect on the Essure placement (1,10,12). A spasmolytic such as butylscopolamine can be administered before the procedure to prevent tubal spasms (12). Use of NSAIDs before the procedure is also associated with better placement rates (1).

Figure 3

The right device has an abnormal position in the pelvis on X-ray, and on HSG the right tube is not obstructed.



In case B, the complete expulsion, the uterine cavity contained some endometrial polyps, which could have blurred vision. The insertion was also more difficult than normal and procedure time was longer than usual. When the procedure was completed, the left insert, which would later be expelled, was not clearly visible. In this case, there were multiple suboptimal conditions that could have caused the insert misplacement. Failure to place the Essure microinserts bilaterally is more often seen in the presence of abnormalities of the uterine cavity or openings of the fallopian tubes (1,2,9,10).

In the case of expulsion into the uterine cavity, case C, the procedure time was significantly longer than average. This was due to removal of the intrauterine device in the beginning of the procedure and to the placement procedure that turned out to be difficult on both sides. The first device was placed on the side with adhesions, which was thought to be the most difficult side to place, but because of the prolonged procedure time, the other side turned out to be difficult to place as well. This last microinsert was later expelled into the uterine cavity. After placement, both sides showed a normal number of coils extending from the uterotubal corner. We think the prolonged procedure time caused a fluid collection to form under the endometrium and thus complicated the placement of the second insert. The second insert was probably placed under a layer of endometrium instead of in the opening of the tube, and a shedding of endometrium, such as in a menstrual bleeding, released the insert.

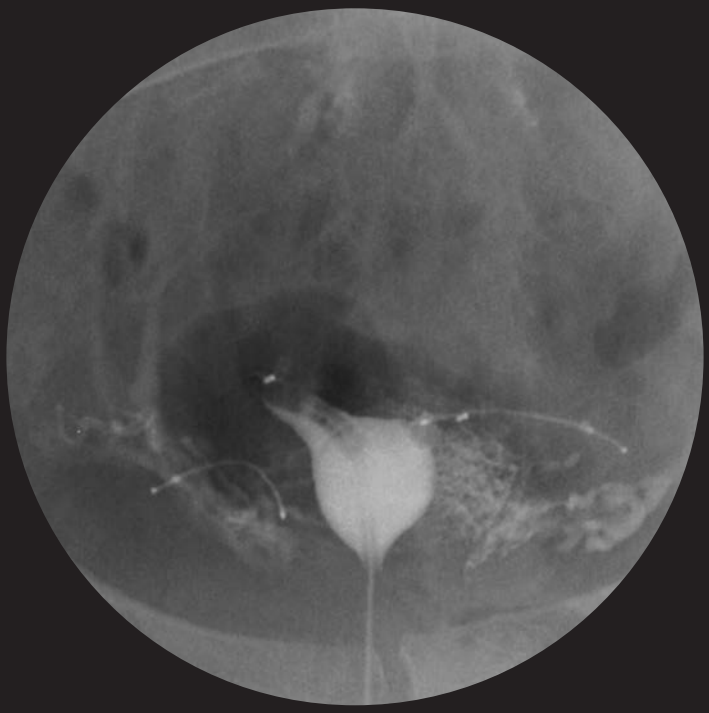
In conclusion, perforation into the abdominal cavity and expulsion from the fallopian tube can occur with or after placement of Essure microinserts, even in the hands of experienced physicians. It is important that patients are seen at follow-up with at least TVU to make sure that microinserts are in the correct position. Only after normal findings at followup examination should patients get the advice to stop contraception.

Complications can be detected during the procedure itself or at follow-up. When, during the procedure, there is doubt about the position of a microinsert, a TVU can be performed at that time. But one should realize that in case of perforation and expulsion, most incorrectly placed microinserts will migrate in the period after the procedure. A majority of cases will not be detected during or directly after the procedure.

We advise screening patients with apparent successful bilateral placement but with difficult placement procedures, other suboptimal conditions during the procedure, or abdominal pain earlier than 3 months after the procedure. Initially this can be done with TVU after the patient's first period or withdrawal bleeding (approximately 4 weeks), and when in doubt, a pelvic X-ray can be performed. Perforation and expulsion do not seem to cause serious adverse events in patients. These women will have to undergo a laparoscopy to trace and remove the missing insert in case of perforation, and undergo a new Essure insertion procedure or choose a different form of birth control.

References

1. Cooper JM, Carignan CS, Cher D, Kerin JF. Microinsert nonincisional hysteroscopic sterilization. Obstet Gynecol 2003;102:59-67.
2. Kerin JF, Cooper JM, Price T, Van Herendael BJ, Cayuela-Font E, Cher D, et al. Hysteroscopic sterilization using a microinsert device: results of a multicenter phase II study. Hum Reprod 2003;18:1223-30.
3. Kerin JF, Carignan CS, Cher D. The safety and effectiveness of a new hysteroscopic method for permanent birth control: results of the first Essure PBC clinical study. Aus N Z J Obstet 2001;41:364-70.
4. Valle RF, Carignan CS, Wright TC. Tissue response to the Stop microcoil transcervical permanent contraceptive device: results from a prehysterectomy study. Fertil Steril 2001;76:974-80.
5. Teoh M, Meagher S, Kovacs G. Ultrasound detection of the Essure permanent birth control device: a case series. Aust N Z J Obstet Gynecol 2003;43:378-80.
6. Thiel JA, Suchet IB, Lortie K. Confirmation of Essure microinsert tubal coil placement with conventional and volume-contrast imaging three-dimensional ultrasound. Fertil Steril 2005;84:504-8.
7. Kerin JF, Levy BS. Ultrasound: an effective method for localization of the echogenic Essure sterilization microinsert: correlation with radiologic evaluations. J Minim Invasive Gynecol 2005;12:50-4.
8. Veersema S, Vleugels MP, Timmermans A, Brolmann HA. Follow-up of successful bilateral placement of Essure microinserts with ultrasound. Fertil Steril 2005;84:1733-6.
9. Kerin JF, Munday DN, Ritossa MG, Pesce A, Rosen D. Essure hysteroscopic sterilization: results based on utilizing a new coil catheter delivery system. J Am Assoc Gynecol Laparosc 2004;11:388-93.
10. Ubeda A, Labastida R, Dexeus S. Essure: a new device for hysteroscopic tubal sterilization in an outpatient setting. Fertil Steril 2004;82:196-9.
11. Litta P, Cosmi E, Sacco G, Saccardi C, Ciavattini A, Ambrosini G. Hysteroscopic permanent tubal sterilization using a nitinol-dacron intratubal device without anesthesia in the outpatient setting: procedure feasibility and effectiveness. Hum Reprod 2005;20:3419-22.
12. Chern B, Siow A. Initial Asian experience in hysteroscopic sterilization using the Essure permanent birth control device. BJOG 2005;112:1322-7.
13. Karthigasu KA, Garry R, Hart R. Case report of failed tubal occlusion using Essure pbc (permanent birth controle) hysteroscopic sterilization procedure. Aust N Z J Obstet Gynecol 2006;46:365-7.



6 Unintended pregnancies after Essure sterilization in the Netherlands

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Abstract

Objective To analyze the data of cases of unintended pregnancies after Essure sterilization.

Design Retrospective case series analysis.

Setting National multicenter.

Patient(s) Ten cases of unintended pregnancies after Essure sterilization in the Netherlands were reported from August 2002 through May 2008.

Intervention(s) Data on the hysteroscopic Essure sterilization procedures and post-procedure confirmation tests of the reported cases were reviewed and analyzed by two authors. The causes of the unintended pregnancies were determined in agreement with the physicians who performed the sterilizations.

Main Outcome Measure(s) Most pregnancies occurred in patients with only one device placement and bilateral occlusion on hysterosalpingography (HSG). Other cases included misinterpretation of HSG, undetected abnormal device position by ultrasound, one undetected pre-procedure pregnancy, and two patient failures to follow up with the physician advice.

Conclusion(s) The risk of pregnancy after hysteroscopic sterilization may be reduced by strictly following the follow-up protocol, performing a urinary pregnancy test on the day of the procedure, and instructing the patient to return for the follow-up visit. A procedure with only a single device placement in a patient without a history of salpingectomy of the heterolateral tube should be considered unsuccessful.

Key Words Essure sterilization, Confirmation test, Unintended pregnancy, Hysterosalpingography, Ultrasound

Introduction

Transcervical sterilization using the Essure System (Conceptus, Mountain View, CA) is becoming increasingly popular as a means of permanent birth control. Worldwide, more than 200,000 women have been sterilized with this method. In combination with the vaginoscopic no-touch technique of hysteroscopy, it is a patient-friendly procedure that does not require general or regional anesthesia or surgical incisions (1,2). In the Netherlands, around 9,000 women are sterilized each year (3). In May 2008, Essure sterilization was first offered to patients who requested permanent contraception in 45 out of 100 Dutch hospitals. Since its introduction in 2002, more than 6000 procedures have been performed. All gynecologists performing the Essure method are appropriately trained gynecologists with experience in office hysteroscopy who have been trained by a precept in the procedure. During office hysteroscopy, the uterine cavity is inspected and the tubal openings are identified. The introduction device is inserted into the fallopian tube, after which the device is allowed to expand while the Essure microinsert remains in position. After insertion and expansion of the microinsert,ideally three to eight coils of the insert are visible outside the tubal opening (2). The Essure microinsert consists of a stainless steel inner coil, a nickel titanium alloy outer coil, and polyethylene terephterate (PET) fibres covering the inner coil (1,4). The PET fibres induce a tissue response, which causes fibrous tissue to grow and hence tubal occlusion (4,5). Patients have to use additional contraception until correct placement of the inserts and/or tubal obstruction is proven at 3-month follow-up. Transvaginal ultrasound examination has proven to be an adequate method to confirm the microinsert position at follow-up (6-9). When ultrasound examination is inconclusive or an abnormal location of a microinsert is suspected, a hysterosalpingography (HSG) is indicated.

The inability to place the inserts bilaterally, perforation, and/or expulsion are known undesirable events of the Essure placement procedure. Most of these events described in previous studies have been detected during the procedure itself and were either attributed to a design problem of the material that was subsequently improved or to incorrect placement procedures (4,5). Malformations or abnormalities of the uterine cavity and the fallopian tubes are associated with placement failure (1,2,10,11). Other factors, such as tubal spasms, are also suspected to have a negative influence on Essure placement procedures (1,11,12).

Because hysteroscopic sterilization is a rather new method, it is important that all pregnancies are reported and that the cases are reviewed to determine the cause of the unintended pregnancy. Some of the causes might be preventable. Understanding these causes can be helpful to improve the follow-up protocols and reduce the number of failures in the future.

Table 1
Overview of 10 cases of unintended pregnancies after Essure sterilization .

Case	Age	Parity	Year	Confirmation test	Interval[a], months	Cause of failure	Conclusion [B]
A	36	0	2004	US, HSG	8	Perforation	Misread
B	31	4	2005	US	3	Expulsion	NC
C	41	2	2005	HSG	24	Unilateral placement	NA
D	38	3	2006	US	10	Expulsion	Misread?
E	36	1	2006	US	11	Unknown	Unknown
F	40	2	2006	US	7	Perforation	NA
G	39	5	2007	—	6	Partial expulsion	NC
H	41	2	2007	HSG	6	Unilateral placement	NA
I	41	1	2007	HSG	4	Unilateral placement	NA
J	24	3	2007	—	0	Luteal pregnancy	NA & NC

[a] Interval between Essure placement and pregnancy. US = ultrasound.
[b] NA = nonadherence to protocol; NC = patient noncompliance.

Materials and methods

This study is a retrospective multicenter case series in the Netherlands. An estimated 6,000 hysteroscopic sterilizationswere performed in 45 hospitals in the Netherlands from August 2002 to May 2008 as estimated from the data from the Dutch distributor. All procedures were performed by appropriately trained gynecologists with experience in office hysteroscopy who participated in a training course for hysteroscopic sterilization with Essure. The procedures were scheduled in the proliferative phase of the cycle or shortly after a withdrawal bleeding if patients were using oral contraceptives. Women were advised to take a non-steroidal anti-inflammatory drug on the evening before and 1 hour before placement of the Essure microinserts. The majority of procedures were performed by a vaginoscopic approach hysteroscopy, using a 4.2 to 5.5 mm continuous-flow rigid hysteroscope without the use of local or general anesthesia. Uterine distension was obtained using saline that was introduced through a fluid management system or by gravity. From the beginning, all patients underwent a HSG after 3 months of follow-up. Since the introduction of the Dutch protocol for the follow-up of Essure sterilization in 2005, vaginal ultrasound has been used for confirmation of tubal-cornual location of the

microinserts after an uncomplicated successful bilateral placement. In all other cases, an HSG is still indicated (6). Patients were instructed to continue alternative contraception until the follow-up visit at 3 months.

The reported cases were reviewed by one of two authors who participated in the faculty of the physician training courses and who supervised as preceptors all first three to five procedures of beginning gynecologists of Essure sterilization in The Netherlands.

Results

As of May 2008, 10 pregnancies were reported to the authors. Table 1 provides the causes of the pregnancies as determined by the reporting physicians in collaboration with the reviewers. In case A, there was a misinterpretation of the HSG at follow-up. The right device was in an unsatisfactory position (perforation), with patency of the right tube. This patient was also examined with ultrasound before the HSG, and an abnormal location of the microinsert or even perforation was not recognized. In two cases, the reported pregnancy was associated with a noncompliance of the patient. In case B, the physician suspected an abnormal location of one microinsert on ultrasound at the 3-month follow-up, but the patient did not return for HSG. One patient, patient G, failed to return for the 3-month follow-up. After delivery of a healthy child, ultrasound examination showed both devices to be in an apparently normal position, while on HSG there was an unsatisfactory device location, with kinking of the left device and patency of the left tube.

One patient, patient D, showed a complete expulsion of one device on X-ray after the delivery of a child. In this case, the ultrasound examination at her 3-month follow-up had probably been misinterpreted. A second patient, patient F, who had a misinterpretation of the ultrasound at 3 months of follow-up, had a complicated placement, with placement of a third device after a spontaneous expulsion of the first device. During laparoscopic sterilization after termination of pregnancy, one device was located intramurally under the serosa because of partial perforation, while the other one was in a proper position in the other tube (13).

One pregnancy occurred before the device placement was done (patient J). Taking the probable date of conception into account, it must have been a luteal-phase pregnancy due to a failure of contraception before the procedure. A urinary pregnancy test on the day of the procedure was not performed.

In three patients (C, H, and I) there was a unsuccessful attempt of device placement on one side, and only one device was placed. On HSG, the heterolateral tube seemed to be occluded.

One patient, patient E, delivered a healthy child by caesarean section. Tubal sterilization was performed during the procedure, but no information was obtained about the location of the device and patency of the tubes during surgery. At the 3-month follow-up after the initial uneventful procedure, both microinserts were in normal position on ultrasound.

Discussion

The Essure device has become an increasingly popular alternative for laparoscopic sterilization in the Netherlands and other Western countries because of its minimally invasive and well-tolerated placement without the need for general or local anesthesia. Since its introduction in the Netherlands in 2002, 10 unintended pregnancies have been reported. The majority of these pregnancies (cases B, C, F, G, H, I, and J) are associated with patient noncompliance or non-adherence to the Dutch follow-up protocol introduced in 2005.

It is apparent that Essure sterilization will not prevent pregnancy in all cases. It is impossible to prevent pregnancy in all cases with any contraceptive technique other than bilateral oophorectomy. There will always be product failures and human errors that result in pregnancy.

Until now, no pregnancies have been reported in patients from the phase II or pivotal trial, but recently Levy et al. reported about 64 pregnancies after Essure sterilization that were reported to the device company from countries all over the world up until December 2005 (14). The most important cause of reported pregnancies was patient or physician non-adherence to protocol (47%). The most common manifestation of non-adherence was the patient failure to return to the follow-up visit. The second most common finding was misinterpretation of X-ray films or HSG at the follow-up visit. Improperly read or interpreted results accounted for 18 (28%) of the reported unintended pregnancies. Contraceptive failure before device placement occurred in eight (12.5%) of the reported pregnancies; seven of these pregnancies were luteal-phase pregnancies.

Two more cases of pregnancy were reported (15). One patient cancelled the HSG due to financial concerns and was lost to follow-up. The second patient underwent a followup evaluation appropriately at 3 months. Her HSG appeared to indicate proper placement of the microinserts with subsequent bilateral tubal occlusion. Upon removal of the uterus by vaginal hysterectomy 6 months after termination of pregnancy, a microinsert was noted protruding through the upper myometrium at the left cornu of the uterus.

In this series of 10 cases of unintended pregnancies in the Netherlands, there were only two cases (B and G) of non-compliance of the patient (20%) Only one patient failed to return for the 3-month follow-up visit.

In three cases (A, D, and F), an abnormal position of one device was not recognized by the confirmation test (A: HSG + ultrasound; D and F: ultrasound) at the follow-up. The ultrasound images are not useful for reviewing because the final decision and results of the ultrasound examination are made by the physician performing a real-time ultrasound scan. The real-time images of ultrasound examination are not recorded and therefore not available for reviewing. This is one of the main disadvantages of ultrasound used as a diagnostic tool to confirm satisfactory device localization after Essure sterilization. Saved three-dimensional (3D) ultrasound volume data may serve that purpose in the future. Patient A, with the misinterpretation of the HSG (perforation of left device), was also examined by ultrasound during the 3-month follow-up visit. An abnormal position of one of the devices was not suspected. The procedure of case F was complicated by a spontaneous expulsion of the first device and placement of a third device. Only an ultrasound examination was done to confirm bilateral localization. According to the Dutch follow-up protocol, in this case an HSG was indicated. In addition, one patient who was lost to follow-up had a normal ultrasound after termination of pregnancy, while on HSG there was an abnormal positioning of one device with tubal patency. The explanation for these contradictions in the results of these different diagnostic tests could be that it is difficult to visualize the entire device on a single image plane. The full distal (tubal) extent of the device cannot always be followed.

The radio opaque markers at the ends of the coils are not visible on ultrasound images. The outer coil is always visible as two interrupted echogenic lines. The inner coil can be incidentally seen as a central linear echogenic line (16). In case of a partial perforation with the outer coil located intramurally or near the cornual-isthmic junction, the location of the microinsert could resemble a normal position on ultrasound. This means that if there is any suspicion of tubal or myometrial perforation (i.e., a sudden drop in resistance or difficult sounding of the tube) an HSG should be performed. It may be that 3D ultrasound with or without contrast infusion improves the diagnostic characteristic of two-dimensional imaging (8,17). Another pitfall of ultrasound could be that one device is recognized twice by turning the ultrasound probe from one site to the other. The same device will be seen at the opposite site of the uterus after turning the probe 180 degrees. According to the instructions to the physicians in the training courses, both devices have to be recognized at the same time in one single plane during ultrasound examination to be sure that two devices are examined. A print or recording of this view is recommended. Training should be initiated to guarantee the specific ultrasound

skills needed to recognize adequate placement of the microinserts in the patients undergoing Essure sterilization.

In the three patients with failed attempts on one side (C, H, and I), the delivery system could not be advanced to the ostia, and only one device was placed in a proper position. Subsequent HSGs showed occlusion of both tubes, which was thought to be caused by fibrosis of the tube. In an earlier report, such cases were omitted from the failures and considered to be successful (11). We advise that in case of a unilateral placement and an unsuccessful placement at the opposite site, without a history of tubectomy for this site, the procedure is considered to be unsuccessful and no HSG or other technique for evaluation should be performed. Even in instances in which the follow-up HSG shows occlusion of the tube, the occlusion could be caused by factors other than the device. Therefore, to rely on the device for contraception, it must be in a proper position and show occlusion on HSG.

Probably not all cases of pregnancy have been reported to the authors, although the estimated number of unreported cases is low. The number of pregnancies, 10 in 6,000, is similar to the number published earlier for global data, 64 in 50,000. The pregnancy rate is low, and it seems that the majority of the cases appear to be preventable. Misinterpretation of radiological as well as ultrasound imaging does occur.

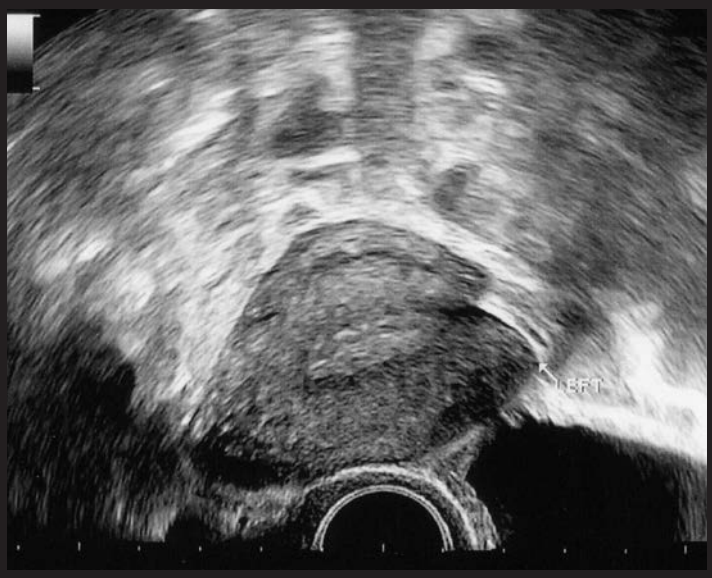
The use of ultrasound imaging diminishes the need for radiological assessment, although the printed images are not useful for retrospective evaluation of abnormal localization of devices and other complications after microinsert placement. Procedures have to be performed by a gynecologist who has been properly trained in the technique as well as in the diagnostic tests during the follow-up visit. Patients have to be informed about the complication risks of hysteroscopic sterilization and the need for adequate contraception before the procedure and until the 3-month confirmation test has shown a satisfactory position of both devices.

Conclusion

This study illustrates that hysteroscopic sterilization with Essure is a popular and reliable alternative for laparoscopic sterilization in the Netherlands. The risk of pregnancy with hysteroscopic sterilization may be reduced by strictly following the protocol for follow-up, performing a urinary pregnancy test on the day of the procedure, and instructing the patient to return for the follow-up visit. A procedure with only a single device placement in a patient without a history of tubectomy of the heterolateral tube should be considered as unsuccessful.

References

1. Cooper JM, Carignan CS, Cher D, Kerin JF. Microinsert nonincisional hysteroscopic sterilization. Obstet Gynecol 2003;102:59-67.
2. Kerin JF, Cooper JM, Price T, Van Herendael BJ, Cayuela-Font E, Cher D, et al. Hysteroscopic sterilization using a microinsert device: results of a multicenter phase II study. Hum Reprod 2003;18:1223-30.
3. Prismant HCaAI. Landelijke LMR-informatie. Verrichtingen: destructie of afsluiting van tubae faloppii mbv endoscopie. 2004. Utrecht, the Netherlands, Prismant, Health Care and Advise Institute.
4. Kerin JF, Carignan CS, Cher D. The safety and effectiveness of a new hysteroscopic method for permanent birth control: results of the first Essure PBC clinical study. Aus NZ J Obstet 2001;41:364-70.
5. Valle RF, Carignan CS, Wright TC. Tissue response to the STOP microcoil transcervical permanent contraceptive device: results from a prehysterectomy study. Fertil Steril 2001;76:974-80.
6. Veersema S, Vleugels MP, Timmermans A, Br€olmann HA. Follow-up of successful bilateral placement of Essure microinserts with ultrasound. Fertil Steril 2005;84:1733-6.
7. Teoh M, Meagher S, Kovacs G. Ultrasound detection of the Essure permanent birth control device: a case series. Aus NZ J Obstet 2003;43: 378-80.
8. Thiel JA, Suchet IB, Lortie K. Confirmation of Essure microinsert tubal coil placement with conventional and volume-contrast imaging three-dimensional ultrasound. Fertil Steril 2005;84:504-8.
9. Kerin JF, Levy BS. Ultrasound: an effective method for localization of the echogenic Essure sterilization microinsert: correlation with radiologic evaluations. J Minim Invasive Gynecol 2005;12:50-4.
10. Kerin JF, Munday DN, Ritossa MG, Pesce A, Rosen D. Essure hysteroscopic sterilization: results based on utilizing a new coil catheter delivery system. J Am Assoc Gynecol Laparosc 2004;11:388-93.
11. Ubeda A, Labastida R, Dexeus S. Essure: a new device for hysteroscopic tubal sterilization in an outpatient setting. Fertil Steril 2004;82:196-9.
12. Chern B, Siow A. Initial Asian experience in hysteroscopic sterilization using the Essure permanent birth control device. Br J Obstet Gynecol 2005;112:1322-7.
13. Langeveld J, Veersema S, Bongers MY, Koks C. Tubal perforation by essure; three different clinical presentions. Fertil Steril. Published online 8 August 2008 [Epub ahead of print].
14. Levy B, Levie MD, Childers ME. A summary of reported pregnancies after hysteroscopic sterilization. J Min Invas Gynaec 2007;14:271-4.
15. Moses AW, Burgis JT, Bacon JL, Risinger J. Pregnancy after Essure placement: report of two cases. Fertil Steril 2008;89:724.e9-11.
16. Wittmer MH, Brown DL, Hartman RP, Famuyide AO, Kawashiuma A, King BF. Sonography, CT, and MRI appearance of the Essure microinsert permanent birth control device. Am J Reprod 2006;187:959-64.
17. Connor VF. Contrast infusion sonography to assess microinsert placement and tubal occlusion after Essure. Fertil Steril 2006;85:1791-3.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7 Confirmation of Essure placement using transvaginal ultrasound.

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Abstract

Objective To evaluate the protocol for confirmation of satisfactory Essure placement using transvaginal ultrasound.

Design Prospective multicenter cohort study (Canadian Task Force classification II-2).

Setting Outpatient departments of 4 teaching hospitals in the Netherlands.

Patient(s) Eleven hundred forty-five women who underwent hysteroscopic sterilization using the Essure device between March 2005 and December 2007.

Intervention Transvaginal ultrasound examination 12 weeks after uncomplicated successful bilateral placement or as indicated according to the transvaginal ultrasound protocol after 4 weeks, and hysterosalpingography (HSG) at 12 weeks to confirm correct placement of the device after 3 months.

Measurements & Main results The rate of successful placement was 88.4% initially. In 164 women (15%), successful placement was confirmed at HSG according the protocol. In 9 patients (0.84%), incorrect position of the device was observed at HSG. The cumulative pregnancy rate after 18 months was 3.85 per thousand women.

Conclusion(s) Transvaginal ultrasound should be the first diagnostic test used to confirm the adequacy of hysteroscopic Essure sterilization because it is minimally invasive, averts ionizing radiation, and does not decrease the effectiveness of the Essure procedure.

Key Words Essure, Confirmation test, Transvaginal ultrasound, HSG, Placement rate, Cumulative pregnancy rate

Introduction

Transcervical sterilization with Essure (Conceptus Inc., Mountain View, CA) is becoming increasingly popular in the Netherlands. In combination with the vaginoscopic procedure of hysteroscopy, it is a patient friendly procedure that does not require general or regional anesthesia (1,2). It is highly effective, with a 5-year effectiveness rate of 99.8% (3). Consequently, hysteroscopic sterilization is rapidly replacing interval laparoscopic sterilization. More than 9,000 women have been sterilised in 60 Dutch clinics using this method since its introduction in 2002 (Sigma Medical BV, Apeldoorn, the Netherlands).

The European Health Office approved the Essure method in 2001, and the US Food and Drug Administration (FDA) approved the method in 2002. Because the microinserts are highly effective when placed in the proper site and configuration, the European Health Office requires radiographic examination to confirm adequate position and configuration (4), and the FDA requires hysterosalpingography (HSG) at 3 months after placement of the device.

Transvaginal ultrasound (TVU) has proved to be an adequate alternative method for confirmation of the microinsert placement at follow-up (5-8).

It has great advantages over radiographic examination and HSG because it is a nonionizing method of imaging. It has the ability to locate the device within the enveloping tissue, and additional information is gained about surrounding soft-tissue structures. It can be performed on an outpatient basis in departments of gynecology by the patient's own physician, and can be repeated at any time without risk to the patient. However, systematic use of TVU as a first-line confirmation test has not been studied in detail.

Since the introduction of Essure in the Netherlands in 2002, HSG is scheduled at 3 months after an Essure procedure according the recommendations of the FDA. The first scout film of the HSG, without constrast medium, was regarded as the X pelvis requested by the European Health Organization. In January 2005, a revised protocol for follow-up after Essure sterilization was introduced in the Netherlands (Fig. 1) to reduce the need for radiologic confirmation (X-ray examination and HSG), without compromising the effectiveness of Essure (5). In January 2005, a revised protocol for follow-up of Essure sterilization was introduced in the Netherlands (Fig. 1) to reduce the number of HSGs without compromising the effectiveness of Essure.

With this new Dutch protocol, TVU is used for the 3-month confirmation of tubocornual location of the microinserts after an uncomplicated successful bilateral placement.

The criteria for a normal successful bilateral procedure include procedure time of 15 minutes or less, microinsert visible after placement, fewer than 9 coils protruding into the uterine cavity, and no unusual events during the procedure. In all other cases, HSG is still indicated (5). A procedure with only a single device placement in a patient without a history of tubectomy of the heterolateral tube should be considered unsuccessful, and HSG should be abandonded, because of a high risk of false positive confirmation of occlusion of the heterolateral tube. When findings at ultrasound examination are inconclusive or abnormal location of a microinsert is suspected, HSG is indicated.

The objectives of the present study was to evaluate the revised protocol based on first-line confirmation using TVU at 3 months after uncomplicated successful Essure sterilization and to analyze the rate of success of placement and effectiveness of the method.

Figure 1

Flow chart of follow-up protocol after Essure sterilization. a. Begin hysterosalpingography with plain scan (without contrast medium). b. If patient uses non-steroidal anti-inflammatory drugs, corticoids, or cytostatic agents, perform hysterosalpingography after 6 months.

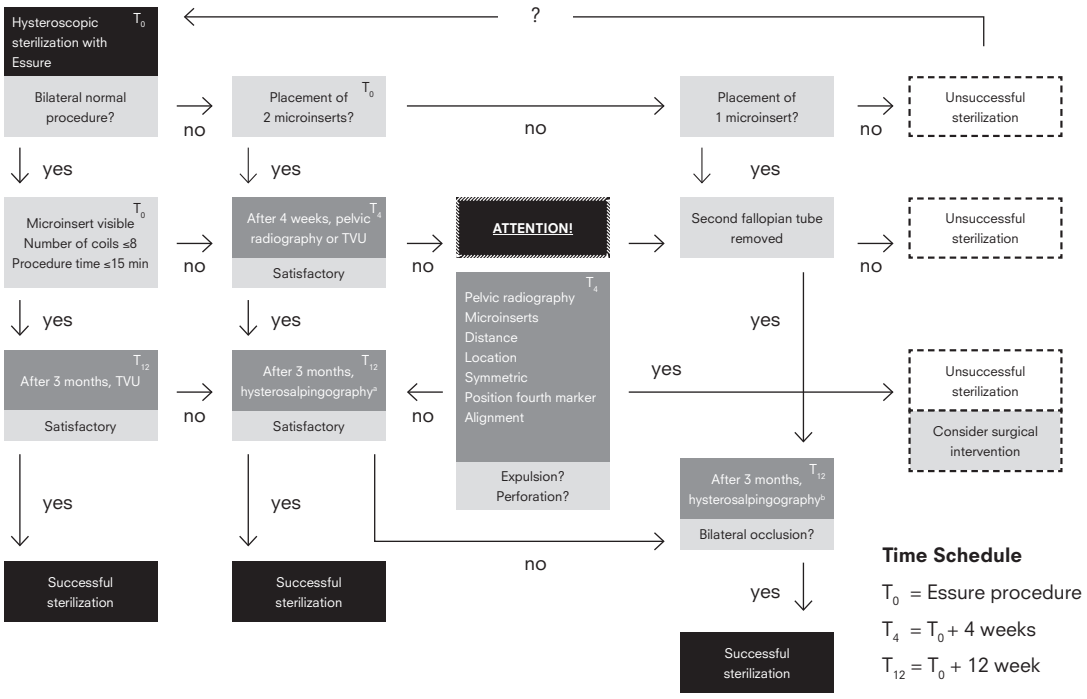


Table 1
Patient demographic characteristics

Variable	Value
No. of patients	1145
Age, mean (SD; 95% CI), y	39.2 6 4.7 (38.9–39.5)
Body mass index, mean (SD; 95% CI)	25.1 6 5.1 (24.8–26.0)
Parity, No. (%)	
0	116 (10.1)
1	159 (14.0)
2	543 (47.4)
3	225 (19.7)
0,3	92 (8.0)
Contraception, No. (%)	
Condom	301 (26.3)
Oral contraceptive/vaginal ring	512/6 (45.2)
LNG IUD/MLCu-375	70/27 (8.5)
Other/none	262 (22.9)

LNG IUD = levonorgestrel intrauterine device; MLCu-375 = multiload copper contraceptive device.

Materials and Methods

All 1145 patients who underwent hysteroscopic sterilization using Essure at 5 clinics from March 2005 up to, but not including, January 2008 were enrolled in the study. The procedures were performed by 9 appropriately trained gynecologists with experience in office hysteroscopy and who participated in a training course for hysteroscopic sterilization using Essure. The procedures were scheduled in the proliferative phase of the cycle or shortly after withdrawal bleeding if patients were using oral contraceptives. Women were advised to take a non-steroidal anti-inflammatory drug on the evening before the procedure and 1 hour before placement of the Essure microinserts. Procedures were performed via vaginoscopic hysteroscopy using a 4.2 to 5.5mm continuous-flow rigid hysteroscope, without the use of local or general anesthesia. Uterine distension was obtained using saline solution via a fluid management system used in the hospital setting or via gravity.

Three months after successful uncomplicated bilateral placement as defined by the protocol, TVU was planned according to the Dutch protocol to confirm correct intramural position of the device at the tubocornual junction of the uterus. In case of difficult placement, procedure time longer than 15 minutes, incorrect number of coils (none or more than 10), or prolonged pain after the procedure, patients were scheduled to undergo an additional TVU examination at 4 weeks after the procedure, followed by HSG at 3 months after the procedure.

If the ultrasound examination after 3 months was inconclusive because the microinserts were not visible or seemed to be in a location other than the tubocornual junction, HSG was indicated. In cases of successful placement in a patient with a history of salpingectomy on the other side, HSG was also required according the protocol (Fig. 1).

Patients were instructed to continue alternative contraception until the 3-month follow-up visit. After correct positioning of the microinserts was proved at follow-up, patients were advised to discontinue other methods of contraception. They were instructed to contact the hospital in case of any complication or unintended pregnancy.

Written informed consent was obtained from all patients. Patient characteristics, procedure features, and results of TVU and HSG were recorded in a database. Institutional review board approval was not necessary for this study.

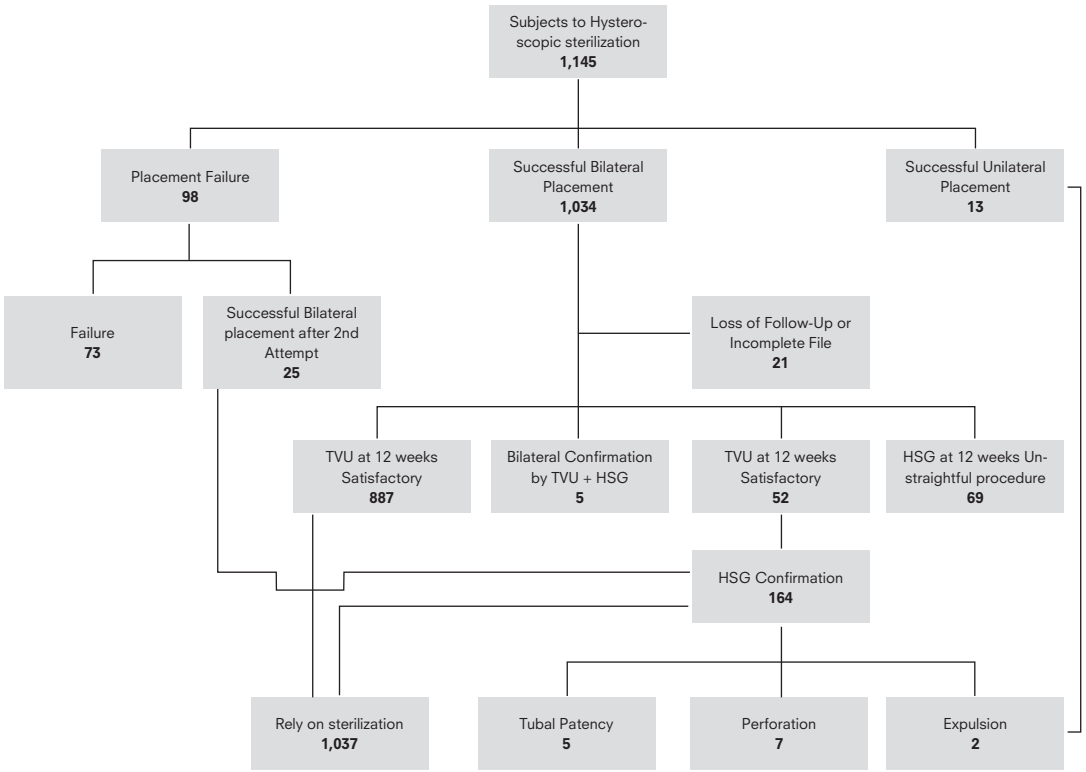
Results

Patient demographic data are given in Table 1. Of 1145 hysteroscopic sterilization procedures, bilateral placement was successful in 1,034 (90.3%), unilateral placement was successful in 13 patients (1.1%), and bilateral placement was successful after the second attempt in 25 patients (2.2%) (Fig. 2). The overall successful placement rate was 93.6% (1,072 of 1,145 intentions to treat). Thirty-five intrauterine devices (IUDs) were left in situ during the procedure, and were removed at the 3-month follow-up visit. Mean procedure time (scope in to scope out) of all procedures was 7.2 minutes (95% CI: 7.0-7.4). Mean procedure time for successful bilateral placement was 6.73 minutes (95% CI: 6.52-6.94), while for unsuccessful placement was 11.84 minutes (95% CI: 10.26-12.70). Mean procedure time for successful single placement in patients with only 1 tube was 5.82 minutes (95% CI: 3.76-7.88).

In 69 of 1,145 patients with intention to treat (6.0%), Essure sterilization was successfully completed; however, the procedure was not considered straightforward. According to the Dutch protocol, TVU was scheduled at 4 weeks after the procedure, and HSG at 3 months. In 52 cases (4.5%), the ''standard'' 3-month TVU was inconclusive; thus, HSG was scheduled as outlined in the protocol.

Figure 2

Flow diagram of enrolled patients.



In 50 of these 52 patients, HSG confirmed bilateral occlusion with normal position of the devices. Only in 2 of these patients was there abnormal positioning of 1 device: expulsion and perforation, respectively. Including patients with a successful second attempt and successful single placement, in 159 patients HSG was indicated at 3 months. In 1 patient who refused HSG, pelvic radiographic examination confirmed adequate localization and configuration of the devices (Fig. 3).

Another 5 women underwent HSG outside of the agreed protocol despite uncomplicated Essure procedures (Fig. 4). Thus, 14.3% of patients (164 of 1145) with intention to treat underwent HSG. In 7 patients (4.3%), HSG demonstrated patency of 1 or both tubes, with normal positioning of the devices.

In 2 of these 7 patients, the second HSG at 6 months after the procedure still showed patency of 1 tube. Three patients decided not to undergo a second HSG, and relied on operative sterilization while there was still patency as demonstrated at HSG.

Figure 3

X-ray film shows a levonorgestrel intrauterine device and Essure microinserts.

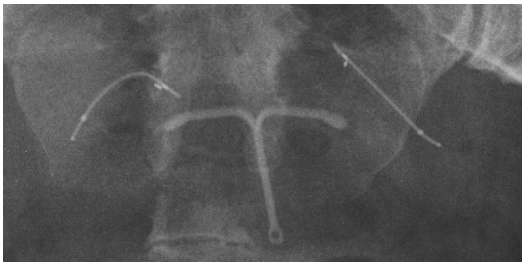
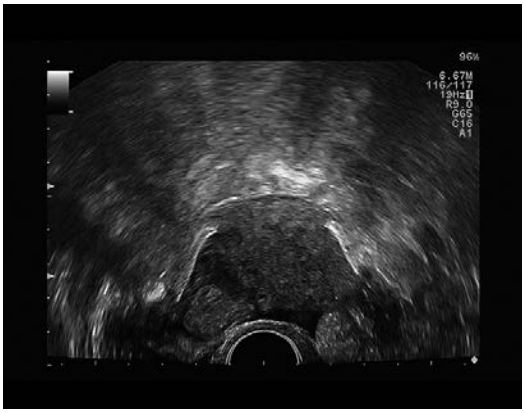


Figure 4

Transvaginal ultrasound image of both Essure microinserts.



In 9 patients, HSG showed evidence of an abnormal position of 1 or 2 devices (2 expulsions and 7 perforations), and these patients were instructed not to rely on the sterilization procedure.

At 3-months, 21 patients were lost to follow-up. Moreover, because of missing data in the files, only 1037 patients were instructed to rely on the sterilization.

The 24-month pregnancy rate was 3.86 per 1,000 (4 of 1,037 patients). In 1 patient, radiographic examination demonstrated complete expulsion of 1 device after delivery of a healthy child. It is probable that findings at TVU examination at 3-month follow-up were misinterpreted or that expulsion occurred after the 3-month visit. In the second patient, placement was complicated, and a third device was placed after spontaneous expulsion of the first device. Violation of the control

protocol occurred in that only TVU was performed instead of HSG at 3 months. At this TVU, the position of the devices was misinterpreted. During laparoscopic sterilization after termination of pregnancy, 1 device was located intramural under the serosa due to partial perforation, and 1 was in the proper position in the contralateral tube. In the third patient, device placement was unsuccessful on 1 side, and only 1 device was placed. At HSG, the contralateral tube seemed to be occluded, and the patient was instructed incorrectly to cease alternative contraception. This was also a violation of the Dutch protocol. In the fourth patient, placement was complicated, with a levonorgestrel IUD in situ. After placement of the first device, the IUD was removed; however, the other ostium could not be observed. During the second attempt with the patient under general anesthesia in the operating room, this ostium was opened with a grasping forceps, and a second device was placed easily. The TVU at 4 weeks after the second procedure showed both devices in a normal tubocornual position. The HSG after 3 months showed bilateral tubal occlusion. During laparoscopic examination after termination of pregnancy, 1 device was intramural under the serosa due to partial perforation, and the other was in a proper position in the contralateral tube. During laparoscopy, tubal patency could be evoked using methylene blue pertubation with high pressure.

Discussion

With the introduction of the revised protocol for confirmation of Essure sterilization, the number of radiologic diagnostic HSGs for verification of hysteroscopic sterilization has been reduced dramatically, from 100% to 14.3% of all successful placements, without compromising the reliability of the sterilization. With this new protocol, it is possible to identify a large subgroup of patients who can rely on Essure sterilization without the standard 3-month HSG confirmation. In a multicenter cohort study, the rate of successful placement was 93.6%. Patient compliance with the 3-months control with TVU as the confirmation test was 98%. The 24-month cumulative pregnancy rate was 3.86 per 1000, which is lower than the cumulative pregnancy rate with laparoscopic sterilization methods (e.g., 5 to 19 per 1000 with the Filshie Clip) (9). None of the 4 pregnancies was related to failure of the sterilization method when the device was properly placed; in 1, the device was absent or incorrectly positioned, and in 3, there was noncompliance with the protocol. This illustrates that strict follow-up of the protocol may reduce the failure rate.

In the United States, the FDA requires HSG after hysteroscopic sterilization. However, in an urban clinic population in Michigan, compliance to a protocol including HSG was revealed to be only 12.7% (10). In Europe, pelvic radiographic

examination is recommended. The diagnostic characteristics of a plain abdominal radiographic examination to confirm satisfactory localization of Essure microinserts are equal to those of ultrasound for confirmation of satisfactory placement. The results of TVU compared with HSG, the ''reference test,'' showed sensitivity of 50% and specificity of 95%. The predictive positive value of a satisfactory TVU result was 99% (5).

Analysis of data from 169 unintended pregnancies after Essure sterilization worldwide revealed that in 30%, the HSG or radiographic examination was misinterpreted (4). In 37% of cases, there was patient noncompliance, primarily with the HSG confirmation test.

In the present study, 3 patients decided to rely on Essure sterilization when the HSG demonstrated that there was still patency, and none of them became pregnant. It has been postulated that the absence of absolute physical occlusion of the tubes does not necessarily equate with failure of sterilisation. There is a well-documented discrepancy between histologic and functional occlusion of the fallopian tubes (3).

In 9 of 164 patients (5%), failed sterilization was due to incorrect positioning of 1 of the devices (i.e., 2 expulsions and 7 perforations). This relatively high number enforces the need for strict compliance with the criteria for indications of HSG after Essure sterilization in our protocol. Two patients in the present study became pregnant after HSG confirmation of occluded tubes. It should be remembered that HSG was developed as a diagnostic test for the fertility workup to diagnose tubal disease. Limiting technical factors include excessive or insufficient pressure during dye instillation, and false-positive or false-negative results because of tubal spasm or intravasation (6).

The revised protocol for confirmation of hysteroscopic sterilization with Essure confirmed the theory that correct placement of the microinserts correlates well with tubal occlusion. No higher failure rate seems to occur when the microinserts were identified at TVU and HSG was substituted after uncomplicated procedures. Two of 4 pregnancies demonstrated violation of the protocol.

Conclusion

Transvaginal ultrasound has great advantages over radiographic examination or HSG because it causes less inconvenience to the patient. It is a nonionizing method of imaging, and can be performed on an outpatient basis by the patient's own physician and can be repeated at any time without risk to the patient.

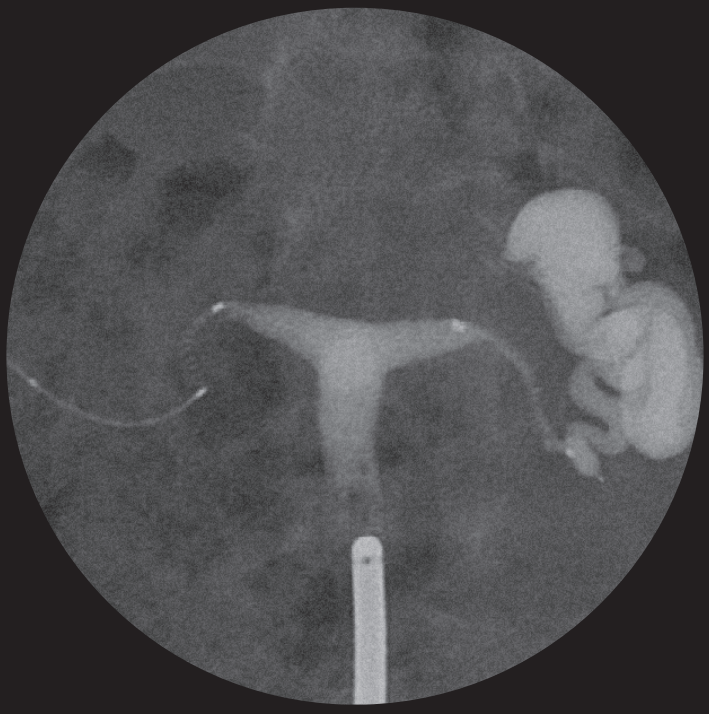
In patients in whom placement is unsatisfactory or TVU cannot confirm satisfactory placement, a complementary HSG is required. The Dutch protocol for

confirmation of Essure sterilization reduced the number of HSGs, thus reducing costs, inconvenience, and discomfort without influencing the effectiveness of the sterilization. Compared with the FDA protocol, the Dutch control protocol is associated with high patient compliance.

In cases of difficult placement, the extra TVU confirmation at 4 weeks did not reduce the number of HSGs. Thus, the need for routine TVU after a difficult hysteroscopic procedure should be abandoned, with sole reliance on the 3-month HSG as a confirmatory test.

References

1. Cooper JM, Carignan ChS, Cher D, Kerin JF. Microinsert nonincisional hysteroscopic sterilization. Obstet Gynecol. 2003;102:59-67.
2. Kerin JF, Cooper JM, Price T, et al. Hysteroscopic sterilization using a microinsert device: results of a multicenter phase II study. Hum Reprod. 2003;18:1223-1230.
3. Connor V. Essure: a review six years later. J Minim Invasive Gynecol.2009;16:282-290.
4. Heredia F, Cos R, Moros S, Torrabadella L, Cayuela E. Radiological control of Essure placements. Gynecol Surg. 2004;1:201-203.
5. Veersema S, Vleugels MP, Timmermans A, Brolmann HAM. Follow-up of successful bilateral placement of Essure microinserts with ultrasound. Fertil Steril. 2005;84:1733-1736.
6. Teoh M, Meagher S, Kovacs G. Ultrasound detection of the Essure permanent birth control device: a case series. Aust NZ J Gynecol. 2003; 43:378-380.
7. Thiel JA, Suchet IB, Lortie K. Confirmation of Essure microinsert tubal coil placement with conventional and volume-contrast imaging three-dimensional ultrasound. Fertil Steril. 2005;84:504-508.
8. Kerin JF, Levy BS. Ultrasound: an effective method for localization of the echogenic Essure sterilization microinsert: correlation with radiologic evaluations. J Minim Invasive Gynecol. 2005;12:50-54.
9. Peterson HB, Xia Z, Hughes JM, et al. The risk of pregnancy after tubal sterilization: findings from the US Collaborative Review of Sterilization. Am J Obstet Gynecol. 1996;174:1161-1170.
10. Shavel VI, Abdallah ME, Diamond MP, Berman JM. Placement of a birth control device at a university medical center. J Reprod Med. 2009;54:218-222.



8 **Essure hysteroscopic tubal occlusion device for the treatment of hydrosalpinx prior to in vitro fertilization-embryo transfer in patients with a contraindication for laparoscopy.**

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Abstract

Objective To investigate the success rate of proximal tubal occlusion with Essure devices in subfertile women with hydrosalpinges, and to observe the results of subsequent treatment with IVF.

Design Prospective, single arm, clinical study.

Setting University hospital and teaching hospital.

Patient(s) Ten women with uni- or bilateral hydrosalpinges prior to IVF. In all patients laparoscopy was contraindicated.

Intervention(s) Hysteroscopic placement of Essure devices in an office setting.

Main Outcome Measure(s) Placement rate, successful proximal tubal occlusion, and pregnancy rate after IVF. Result(s): All patients had successful placement of the Essure devices without any complications. Proximal tubal occlusion was confirmed by hysterosalpingography in 9 out of 10 patients. A 40% ongoing pregnancy rate was achieved with 20% life births after one IVF cycle and/or frozen embryo transfer.

Conclusion(s) Proximal occlusion of hydrosalpinges with Essure devices before IVF is a successful treatment for patients with a contraindication for salpingectomy.

Key Words Essure hysteroscopic tubal occlusion, Hydrosalpinges, IVF-ET

Introduction

The tubal factor accounts for up to 35% of female infertility, and is the most obvious indication for in vitro fertilization-embryo transfer (IVF-ET). Distal tubal occlusion may lead to formation of hydrosalpinges, which are found in 10% to 30% of all patients undergoing IVF-ET (1).

Patients with hydrosalpinges have been identified as a subgroup with significantly poorer outcomes of IVF-ET compared to tubal factor patients without hydrosalpinges. This has been demonstrated in two meta-analysis of retrospective studies concluding that hydrosalpinges were associated with a reduced chance of implantation and a increased risk of miscarriage (2,3). Especially patients with hydrosalpinges large enough to be visible on ultrasound are associated with the poorest IVF-ET prognosis (4,5).

The theories explaining the harmful effect of hydrosalpinges on IVF outcomes are multiple, and include the following: [1] a mechanical washout of the transferred embryos through tubouterine reflux of hydrosalpinx fluid, [2] a direct embryotoxic effect even when a low concentration of hydrosalpinx fluid is present in the uterine cavity, [3] a lower endometrial receptivity as an effect of disturbed expression of the cytokine and integrin system by the presence of a hydrosalpinx, thus impairing the implantation potential.

Laparoscopic salpingectomy before IVF-ET has been shown to restore IVF-ET outcomes in patients with hydrosalpinges (6-10). However, this procedure is associated with an increased risk for complications in patients with severe pelvic adhesions. Proximal occlusion of a hydrosalpinx by hysteroscopic placement of an Essure device may offer an alternative to laparoscopic surgery in these patients. Therefore, we conducted a prospective, single-arm, clinical study aiming to investigate the success rates of proximal tubal occlusion with Essure devices in subfertile women presenting with hydrosalpinges in which laparoscopy was felt to be contraindicated, as well as to observe the results of subsequent treatment with IVF-ET or frozen embryo transfers with follow-up including pregnancy and delivery.

Materials and methods

Ten patients with uni- or bilateral hydrosalpinx undergoing IVF-ET or frozen embryo transfers were included in this clinical study. A hydrosalpinx was defined as a distally occluded fallopian tube that was pathologically dilated or became pathologically dilated when patency was tested by hysterosalpingography (HSG). We included patients in this study after confirming the presence of hydrosalpinges with transvaginal ultrasound (midcyclic) and when laparoscopic surgery was

considered to be contraindicated because of extensive pelvic adhesions. Patients were excluded if their age was over 40 years and if they were not suitable for IVF treatment. Approval of the institutional review board was obtained.

The Essure device was approved by the U.S. Food and Drug Administration in 2002, and indicated for hysteroscopic tubal sterilization. Essure (Conceptus Inc., San Carlos, CA) is an expanding spring device (diameter: 2 mm; length: 40 mm) made of Nitinol and stainless steel, which contains Dacron fibres that induce a local inflammatory response and subsequent fibrosis of the proximal part of the tube. Nitinol consists of nearly equal atomic nickel–titanium (NiTi) alloy. The presence of nickel is a cause of concern related to embryologic development, but the NiTi alloy showed no cytotoxic, allergic, or genotoxic activity in animal studies, and was similar to the clinical reference material, 316 stainless steel (11). The hysteroscopic placement of the Essure devices was done under antibiotic prophylaxis (Doxycyclin: 200 mg, 5 days) in the second week of the patient's menstrual cycle. The Essure devices were placed with up to four coils visible in the uterine cavity under direct hysteroscopic view using a special delivery system. Three months postprocedure an HSG was performed to evaluate proximal tubal occlusion. Thereafter, all patients underwent IVF-ET and/or frozen embryo transfer. Patients with severe endometriosis were pretreated with long-term (≤3 months) GnRH-agonists before IVF-ET according to Sallam et al. (12).

Results

Ten women (mean age: 33.5 years; range: 28-38 years) with unilateral (N=7) or bilateral hydrosalpinges (N=3), because of undergoing IVF, were included (Table 1). Laparoscopy was felt to be contraindicated because of previous extensive pelvic surgery because of endometriosis (N=7) and Crohn's disease (N=1) or frozen pelvis as a result of pelvic inflammatory disease (N=2). Before the placement of the Essure devices six patients underwent unsuccessful IVF treatment.

All Essure procedures were performed in an office setting. No anaesthetics were administered, except for two cases where a paracervical block was needed. Successful placement was achieved in all patients. A mean number of three coils (range: 1-4 coils) of the device spring were left protruding into the uterine cavity. No intraoperative or postoperative complications occurred. The procedure times ranged between 5 and 8 minutes. An HSG was performed after 3 months, demonstrating tubal occlusion in 9 patients.

IVF was started after a mean duration of 4.5 months following the Essure procedure (Table 2). The first two patients (cases A and B) became pregnant on their

Table 1
Demographics and Essure data.

Case	Age (years)	Duration subfertility (years)	IVF-ET prior to Essure	Pathology	Hydrosalpinx (uni/bilateral)	Essure coils in uterine cavity (N)	Tubal patency postprocedure[a]
A	32	2	Yes	Endometriosis	Unilateral	1	No
B	30	5	Yes	Endometriosis	Bilateral	3 + 3	No
C	32	3	Yes	Endometriosis	Unilateral	4	No
D	38	9	Yes	Endometriosis	Bilateral	2 + 3	Yes (Left side)
E	34	8	No	Endometriosis	Bilateral	4 + 4	No
F	36	3	No	Endometriosis	Unilateral	3	No
G	28	4	No	Endometriosis	Unilateral	3	No
H	30	2	Yes	Frozen pelvis (post-PID)	Unilateral	4	No
I	37	4	Yes	Morbus Crohn	Bilateral	4 + 3	No
J	38	3	No	Frozen pelvis (post-PID)	Unilateral	2	No

Note: PID = pelvic inflammatory disease; IVF-ET = in vitro fertilization-embryo transfer.
[a]Determined with hysterosalpingography 3 months after Essure placement.

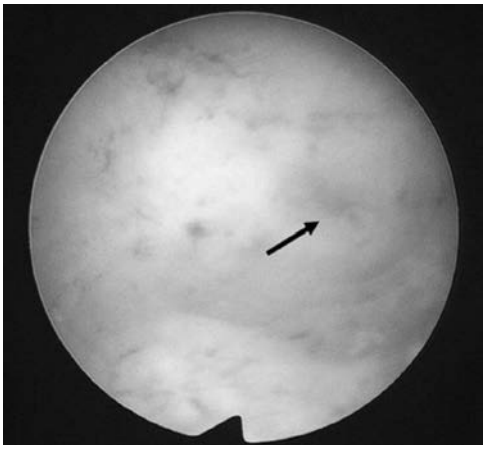
first IVF treatment cycle. The course of these pregnancies was normal, and both patients had a spontaneous term vaginal delivery of healthy infants. Postpartum hysteroscopy showed in both cases complete tissue encapsulation of the Essure devices (Fig. 1).

In case C, the patient experienced a miscarriage nearly 7 weeks after oocyte retrieval in her first IVF cycle. Frozen embryo transfer is now pending for this patient.

Case D involved a patient in which two Essure devices were placed bilaterally. One of them (the left side) showed tubal patency at the HSG (Fig. 2). A repeat HSG has not been performed and she became pregnant after a frozen embryo transfer performed 5 months postprocedure. (The patency rate in earlier studies with HSG 3 months after hysteroscopic sterilization with Essure was 3-4%, and in all cases a repeat HSG after 6-7 months showed bilateral occlusion) (13).

Figure 1

Hysteroscopic view 3 months after vaginal delivery (patient B): complete tissue encapsulation of the Essure device. The arrow is pointing at the tissue overgrowth at the ostium tubae.



Unfortunately, she delivered at 24 weeks of gestation and her child died shortly after birth. Two weeks earlier she was admitted to an obstetric ward with complaints of discomfort in the lower abdomen and back in combination with sonographic observations of shortening cervical length. During the admission she developed a chorioamnionitis with subsequent rupture of membranes, which made the placement of an emergency cerclage impossible. Hysteroscopic evaluation after the delivery demonstrated in this case total tissue encapsulation of the left sided Essure device. On the right side only the tip of the device was visible. Six months after the delivery a frozen embryo transfer was performed, which was unsuccessful. A second frozen embryo transfer resulted in a ongoing pregnancy.

One patient, case E, did not achieve pregnancy after three IVF cycles and one frozen embryo transfer despite goodquality embryos. Two patients (cases F and G) ceased their IVF treatment after their first cycle because of partner separation. The last three patients (cases H, I, and J) from our study underwent all one unsuccessful IVF treatment cycle. One of them is currently undecided as whether to proceed with further treatment.

Discussion

In line with the pathophysiologic concepts of hydrosalpinges, any surgical intervention interrupting the communication between hydrosalpinx and uterine cavity would stop the leakage of hydrosalpinx fluid and would improve the endometrial environment for implantation. Laparoscopic salpingectomy before IVF in patients with hydrosalpinges restores IVF-ET outcomes but carries also all the risks (visceral injury, vascular damage, and unintended laparotomy) associated with laparoscopic intervention and general anesthesia (14). Our study shows that a hysteroscopic approach to proximal occlusion of hydrosalpinges with Essure devices is safe, highly effective, and feasible in an ambulatory setting. In the 10 patients that were treated no intraoperative or postoperative complications occurred. Successful placement was achieved in all patients using local anaesthetics only in 20% of the cases. The Essure devices induced complete proximal occlusion in 9 out of 10 patients.

Only in one patient (case D) was one-sided patency observed during HSG. On the other hand, hysteroscopy after her immature delivery showed total tissue encapsulation of this device, suggesting that the induced fibrosis by the Dacron fibres may take >3 months to establish complete occlusion of the proximal tubal lumen.

In the last 3 years four reports (15-18) on the use of Essure devices for the treatment of hydrosalpinx before IVF have been published. As far as we know, our study is the largest case-series on this topic. A similar study, but slightly smaller with respect to the number of patients (N=7), was presented at the annual meeting

Figure 2

Hysterosalpingogram 3 months after Essure placement (patient D).

Two devices are visible with contrast medium in the left hydrosalpinx.

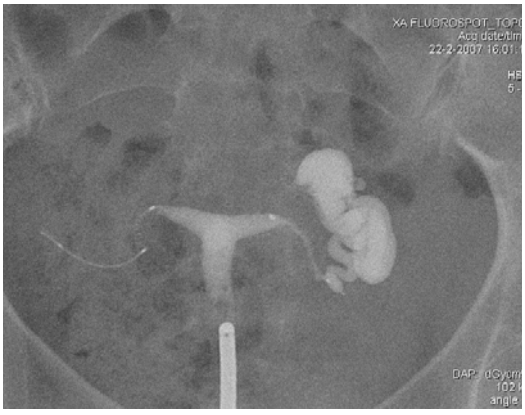


Table 2
Artificial reproductive treatments and their subsequent outcomes after hysteroscopic placement of Essure devices.

Case	ART 1	Outcome	ART 2	Outcome	ART 3	Outcome	ART 4	Outcome
A	IVF	Life birth	—	—	—	—	—	—
B	IVF	Life birth	—	—	—	—	—	—
C	IVF	Miscarrage	Frozen ET	No pregnancy	—	—	—	—
D	Frozen ET	Immature delivery	Frozen ET	No pregnancy	Frozen ET	Ongoing pregnancy	—	—
E	IVF	No pregnancy	IVF	No pregnancy	IVF	No pregnancy	Frozen ET	No pregnancy
F	IVF	No pregnancy	—	—	—	—	—	—
G	IVF	No pregnancy	—	—	—	—	—	—
H	IVF	No pregnancy	—	—	—	—	—	—
I	IVF	No pregnancy	—	—	—	—	—	—
J	IVF	No pregnancy	—	—	—	—	—	—

Note: ART = artificial reproductive treatment; IVF = in vitro fertilization; ET = embryo transfer. 2009.

of the ASRM in 2007 (17). Both case-series show good pregnancy rates with IVF-ET following Essure placement, which are in line with those found after laparoscopic salpingectomy (10).

In our study five pregnancies occurred, including two term vaginal deliveries of healthy infants, a miscarriage, and a immature delivery. In case D, the immature delivery appears primary to be related to cervical insufficiency (although risk factors for cervical insufficiency are lacking), leading to a chorioamnionitis and subsequent rupture of the membranes. However, it remains difficult to rule out any influence of the visible Essure tip (seen on the right side at postpartum hysteroscopy) on this chain of events in this case.

A significant concern in using Essure devices for the treatment of hydrosalpinx in women wishing to conceive is the trailing of Essure coils into the uterine cavity and its possible effects on implantation as well as on pregnancy. Therefore, we decided, in line with other investigators (16-18), to limit the number of coils remaining in the cavity to three. Our experience is that this is usually feasible. The second-look hysteroscopies performed after delivery in our study confirmed earlier observations that deep placement of the Essure devices usually leads to total encapsulation of the device with exclusion from the uterine cavity, which is reassuring (19).

In conclusion, our study confirms earlier reports on the effectivity of Essure devices in inducing proximal tubal occlusion in infertile patients with ultrasound visible hydrosalpinges. Up to now, our study is the largest prospective case-series on this subject including second-look hysteroscopies after childbirth. Our data show successful placement in all cases without intraoperative or postoperative complications. A 40% ongoing pregnancy rate was achieved with 20% life births after one IVF-ET cycle and/or frozen embryo transfer (in this same time frame an overall live birth rate of 26% was achieved in women without hydrosalpinx (or Essure placement) treated at our IVF center). In our opinion, these results warrant a randomized comparison between laparoscopic salpingectomy and hysteroscopic placement of Essure devices for ultrasound visible hydrosalpinges in patients before IVF-ET.

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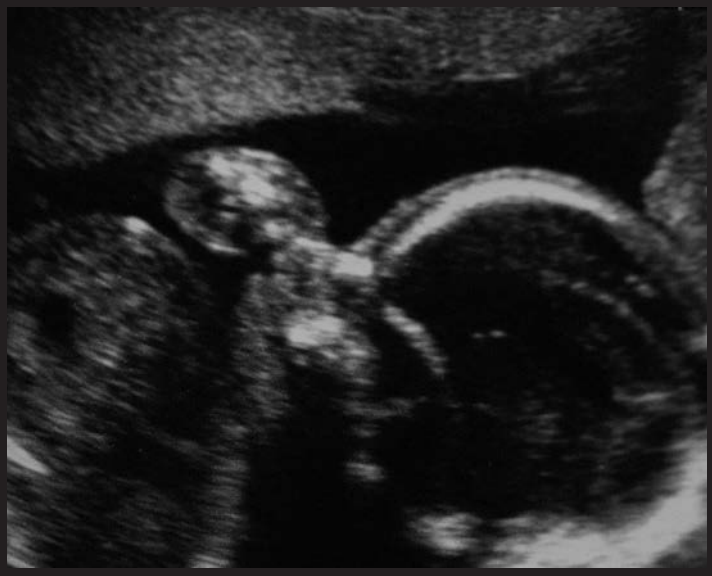
References

1. Andersen AN, Lindhard A, Loft A, Ziebe S, Andersen CY. The infertile patient with hydrosalpinges. IVF with or without salpingectomy? Hum Reprod 1996;11:2081-4.
2. Zeyneloglu HB, Arici A, Olive DL. Adverse effects of hydrosalpinx on pregnancy rates after in vitro fertilization-embryo transfer. Fertil Steril 1998;70:492-9.
3. Camus E, Poncelet C, Goffinet F, et al. Pregnancy rates after IVF in cases of tubal infertility with and without hydrosalpinx: meta-analysis of published comparative studies. Hum Reprod 1999;14:1243-9.
4. De Wit W, Gowrising CJ, Kuik DJ, Lens JW, Schats R. Only hydrosalpinges visible on ultrasound are associated with reduced implantation and pregnancy rates after in vitro fertilization. Hum Reprod 1998;13: 1696-701.
5. Strandell A, Lindhard A, Waldenstrom U, Thorburn J. Hydrosalpinx and IVF outcome: cumulative results after salpingectomy in a randomzed controlled trial. Hum Reprod 2001;16:2403-10.
6. Dechaud H, Daures JP, Amal F, Humeau C, Hedon B. Does previous salpingectomy improve implantation and pregnancy rates in patients with severe tubal factor infertility who are undergoing in vitro fertilization? A pilot prospective randomized study. Fertil Steril 1998;69:1020-5.
7. Goldstein DB, Sasaran LH, Stadtmaner L, Popa R. Selective salpingostomy-salpingectomy and medical treatment prior to IVF in patients with hydrosalpinx. Fertil Steril 1998;70(Suppl 1):S320.
8. Strandell A, Lindhard A, Waldenstrom U, Thorburn J, Janson PO, Hamberger L. Hydrosalpinx and IVF outcome: a prospective randomized multicenter trial in Scandinavia on salpingectomy prior to IVF. Hum Reprod 1999;14:2762-9.
9. Kontoravdis A, Makrakis E, Pantos K, Botsis D, Deligeoroglou E, Creatsas G. Proximal tubal occlusion and salpingectomy result in similar improvement in in vitro fertilization outcome in patients with hydrosalpinx. Fertil Steril 2006;86:1642-9.
10. Johnson NP, Mak W, Sowter MC. Surgical treatment for tubal disease in women due to undergo in vitro fertilization. Cochrane Database Syst Rev 2004;3:CD002125.
11. Wever DJ, Veldhuizen AG, Sanser MM, Schakenraad JM, van Horn JR. Cytotoxic, allergic, and genotoxic activity of a nickel-titanium alloy. Biomaterials 1997;18:1115-20.
12. Sallam HN, Garcia-Velasco JA, Diaz S, Arici A. Long-term pituitary down-regulation before in vitro fertilization (IVF) for women with endometriosis. Cochrane Database Syst Rev 2006;4.
13. Kerin JF, Cooper JM, Price T, Van Herendael BJ, Cayuela-Font E, Cher D, et al. Hysteroscopic sterilization using a microinsert device: results of a multicenter phase II study. Hum Reprod 2003;18:1233-30.
14. Practice committee of the American Society for Reproductive Medicine.
15. Salpingectomy for hydrosalpinx prior to IVF. Fertil Steril 2004;82: 117-9.

16. Rosenfield RB, Stones RE, Coates A, Matteri RK, Hesla JS. Proximal occlusion of hydrosalpinx by hysteroscopic placement of microinsert before in vitro fertilization-embryo transfer. Fertil Steril 2005;83:1547-50.
17. Kerin JF, Cattanach S. Successful pregnancy outcome with the use of in vitro fertilization after Essure hysteroscopic sterilization. Fertil Steril 2007;87:1212.e1-4.
18. Galen DI. Utilization of the Essure microinsert for the treatment of hydrosalpinx prior to IVF. Fertil Steril 2007;88(Suppl 1):16.
19. Hitkari JA, Singh SS, Shapiro HM, Leyland N. Essure treatment of hydrosalpinges. Fertil Steril 2007;88:1663-6.
20. Kerin JF. Tissue encapsulation of the Essure device from the uterine cavity after hysteroscopic sterilization. J Minim Invasive Gynecol 2007;14:202-4.



9 Outcomes of pregnancies in women with hysteroscopically placed microinserts in situ.

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Abstract

This was a retrospective review of all pregnancies reported after Essure in situ in the Netherlands. Pregnancies included those that were unintentional (resulting from lack of protocol adherence and/or misread confirmation tests) and those that were intentional (resulting from off-label use of Essure microinserts for hydrosalpinx closure before in vitro fertilization/intracytoplasmic sperm injection with embryo transfer or in vitro fertilization with embryo transfer after regret of sterilization). The outcomes of 50 pregnancies in women with 1 or 2 microinserts in situ were evaluated. Eight unintended pregnancies and 18 intended pregnancies resulted in birth of a full-term healthy baby. Seven infants were delivered via Caesarean Section. Two women delivered prematurely by C-section, (singleton after 34 weeks 1 day, twins after 35 weeks 3 days). All babies are healthy and without any congenital anomalies. There were 2 stillbirths after 20 weeks; however, it is unlikely that this was related to the presence of the microinserts. In conclusion, it is unlikely that the presence of intratubal microinserts interferes with implantation and the developing amniotic sac and fetus.

Key Words Essure microinserts; Hysteroscopic sterilization ; Hydrosalpinges; In vitro fertilization; Permanent birth control; Pregnancy outcomes; Unintended pregnancies

Introduction

The Essure hysteroscopic sterilization method has been in use worldwide for >10 years. From 2001 through 2010, almost 500,000 Essure kits were distributed worldwide. During that time, 748 pregnancies were reported, or 15% of the estimated user population of distributed kits. Of these, most were due to patient or physician noncompliance or misinterpreted confirmation test results (n=476). Luteal phase pregnancies or pregnancy at the time of the procedure resulted in 32 reported pregnancies. The remaining 240 reports of pregnancy lacked sufficient information to evaluate causality (1).

Patients who regret sterilization after Essure placement and desire to become pregnant must rely on in vitro fertilization and embryo transfer (IVF/ET). Although not an approved use, successful pregnancy outcomes with the use of IVF after Essure sterilization has been documented (2). Several studies have reported successful pregnancies with IVF after proximal occlusion of hydrosalpinges via hysteroscopic placement of Essure microinserts (2-7).

A theoretical concern for all women who want to become pregnant or who have an unintended pregnancy after Essure placement is the trailing microinsert coils in the uterine cavity and their possible effects on pregnancy. In theory, the microinserts could cause similar tissue effects as with an intrauterine device, and consequent myometrial contractions or rupture of membranes could be considered a possible cause of premature birth; the literature reports an increased risk of preterm delivery and chorioamnionitis with the use of intrauterine copper devices (8).

This retrospective analysis was designed to review all pregnancies reported in the Netherlands from 2002 to 2010, whether unintended or intended as part of IVF-ET, subsequent to Essure placement and to analyze the obstetric outcomes of the subsequent pregnancies.

Material and Methods

All 136 gynecologists in the Netherlands who perform Essure sterilization were asked via E-mail in December 2010 about either intended (IVF-ET) or unintended pregnancies in patients after the Essure procedure. After a positive reply, a questionnaire was sent to collect data about patient history, the Essure procedure, and obstetric outcomes. Data from patients with a successful IVF-ET and/or frozen embryo transfer (FET) after Essure who participated in a previous prospective clinical study were included (6,7).

Data sources included information retrieved from the Dutch National Perinatal Registry, data from a previous prospective trial (N=22), and responses (N=28) to E-mails sent to physicians who perform Essure procedures (N=136). The data on pregnancies and outcomes were collected from the national perinatal registry (Landelijk Verloskunde Registratie (LVR)) used by all obstetric departments in the Netherlands. All professional organizations have their own voluntary medical registry: the LVR1 registry (midwives), the LVR1 registry (general practitioners),

Table 1
Outcome of unintended not terminated pregnancies after failed Essure sterilization in the Netherlands, 2002–2011

Pat.	Age, yrs	Parity	Year of sterilization	No. of coils, left/right	Months of reliance on sterilization	Pregnancy, weeks + days	Outcome
1	36	0	2004	5/2	< 12	40 + 4	Vaginal delivery, healthy boy, 2970g
2	31	4	2005	7/4	< 12	19 + 4	Vaginal delivery, healthy boy, 3750g
3	36	1	2006	3/1	< 12	38 + 1	Caesarean section, healthy girl, 3755g
4	38	3	2006	5/3	< 12	41 + 6	Vaginal delivery, healthy boy, 4020g
5	37	2	2008	3/1	< 12	40 + 5	Vaginal delivery, healthy girl
6	31	2	2009	2/2	NA	40 + 3	Healthy girl, 3680g
7	41	2	2009	1/1	NA	NA	NA, healthy boy
8	35	3	2010	5/5	None	38 + 3	Vaginal delivery, healthy boy
9	36	1	NA	NA	NA	40 + 8	Vaginal delivery, healthy boy

NA = not available

the LVR2 registry (obstetricians), and the LNR registry (paediatricians and neonatologists). The LVR1, LVR2, and LNR registries are linked to one combined PRN registry. All patient identification information was de-identified, and institutional review board approval was obtained to collect the data.

Results

De-identified data were collected for 50 pregnancies in 43 patients in the Netherlands who became pregnant with 1 or 2 Essure microinserts in situ. In 26 patients an unintended pregnancy occurred after hysteroscopic sterilization with Essure. Twenty-two pregnancies occurred in 15 patients who underwent IVF-ET because of infertility due to unilateral (n=9) or bilateral (n=6) hydrosalpinges. In these women, laparoscopic salpingectomy was relatively contraindicated because of extensive endometriosis, a frozen pelvis, or inflammatory bowel disease with a history of multiple abdominal operations. Two patients experienced sterilization regret and subsequently achieved successful pregnancies after Essure and IVF/ET.

Of 26 unintended pregnancies after hysteroscopic sterilization with Essure 17 (65.4%) were electively terminated, and 9 (34.6%) resulted in the birth of a baby (Table 1). In 7 women, pregnancies ended in spontaneous vaginal delivery after uncomplicated pregnancies. One patient delivered via primary caesarean section at 38 weeks 1 day because of breech presentation. Eight healthy babies were born. No information was provided regarding the outcome of 1 pregnancy.

Intended Pregnancies: Pre-IVF Occlusion of Hydrosalpinges

Most of the outcomes of IVF/ET after closure of 1 or 2 hydrosalpinges via hysteroscopic insertion of the Essure microinserts have been published previously (7). In 15 patients, IVF/ET resulted in 1 biochemical pregnancy and 21 pregnancies confirmed via vaginal ultrasound; 6 of these were miscarried at 6 to 11 weeks (Table 2).

Two pregnancies (9.1%) ended in premature delivery, 2 (9.1%) in premature delivery including a twin pregnancy, and 10 (45.5%) term deliveries. Six of these patients delivered via caesarean section. Overall, 15 of 23 pregnancies (65%) were ongoing. Only 2 patients had a microinsert with 5 coils in the uterine cavity. In 1 of these patients, pregnancy ended in miscarriage.

In the other patient, pregnancy ended with stillbirth. This woman became pregnant after a seventh IVF/ET cycle, which was the first IVF treatment after tubal closure of hydrosalpinges. Two Essure microinserts were placed before, with proximal closure of 2 hydrosalpinges. A singleton pregnancy was achieved; however, premature rupture of membranes resulted in stillbirth at 19 weeks 3 days.

Table 2
Pregnancies after ART after proximal tubal occlusion of hydrosalpinges with Essure microinserts

Patient	Age, yr	Parity	Tubal occlusion. Date	No. of microinserts	No. of coils, left/right	ART cycle after tubal occlusion	
1	32	0	12-21-05	1	0/1	IVF 1[b] IVF 2[a] IVF 3[a] IVF 4[a]	
2	30	0	12-30-05	2	3/3	FET 1[b]	
3	32	0	08-05-06	1	5/0	IVF 2	
4	38	0	11-29-06	2	3/2	FET 1[b] FET 2[b]	
5	29	0	4-5-07	1	3/0	FET 2[b] FET 2 Spontaneous	
6	36	1	2-7-08	2	1/1	FET 1[a]	
7	30	1	2006	2	NA	FET 1	
8	33	0	3-12-08	1	2/0	IVF 2[a]	
9	36	0	10-16-08	2	4/1	IVF 2[a] FET 1[a]	
10	32	0	3-17-09	1	2/0	IVF 2[a]	
11	31	0	1-16-08	1	0/1	FET 2a	
12	35	0	4-1-09	1	2/0	IVF 1[a]	
13	38	0	6-19-08	1	4/0	IVF 1[a]	
14	29	0	9-10-10	1	NA	IVF 1[a]	
15	33	0	2009 2011	2 0	0/5 NA	IVF 1 IVF 2	

ART 5 assisted reproduction technology; FET 5 frozen embryo transfer; IVF 5 in vitro fertilization; NA 5 not available.
a Previous published (6).
b Previous published (6,7).

	Duration of pregnancy, weeks + days	**Outcome**
	39 + 2 <12 <12 38 + 4	Vaginal delivery, healthy girl, 3040g Miscarriage Miscarriage Vaginal delivery, healthy girl, 3224g
	40 + 0	Vaginal delivery, healthy boy, 3651g
	<12	Miscarriage
	24 35 + 3	Vaginal delivery, normal infant Caesarean section, breech, healthy girl, 3400g
	<12 < 5 <12	Miscarriage Biochemical Miscarriage
	37 + 2	Vaginal delivery, premature rupture of membranes, healthy girl, 2920g
	39 + 2	Caesarean section, breech, healthy girl, 3236g
	42 + 2	Caesarean section, asphyxia, recovered, boy, 3880g
	<12 41 + 3	Miscarriage Caesarean section, dystocia, healthy girl, 4240g
	38 + 2	Vaginal delivery, healthy boy 3310g
	34 + 1	Caesarean section, healthy boy, 2060g, 1 healthy girl, 1905g
	38 + 5	Caesarean section, breech, healthy girl, 2757g
	<12	Miscarriage
	38 + 3	Vaginal delivery, healthy girl, 3128g
	19 + 3 18+3	Vaginal delivery, normal infant Vaginal delivery, normal infant

No fetal dysmorphias were visible. Several weeks later, hysteroscopy showed an encapsulated microinsert on the left side, and on the right side, 5 outer coils and the inner PET fibres of the microinsert were protruding into the uterine cavity. After several months, laparoscopic tubal coagulation was performed at the left salpinx, and Filshie Clip placement at the right salpinx, and both microinserts were hysteroscopically removed. The eighth IVF cycle resulted in a twin pregnancy. Primary cerclage was performed at gestational week 13, and at 17 weeks 6 days premature rupture of membranes occurred, and the patient delivered 4 days later despite injection of 500 mg hydroxyprogesterone (Proluton). Histologic examination of the placentas showed evidence of chorioamnionitis.

Another woman, became pregnant after frozen embryo transfer at 5 months after bilateral Essure placement. She delivered prematurely at 24 weeks due to cervical insufficiency, and the baby did not survive. Eight months later the patient became pregnant again after a second frozen embryo transfer with the microinserts in place. She carried almost to term with a primary cervical cerclage and delivered a healthy infant at 35 weeks 3 days.

IVF Pregnancies After sterilization Regret

Each of the 2 patients with sterilization regret treated via IVF/ET conceived after the first single embryo transfer. One delivered a healthy baby via caesarean section (indicated because of fetal condition during labour) at 40 weeks 3 days, and the other delivered a healthy baby spontaneously at 36 weeks 6 days.

Discussion

We analyzed the obstetric outcomes of 50 pregnancies in 43 women with 1 or 2 Essure microinserts in place and found a good outcome for ongoing pregnancies. The number of miscarriages in the group who underwent IVF/ET after proximal closure of hydrosalpinges is not unexpectedly high and reflects findings reported in the literature (10). The number of ongoing pregnancies in this group is encouraging and congruent with the literature on pre-IVF salpingectomy or tubal occlusion (9).

To achieve proper location and occlusion and to prevent movement of the device, the manufacturer advises 3 to 8 coils protruding into the uterine cavity for the purpose of permanent birth control. Authors of articles about Essure placement before IVF/ET advise placement of ≤4 intrauterine coils. In the present study, at least 10 patients had microinserts with 4 coils in the uterus after placement. One of these patients delivered prematurely; however, this woman experienced another premature delivery after microinsert removal, indicating that it is unlikely that there is a relation between

the earlier fetal loss and the microinserts or the number of coils in the uterine cavity.

Hydrosalpinges are associated with a reduced chance of implantation and increased risk of miscarriage after IVF (11,12). To exclude negative effects of hydrosalpinges, salpingectomy or occlusion of the fallopian tubes is advised before assisted reproductive techniques (10,12,13). IVF/ET outcomes in a patient with hydrosalpinges was initially studied by Rosenfield et al (3).

Kerin and Cattanach (2) described 2 patients who underwent IVF/ET procedures after Essure. Both patients underwent a second-look hysteroscopy within 3 months after the IVF procedure. Device encapsulation by tissue ingrowth reduced the average number of coils trailing into the uterine cavity from 4 to 1, with no evidence of inflammation or other abnormality. Another study showed that coils protruding into the uterine cavity shortened from 5.7 mm to 2.0 mm and from 5.4 mm to 1.8 mm after a mean of 20 months. Progressive device encapsulation was observed over time in 7 women who underwent hysteroscopic procedures to treat unrelated gynecologic conditions between 4 and 43 months after Essure placement. In these patients the average length of coils in the uterine cavity had decreased from 6 mm to mm at second-look hysteroscopy. Complete encapsulation was observed in 25% of cases after 13 to 43 months (14).

A later prospective 2-center clinical study of 20 women with hydrosalpinx who were recruited for off-label unilateral (n=8) or bilateral (n=8) placement of Essure before IVF/ ET resulted in 12 live births. During placement of the microinserts, the number of coils was limited to 2 to 4. Four obstetric complications not likely related to microinserts were reported including placenta previa, hypertension, maternal diabetes with premature rupture of membranes, and pre-eclampsia. The median gestational age at birth was 37 weeks (range, 33-40 weeks), with 3 pairs of full-term twins, 1 pre-term pair of twins at 33 weeks, 6 full-term singleton births, and 2 preterm singleton births at 33 and 35 weeks. In 1 additional pregnancy, nonviable twins were lost during the first trimester. Six deliveries were via caesarean section because of complications including placenta previa, hypertension, preeclampsia, and maternal diabetes with premature rupture of membranes. Pregnancies and births were otherwise uncomplicated, and the infants were healthy (4).

Thébault et al (5) published successful results of IVF after Essure placement in 7 women with hydrosalpinges. The number of coils left in the uterine cavity was ≤3 in all cases except one with 3 and 6 coils. Four pregnancies ended in miscarriage. and 1 ended in fetal death at 27 weeks due to platelet allo-immunization. The same patient conceived again and delivered twins at 36 weeks via caesarean section. One woman delivered a healthy infant after 41 weeks, and 1 delivered twins via caesarean section at 37 weeks. There were no obstetric complications caused by premature contractions or infection.

In our series, both patients in whom pregnancy ended in stillbirth delivered a second time after consecutive IVF/ET. In 1 woman, cervical cerclage prevented premature birth, indicating cervical incompetence as a cause of earlier fetal loss rather than premature labour induced by the microinserts. In the other woman, both microinserts were removed before a following IVF/ET cycle was started. However, a second stillbirth occurred, indicating that the cause of both fetal losses was not likely related to the presence of microinserts.

Although most women remain satisfied with their decision to undergo Essure placement as a final contraceptive means, there will always be a small group of women who regret sterilization. Careful pre-sterilization counselling, thorough informed consent, and emphasis that sterilization is irreversible will reduce the risk of regret but will not completely eliminate it. There will inevitably be a small number of women who, due to unexpected life events, may wish to have children after sterilization. In the US Collaborative Review of sterilization (CREST) study, the percentage of women expressing regret was 20% for those aged ≤30 years at the time of sterilization , compared with 6% for women aged >30 years at the time of tubal ligation. For women aged <25 years, the rate was as high as 40%. The regret rate was also high for women who were not married at the time of tubal ligation or for those who underwent tubal ligation less than a year after delivery (15). Patients with sterilization regret after Essure who want to become pregnant must rely on IVF/ET. In the present study only 2 patients with sterilization regret were treated via IVF/ET. Both conceived after the first single embryo transfer and delivered a healthy baby.

The Essure contraindication to nickel hypersensitivity has been changed to a warning on the basis of data that suggest that the reported incidence of adverse events suspected related to nickel hypersensitivity is extremely small (1%) and is consistent with data from other nickel-containing devices.

These findings are reassuring and beg the question of whether nickel reactions are clinically relevant in the use of nitinol-containing microinserts for hysteroscopic sterilization (16). Nevertheless, the presence of nickel in the microinserts is a cause of concern related to embryologic development, although animal studies showed no cytotoxic, allergic, or genotoxic activity of the nickel-titanium alloy, and reactions were similar to the clinical reference material, 316 stainless steel (17). In the present study we did not find any indication of nickel-related adverse effects.

To our knowledge, ours is the largest study published to date about the outcomes of pregnancies after hysteroscopic tubal occlusion using Essure microinserts. Limitations of the study are the nonstandardized collection of data, which were combined from a retrospective case series study (unintended pregnancies and intended IVF/ET pregnancies after sterilization regret) and an uncontrolled

cohort study (pre-IVF tubal occlusion), the different populations, and the lack of a control group. However, the potential recall bias associated with retrospective trials is reduced by intensive communication between the Dutch gynecologists and the distributor of Essure to ensure the timely and accurate reporting of all Essure-related events, including pregnancies. Although part of the data were published earlier, those reports focused mainly on the cause of unintended pregnancies and the success rate of IVF treatment after pre-IVF closure of hydrosalpinges rather than evaluation of the potential risks and effects of the microinserts on the pregnancy. Data from the present study and literature review indicate that relevant to subsequent adverse obstetric and perinatal outcome, pregnancies with Essure microinserts in place have a good prognosis.

Larger studies are needed to confirm these findings. Nevertheless, there seems to be no reason to discourage patients who request IVF/ET after hysteroscopic sterilization or with an indication of proximal tubal occlusion of hydrosalpinges. This information can also be helpful for patients with unintended pregnancies who have to make one of the most difficult decisions of their lives as to whether to terminate or continue the pregnancy.

In conclusion, the results of this case series report support the conclusion of earlier reports (3,9,10) that it is unlikely that the presence of Essure microinserts interferes with implantation and the developing amniotic sac and fetus.

Referencs

1. Levy BS, Munro MG, Veersema S, Vleugels M. Reported pregnancies after Essure hysteroscopic sterilization: a retrospective analysis of pregnancy reports worldwide: 2001-2010. Presented at the 40th Annual AAGL Global Congress of Minimally Invasive Gynecology, November 7–10, Hollywood, Florida.
2. Kerin J, Cattanach S. Successful pregnancy outcome with the use of in vitro fertilization after Essure hysteroscopic sterilization. Fertil Steril. 2007;85:1212E1-1212E4.
3. Rosenfield RB, Stones RE, Coates A, Matteri RK, Hesla JS. Proximal occlusion of hydrosalpinx by hysteroscopic placement of microinsert before in vitro fertilization-embryo transfer. Fertil Steril. 2005;83:1547-1550.
4. Galen DI, Khan N, Richter KS. Essure multicenter off-label treatmentfor hydrosalpinx before in vitro fertilization. J Minim Invasive Gynecol. 2010;18:338-342.
5. Th'ebault N, Broux PL, Moy L, Vialard J. Utilization du micro-implant Essure pour exclusion d'hydrosalpinx dans un contexte d'infertilite. J Gynecol Obstet Biol Reprod. 2011;41:145-150.
6. Mijatovic V, Veersema S, Emanuel MH, Schats R, Hompes PGA. Essure hysteroscopic tubal occlusion device for the treatment of hydrosalpinx prior to in vitro fertilization-embryo transfer in patients with a contraindication for laparoscopy. Fertil Steril. 2010;93:1338-1342.
7. Mijatovic V, Dreyer K, Emanuel MH, Schats R, Hompes PG. Essure hydrosalpinx occlusion prior to IVF-ET as an alternative to laparoscopic salpingectomy. Eur J Obstet Gynecol Reprod Biol. 2012;161:42-45.
8. Ganer H, Levy A, Ohel I, Sheiner E. Pregnancy outcome in women with an intrauterine contraceptive device. Am J Obstet Gynecol. 2009;201: 381.e1-381.e5.
9. Hammadieh N, Coomarasamy A, Papaioannou S, Afnan M, Sharif K. Ultrasound-guided hydrosalpinx aspiration during oocyte collection improves pregnancy outcomes in IVF: a randomized controlled trial. Hum Reprod. 2008;23:1113-1117.
10. Practice Committee of the American Society for Reproductive Medicine in collaboration with the Society of Reproductive Surgeons.
11. Salpingectomy for hydrosalpinx prior to in vitro fertilization. Fertil Steril. 2008;90(Suppl 3):S66-S68.
12. Zeyneloglu HB, Arici A, Olive DL. Adverse effects of hydrosalpinx on pregnancy rates after in vitro fertilization-embryo transfer. Fertil Steril. 1998;70:492-499.
13. AC, Muasher SJ. The significance of hydrosalpinx in vitro fertilization. Fertil Steril. 1998;69:373-384.
14. Camus E, Poncelet C, Goffinet F, et al. Pregnancy rates after IVF in cases of tubal infertility with and without hydrosalpinx: meta-analysis of published comparative studies. Hum Reprod. 1999;14: 1243-1249.
15. Kerin JF. Tissue encapsulation of the Essure device from the uterine cavity after hysteroscopic sterilization. J Minim Invasive Gynecol. 2007;14:202-204.
16. Grubb GS, Peterson HB, Layde PM, Rubin GL. Regret after decision to have a tubal sterilization. Fertil Steril. 1985;44:248-253.

17. Zurawin R, Zurawin J. Adverse events due to suspected nickel hyper-sensitivity in patients with Essure microinserts. J Minim Invasive Gynecol. 2011;18:475-482.
18. Wever DJ, Veldhuizen AG, Sanser MM, Schakenraad JM, van Horn JR. Cytotoxic, allergic, and genotoxic activity of a nickel-titanium alloy. Biomaterials. 1997;18:1115-1120.

10 General discussion and future perspectives

Preceding experience with hysteroscopic sterilization

For more than 100 years, physicians have searched for a transcervical way to occlude the fallopian tubes at their uterotubal junction to avoid the complications that are associated with general anesthesia and abdominal instrumentation. Methods using electrocoagulation, cryocoagulation or other techniques of heating the tubal openings by access through the uterine cavity were unsuccessful. Many designs of intratubal mechanical devices (screws, plugs and formed-in-place intratubal devices) have been tried out over the past 60 years, with limited success (1,2).

Only three methods were released on the European Market (Ovabloc Intratubal Device System (1980), Essure System (2002) en Adiana Permanent Contraception System (2009), while the FDA only approved the Adiana (3) en Essure (4,5,6). The Ovabloc and the Adiana were both withdrawn from the market. The Ovabloc in 1988 after reports of disappointing results, technical problems with the cold storage of the silicon and the fact that the claim to be a reversible sterilization technique could not be confirmed by a histological study. The Adiana was withdrawn as part of a deal to settle ongoing patent infringement litigation in March 2012. Currently, the Essure method is the only available hysteroscopic sterilization method.

Placement rates, efficacy and safety of current hysteroscopic sterilization devices.

The latest Cochrane Review of techniques for the interruption of tubal patency for female sterilization concluded in 2011 that data on rare and long-term outcomes are available from cohort studies, rather than from randomised controlled trials (8). Despite the different clinical settings (office or theatre; in-patient or out-patient) and differences in pre-medication and the use of different kind of anaesthetics (none, paracervical block, sedation or general anesthesia,) during the procedures all authors claimed high patient tolerance and satisfaction and a high effectiveness and safety of the methods.

Since the introduction of Essure in 2002 only gynecologists with experience in hysteroscopy were trained to perform this new method of sterilization , but studies have been shown that the learning curve for successful bilateral placement is steep (9). According to Levie the procedure can be recommended to be carried out by general obstetrician/gynecologists after an appropriate training course and supervision for the first several procedures. No differences were found in patient age, nulliparity, and BMI between successful and incorrect placement procedures (10,11). However, second half of menstrual cycle at the time of surgery and an enlarged uterus are predictors of unsuccessful placement. Difficulty to visualize

the tubal ostia, was significantly associated with failure. A longer procedure time was also associated with failure (12), likely due to procedure difficulty rather than as a direct cause of placement failure. In most of the published studies the procedures were scheduled in the proliferative phase of the menstrual cycle or oral contraceptives were prescribed, starting one month before the procedure to induce endometrial suppression.

In chapter 2 we conducted a systematic review to examine the placement rate, efficacy, safety and risk factors for failure of hysteroscopic sterilization techniques. In total, 45 studies were included. Feasibility was expressed as successful bilateral placement rate in one attempt (A, table 1.). For Ovabloc, Essure and Adiana, these placement rates were respectively: 80% (95% CI: 76-83%), 92% (95% CI: 91-94%) and 94.7%. The percentages of women that could rely on successful bilateral placement confirmed at three months follow-up (B, table 1.) were respectively: 0.96% (95% CI: 0.93-0.96), 0.97 (0.95%-0.98) and 0.91. Because of unspecified follow-up data and variation in sample size we were not able to pool the data and calculate cumulative pregnancy rates for Ovabloc and Adiana methods. Twelve pregnancies occurred in 1212 patients who relied on Ovabloc sterilization (1.2%), while 8 pregnancies occurred in 7,706 women after successful Essure sterilization (0.1%). The 36 months cumulative pregnancy rate of Adiana was 1.5%.

Complications during the hysteroscopic procedures were incidentally reported. During the Ovabloc procedures, perforation of the uterine wall occurred in five out of 438 cases (13). The most important risk factors for placement failure of Ovabloc were bad visualization, tubal spasm or inability to obtain linear axis between obturator tip of the catheter and tubal ostium (14) In the Essure studies, two perforations during the procedure were reported (15), while 42 expulsions, 45 perforations and 9 migrations of devices were notified at the three-month control in a total of 10,124 cases. Hyponatremia (sodium 129 mEq/L) occurred in one case of sterilization with Adiana.

Table 1: Feasibility and efficacy of three methods of hysteroscopic sterilization.

	Successful bilateral placement 1st attempt (A)	**Satisfactory confirmation after total bilateral placements (B)**	**Satisfactory confirmation after successful placement 1st attempt (A x B)**	**Pregnancies after confirmation**
Ovabloc	0.80	0.96	0.77	12 / 1212
Essure	92	0.97	0.89	8 / 7706
Adiana	0.95	0.91	0.86	9 /570

Based on this systematic review it seems that the Essure method has the highest successful placement rate at first attempt with proper position at confirmation and the highest efficacy.

Confirmation of correct bilateral placement and bilateral tubal occlusion.

As the primary objective of sterilization is occlusion of both tubes, the obvious 'gold standard' reference test is testing tubal patency. Other, less invasive tests such as transvaginal ultrasound and X-ray aim to confirm the appropriate position of the devices in both tubes, but are constructs for tubal patency. If tubal patency can be predicted accurately by the position of the devices, better tolerated confirmation tests may become the professional standard.

It is remarkable that in the United States of America an hysterosalpinography (HSG) is obligatory after successful bilateral placement, while the European Health Office approved the Essure method requiring only an X-ray or transvaginal ultrasound three months after the procedure accepting the lack of information of tubal occlusion. A review of the clinical data from studies by Kerin et al. and Cooper et al. of more than 700 patients showed that an HSG seems not always necessary (6,16,17). During these phase II and III multicenter clinical trials, satisfactory bilateral insertions were ultimately achieved in 664 of 734 patients (90%). The original protocol required that an HSG has to be performed three months after placement to confirm tubal occlusion. However, in patients in whom a satisfactory bilateral insertion had been achieved, a 100% bilateral occlusion rate was found (18).

A three-month confirmation test is not uncommon after hysteroscopic sterilization methods. Also for the Adiana Permanent Contraception System and Ovabloc Intratubal Device Method, a three months confirmation was indicated. In the late 1970's the three-month HSG was abandoned as a routine follow-up after laparoscopic sterilization because of discordance between tubal patency and pregnancy rates (19). In a pre-hysterectomy study of Valle, with the STOP microcoil device (an earlier type of the Essure ESS 105 with a stainless steel inner coil, an outer coil of nitinol and PET fibres) hysteroscopic placement was performed in women who required hysterectomy. Histology data of the tubes demonstrated that tissue in-growth reaction was predictable, occurred in all fibered specimens collected and was localised to the device. More than 80% occlusion was noted more often in specimens in which the device had been in place for more than four weeks. Histological confirmation of complete occlusion of the tube histologically was difficult, as artefacts may have been introduced during processing. Other studies have demonstrated that an inflammatory response peaks between two and three weeks,

after which the inflammatory response slowly resolves during a 10-week period (20). In the study of Valle (21), tubal occlusion was also evaluated by HSG just prior to hysterectomy. It is remarkable that occlusion was noted in all tubes, even in those cases with device placement less than two weeks before hysterectomy.

In chapter 3, we evaluated the diagnostic characteristics of pelvic X-ray of the pelvis and a transvaginal ultrasound after Essure sterilization with HSG as a reference test. In 9 of 150 patients with successful bilateral placement it was not possible to identify both devices in correct position with ultrasound. In one of these nine patients one microinsert was missing on pelvic X-ray; this patient seemed to have had an expulsion. In the other 149 patients the pelvic X-ray was determined to be satisfactory with both microinserts in situ. In one of these 149 women there was evidence of dye passage (patency) past the microinsert into the distal tubal lumen upon HSG. The sensitivity of transvaginal ultrasound with the HSG as reference test for correct position of the devices and tubal occlusion was 50% (one true positive[a], one false negative[b]), and the specificity was 94.6% (Table 2). If compared with X-ray as reference test sensitivity and specificity were respectively 100% (one true positive[a]) and 94.6% (table 3).

The positive predictive value of ultrasound to diagnose a correctly positioned microinsert was 99 %, while the negative predictive value was only 11%. This means that when a microinsert is not clearly visible by ultrasound one should not conclude that it is an unsatisfactory sterilization but that further evaluation is indicated. In our second study, described in chapter 4, we analyzed the interobserver agreement of X-ray without contrast after Essure sterilization and concluded that interobserver agreement was low. Even gynecologists with extensive experience in reading radiographs after Essure, were not able to recognise suspicious or unsatisfactory X-rays of patients with abnormal positions of the devices. In scoring reliability of the Essure sterilization there was a large difference in the agreement between radiologists (moderate, κ-value: 0.52) and gynecologists (slight, κ-value: 0.09),

Table 2: Counts of position of Essure microinsert, diagnosed by transvaginal ultrasound with HSG as reference test.

HSG	unsatisfactory	satisfactory	**total**
TVU			
unsatisfactory	1[a]	8	9
satisfactory	1[b]	140	141
total	2	148	150

Table 3: Counts of position of Essure microinsert, diagnosed by transvaginal ultrasound with X-ray as reference test

X-ray	unsatisfactory	satisfactory	**total**
TVU			
unsatisfactory	1[a]	8	9
satisfactory	0	141	141
total	1	149	150

Table 4: Counts of position of Essure microinsert, diagnosed by X-ray with HSG as reference test.

HSG	unsatisfactory	satisfactory	**total**
X-ray			
unsatisfactory	1[a]	0	1
satisfactory	1[b]	148	149
total	2	148	150

while for a high number of cases (27/47) at least one of the radiologists advised additional HSG to confirm a reliable sterilization .

In chapter 5, three cases with different types of incorrect position of Essure microinserts at three-months follow-up and their appearance on X-ray and by ultrasound were discussed (one case of complete expulsion with a missing device, one case of perforation and one case of proximal position of a device, which was located in the uterine cavity). In the cases of the perforation and the proximal position, pelvic X-ray demonstrated an abnormal position of one microinsert and abnormal configuration with a deviation of the fourth marker (proximal end of outer coil). In chapter 6 we analyzed data collected from 10 patients with unintended pregnancies after Essure sterilization in the Netherlands and identified one case of luteal pregnancy (pregnancy already occurred before the procedure). In three cases single placement was followed by a three months HSG and bilateral tubal occlusion was concluded. In the other six cases an abnormal position of a microinsert was recognized after termination of pregnancy.

Based on our own findings, conclusion from other studies (18,22,23) and analysis of unintended pregnancies cases we developed a new follow-up protocol for Essure sterilization with transvaginal ultrasound as first-line investigation after an uncomplicated bilateral placement (Addendum Fig. 1):

- No unintended pregnancies occurred after proper demonstration of bilateral occlusion following device placement (24).
- Improper placement of devices was usually preceded by difficult or complicated procedures (25).
- Procedure time of failed procedures was longer than procedure time of bilateral successful placements (26).
- Unilateral device placement in patients with bilateral tubal occlusion on HSG, without a history of salpingectomy was related to unintended pregnancy (24).
- Transvaginal ultrasound (TVU) has proved to be an adequate alternative method for confirmation of the microinsert placement at follow-up (18,23,25,27).

This revised Dutch protocol was validated in a center study, as described in chapter 7. With a reduction of the number of HSG's to less than 15%, the effectiveness of hysteroscopic sterilization was not reduced. The two-years cumulative pregnancy rate was 3.86 per 1,000, while two of four pregnancies occurred after violation of the protocol (VOP). In one case, placement was complicated, and a third device was placed after a spontaneous expulsion of the first device. Ultrasound examination was performed at three months instead of HSG. In the second patient, device placement was unsuccessful on one side, and only one device was placed. At HSG, the contralateral tube seemed to be occluded, and the patient was instructed to cease alternative contraception. This suggests that strict following of the protocol could further reduce the already low pregnancy rate. The extra four-weeks ultrasound examination as suggested by others (27) to detect perforations before the 3 months control, did not cause any deviations from the protocol and should be reserved for specific indications (difficult procedure with high risk for perforation or patient with post-procedure abdominal pain). The results of our study supported the submission to receive the CE mark for transvaginal ultrasound as first-line confirmation test after Essure sterilization , which was assigned in 2011. Others studies (23,28,29,30) confirmed the validity of ultrasound as first-line confirmation test. In 2011 a clinical trial was initiated to obtain FDA approval for transvaginal ultrasound confirmation in the United States.

Thiel et al. (23) and Legendre et al. (32,33) assessed the position of the microinsert with 3D ultrasound. The use of volume-contrast 3D imaging improved the visualization of the microinserts within the uterine cornua and proximal fallopian tube. A classification with four different positions of the microinsert (perfect, proximal, distal

and very distal) was proposed. 3D-US showed a sensitivity of 100% and a Specificity of 58.2% with HSG as reference test and inadequate evaluation of 3D-US was regarded as a positive test result (indicative of sterilization failure), whereas a satisfactory evaluation was regarded as a negative test result (indicative of successful sterilization). The Negative Predictive Value (NPV) of 3D-US was 100% (95% CI: 100–100%) (i.e. proportion of patients with negative results, i.e. satisfactory position and successful sterilization on 3D-US, with actual negative results) and the Positive Predictive Value (PPV) of 3D-US was 23.3% i.e. proportion of women with at least an unsatisfactory position on 3D-US whose sterilization was correctly found to have failed (33). Advantage of the 3D ultrasound compared to 2D is that the volume 3D data can be preserved for a later assessment. As far as we know the performance of 2D and 3D ultrasound to confirm hysteroscopic sterilization has not yet been compared. Connor evaluated Contrast Infusion Sonography (CIS) as a first-line Essure confirmation test (34). The contrast solution infused consists of 1 mL of a perflutren microsphere contrast agent (Bristol Myers-Squibb Medical Imaging, North Billerica, MA) mixed with 20 mL of normal saline. Preliminary data suggested that CIS is a feasible, safe and accurate confirmation test, which is well accepted by patients.

Outcome of unintended pregnancies and IVF pregnancies after regret or pre-procedure closure of hydrosalpinges.

Finally we started a prospective study to investigate the success rate of proximal tubal occlusion with Essure devices in subfertile women with hydrosalpinges and to observe the results of subsequent treatment with IVF. Our case series in chapter 9,shows good pregnancy rates with IVF-ET following Essure placement, and is consistent with rates found after tubal obstruction with microinserts or laparoscopic salpingectomy (35-38).

A significant concern for women with unintended pregnancies and subfertile women wishing to conceive with microinserts in situ, is the trailing of Essure coils into the uterine cavity and its possible effects on implantation as well as on pregnancy.

Although two out of 50 pregnancies in our case series ended with a stillbirth we concluded that it was unlikely that these events were induced by the presence of the microinsert. In a recent review on the efficacy and safety of Essure in the management of hydrosalpinges prior to IVF, data of 115 women in 11 studies were pooled. Successful placement of Essure was achieved in 96.5% (95% CI: 91.1-98.9%) of women and tubal occlusion in 98.1% (95% CI: 93.1-99.9%). Subsequent IVF resulted in 38.6% pregnancy rate (95% CI: 30.9-46.8%),

27.9% live birth rate (95% CI: 21.1-35.8%) and 28.6% combined ongoing pregnancy and live birth rate (95% CI: 21.7-36.6%) per embryo transfer (39).

The strength of this thesis is the high clinical relevance. The outcomes of our studies were used to revise the Dutch follow-up protocol of hysteroscopic sterilization, which was validated in a large multicenter study. The major limitation of the studies is that they were not comparative and based on single-arm prospective cohort studies and case series.

The effectiveness of hysteroscopic sterilization methods is based on correct intra-tubal position of devices confirmed by a diagnostic test after three months. The predictive value of a diagnostic test for recognizing an abnormal position of a device depends on the incidence of these improper placed devices. Because of the low incidence of abnormal positioned devices we found a low negative predictive value. However confirmation of the proper position of the devices makes effective sterilization very likely. To evaluate the diagnostics characteristics of a confirmation test, a larger cohort of patients would have been preferable. Although we studied the interobserver agreement for X-ray we could not study this for transvaginal ultrasound examination. The biggest disadvantage of using ultrasound as a diagnostic test is that it is a real-time examination, while capturing the diagnosis on a hardcopy. We did not succeed in capturing videos of all our ultrasound examinations. 3D ultrasound volumes that can be stored and reviewed, may solve the problem of retrospective analysis of diagnostic data.

Conclusion

At this moment there is only one hysteroscopic sterilization method available. The Essure method can be performed in an office setting without anesthetics during the procedure. Patient satisfaction and tolerance are high. Hysteroscopic sterilization with a strict follow-up protocol with transvaginal ultrasound as first-line test for confirmation is highly effective and reduces the need for radiologic examination. The risk of complications (perforation, expulsion and pregnancy) is low. Radiologic confirmation is only needed for strict indications. The use of microinserts to obstruct hydrosalpinges in an IVF program to improve the “take home baby” rates is promising and related to less burden (in contrast to laparoscopic treatment, hysteroscopic treatment can be performed in an outpatient setting, without use of general anesthesia, with shorter procedure times and a quicker recovery) and possibly also less interventional and/or anesthesiologic risk for the patient. It is unlikely that the presence of Essure microinserts interferes with implantation and the developing amniotic sac and fetus.

Future perspectives

The need for a confirmation test after sterilization is questionable. Because the contraceptive principle of hysteroscopic sterilization methods such as Essure System and Adiana Permanent Contraception System is based on tubal occlusion by tissue in-growth and not by direct tubal occlusion by the device itself, it makes sense to use a tubal patency test for confirmation after the procedure. On the other hand, persisting anatomical tubal patency does not necessarily imply sterilization failure and a negative dye spill post-procedure sterilization HSG does not complete exclude the possibility of pregnancy at a later stage (40). HSG is an ionizing radiation technique inconvenience for the patient and risk of anaphylactic reaction. In the United States it is an obligatory test although the patient-compliance is very low (41). A theoratical risk of flushing the fallopian tube with contrast medium and wash-out of scarred tissue has not been described (21).

One of the outcomes of this thesis is that the chance of an abnormal position of Essure microinserts after bilateral placement (one or more attempts) is less than 3%. Perforation or expulsion happened after complicated procedures. Pregnancies were described after violation of protocol or in patients who were non compliant to the protocol. None of the cases of pregnancy were a method failure but all were related to improper position of a device. Our hypothesis is that a standard confirmation test is not necessary and can be removed from the flow chart. It will not reduce the effectiveness of Essure sterilization. In case of an "abnormal" procedure, with a procedure time of more than 12 minutes, to deep or to proximal placement (more than eight coils visible) or the need for a second attempt, confirmation by transvaginal ultrasound or X-ray is indicated X-ray. In these scenarios X-ray and transvaginal ultrasound are complementary. X-ray verifies devices presence, the position, symmetry and distance between the microinserts and the configuration of the devices with its four markers, while ultrasound visualizes the relation of the microinserts to soft tissue, and the tubocornual junction in particular.

If the first-line test is unsatisfactory, the complementary test has to be performed. If both tests have an unsatisfactory result (meaning: there is doubt in the efficacy of the sterilization), additional HSG should confirm proper position of the device and tubal occlusion. This renewed Dutch protocol has to be validated in a prospective multicenter study (Addendum Fig. 2, page 215).

The "ideal" hysteroscopic sterilization device, with 100% effectiveness and 100% safety and no not need for confirmation, has not been developed yet. There is still a need to improve the available intratubal devices.

Three new hysteroscopic sterilization devices will be launched in the near future. One is a redesigned Ovabloc Intratubal Device System. Challenges related to the design included the storage of material under room temperature conditions achieving reliable curing times and incorporating a contrast agent to facilitate visibility for evaluation. A study with a new model of the Essure System has recently been completed. The investigational device offers immediate, permanent contraception without a three-month confirmation test. A multicenter pivotal study for safety and efficacy of Altaseal will be started this year. The Altaseal (42) is a hysteroscopically placed mechanical occlusion implant for immediate contraception.

In case that in the future confirmation tests are still indicated after hysteroscopic sterilization , a new diagnostic test like 3D ultrasound has to be evaluated to confirm proper placement. Results from earlier studies (32,33,43-45) are promising. If tubal occlusion still has to be confirmed new non-radiation techniques like Contrast Infusion Sonography or Hysterosalpingo Contrast Sonography (HyCoSy) as suggested by Connor in 2008 (34) or the newer Hysterosalpingo-Foaminfusion Sonography (HyFoSy) could be considered to be evaluated as confirmation test for tubal occlusion (46-48).

Patient Outcome Measurement Tool (POMT) is a surgical registry that has recently been introduced in the Netherlands for the collection, analysis and reporting of patient clinical data for gynecological patients undergoing surgical interventions. Procedures and adverse events or complications will be related to patients unique Citizen Service Number (BSN), independent of where the procedure was performed. Registration of sterilization procedures and complication, gives the opportunity for long-term follow-up of all methods of sterilization and life-table mathematics to calculate 2-year, 5-year or 10-year cumulative pregnancy rates. Therefore, we strongly recommend that all data of patients seeking for sterilization will be registered in this module.

Referencs

1. Magos A, Chapman L Hysteroscopic tubal sterilization. Obstet Gynecol Clin N Am 2004;31: 705-719
2. Abbott J. Transcervical sterilization. Best Pract Res Clin Obstet Gynecol 2005:14:1-14
3. Vancaillie TG, Anderson TL, Johns DA. A 12-month prospective evaluation of transcervical sterilization using implantable polymer matrices. Obstet Gynecol.2008;112:1270-7
4. Cooper JM. Hysteroscopic sterilization. Clin Obstet Gynecol. 1992;35:282-98
5. Loffer FD. What's new in female sterilization ? The silicone tubal plug is. Ariz Med. 1982;39:442-5.
6. Kerin JF, Cooper JM, Price T, et al., Hysteroscopic sterilization using a microinsert device: results of a multicenter phase II study, Hum Reprod, 2003;18:1223-30.
7. Asaf a. Abdin F et al. Histopathological effects of silicone rubber Ovabloc on the human fallopian tube. Int J Gynecol Obstet 1993; 43:181-9
8. Lawrie TA, Nardin JM, Kulier R, Boulvain M. Techniques for the interruption of tubal patency for female sterilization. Cochrane Database Syst Rev. 2011.
9. Levie M, Chudnoff SG. A comparison of novice and experienced physicians performing hysteroscopic sterilization: An analysis of an FDA-mandated trial. Fertil Steril. 2011 Sep;96(3):643,648.e1Sinha 2006
10. Savage UK, Masters SJ, Smid MC, Hung YY, Jacobson GF. Hysteroscopic sterilization in a large group practice: Experience and effectiveness. Obstet Gynecol. 2009;114:1227-31.
11. Sinha D, Kalathy V, Gupta JK, Clark TJ. The feasibility, success and patient satisfaction associated with outpatient hysteroscopic sterilization. BJOG. 2007;114:676-83.
12. Shavell VI, Abdallah ME, Diamond MP, Berman JM. Placement of a permanent birth control device at a university medical center. J Reprod Med. 2009;54:218-22.
13. Reed TP,3rd. Ovabloc. five years of experience. J Reprod Med. 1984;29:601-2.
14. Houck RM, Cooper JM, Rigberg HS. Hysteroscopic tubal occlusion with formed-in-place silicone plugs: A clinical review. Obstet Gynecol. 1983;62:587-91.
15. Lett CD, Thiel JA. The effect of menstrual phase and hormonal contraception on successful bilateral placement of the essure microinsert tubal coil. Gynecol Surg. 2009;6:219-22.
16. Cooper JM, Carignan CS, Cher D, Kerin JF, Microinsert nonincisional hysteroscopic sterilization , Obstet Gynaeol, 2003;102: 59-67.
17. Conceptus USA, US Physician Training Manual: HSG Protocol, TR-0679 2003;101.
18. Kerin JF, Levy BS. Ultrasound: an effective method for localization of the echogenic Essure sterilization microinsert: correlation with radiologic evaluations. J Minim Invasive Gynecol. 2005;12:50-54
19. Seikh. 1976: Am J Obst Gynaeol 126:181-185
20. Estridge TD, Feldman DS. Quantification of vascular ingrowth into Dacron velour. J Biomater Appl. 1991;6:157-69.
21. Valle RF, Carignan CS, Wright TC and the STOP Prehysterectomy Investigation Group. Fertil steril. 2001;76:974-980

22. Weston G, Bowditch J. Office ultrasound should be the first-line investigation for confirmation of correct ESSURE placement. Aust N Z J Obstet Gynecol. 2005;45:312-5.
23. Thiel JA, Suchet IB, Lortie K. Confirmation of essure microinsert tubal coil placement with conventional and volume-contrast imaging three-dimensional ultrasound. Fertil Steril. 2005;84:504-8.
24. Veersema S. Vleugels MPH, Moolenaar LM, Janssen CAH, Brölmann HAM. Unintended pregnancies after Essure sterilization in the Netherlands. Fertil Steril. 2010;93:35-8.
25. Veersema S, Vleugels MP, Timmermans A, Brolmann HAM. Follow-up of successful bilateral placement of Essure microinserts with ultrasound. Fertil Steril. 2005;84:1733-1736
26. Levie B Levie MD, Childer ME. A summary of reported pregnancies after hysteroscopic sterilization. Presented at 34th Annual meeting AAGL Chicago, 2005. J Minim Invasive Gynecol. 2007;14:271-274
27. Teoh M, Meagher S, Kovacs G. Ultrasound detection of the Essure permanent birth control device: a case series. Aust NZ J Gynecol. 2003; 43:378380.
28. Arjona JE, Mino M, Cordon J, Povedano B, Pelegrin B, Castelo-Branco C. Satisfaction and tolerance with office hysteroscopic tubal sterilization. Fertil Steril. 2008;90:1182-6.
29. Andersson S, Eriksson S, Mints M. Hysteroscopic female sterilization with essure in an outpatient setting. Acta Obstet Gynecol Scand. 2009;88:743-6.
30. Chapa HO, Venegas G. Preprocedure patient preferences and attitudes toward permanent contraceptive options. Patient Prefer Adherence. 2012;6:331-6 Epub
31. Thiel JA, Suchet I, Tyson N, Price P. Outcomes in the ultrasound follow-up of the essure microinsert: Complications and proper placement. J Obstet Gynecol Can. 2011;33:134-8.
32. Legendre G, Gervaise A, Levaillant JM, Faivre E, Deffieux X, Fernandez H. Assessment of three-dimensional ultrasound examination classification to check the position of the tubal sterilization microinsert. Fertil Steril. 2010;94:2732-5.
33. Legendre G, Levaillant JM, Faivre E, Deffieux X, Gervaise A, Fernandez H. 3D ultrasound to assess the position of tubal sterilization microinserts. Hum Reprod. 2011;26:2683-9.
34. Connor VF. Clinical experience with contrast infusion sonography as an essure confirmation test. J Ultrasound Med. 2011;30:803-8
35. Rosenfield RB, Stones RE, Coates A, Matteri RK, Hesla JS. Proximal occlusion of hydrosalpinx by hysteroscopic placement of microinsert before in vitro fertilization-embryo transfer. Fertil Steril 2005;83:1547-50.
36. Kerin JF, Cattanach S. Successful pregnancy outcome with the use of in vitro fertilization after essure hysteroscopic sterilization. Fertil Steril. 2007;87:1212.e1,1212.e4.
37. Galen DI. Utilization of the Essure_ microinsert for the treatment of hydrosalpinx prior to IVF. Fertil Steril 2007;88(Suppl 1):16.
38. Hitkari JA, Singh SS, Shapiro HM, Leyland N. Essure_ treatment of hydrosalpinges. Fertil Steril 2007;88:1663-6.
39. Arora P, Arora R, Cahill D. Essure for management of hydrosalpinx prior to in vitro fertilization- a systematic review and polled analysis. BJOG 2014; epub ahead.

40. Varma R, Gupta JK.Failed sterilization : evidence-based review and medico-legal ramifications. BJOG. 2004;111:1322-32
41. Shavell VI, Abdallah ME, Diamond MP, Kmak DC, Berman JM. Post-essure hysterosalpingography compliance in a clinic population. J Minim Invasive Gynecol. 2008;15:431-4.
42. Thurkow A. AltaSeal Hysteroscopic sterilization : The New Challenger to Essure? J Minim Invasive Gynecol. 2011;18:38
43. Pachy F, Bardou D, Piovesan P, Jeny R. Vaginal tridimensionel ultrasound interest for the assessment of correct Essure sterilization microinsert placement. J Gynecol Obstet Biol Reprod (Paris). 2009 Jun;38(4):321-7
44. Oliviera M, Johnson D, Switalski P et al. Optimal Use of 3D and 4D Transvaginal Sonography in Localizing the Essure Contraceptive Device. J Diagn Med Sonography 2009;25: 163-167
45. Thiel JA, Suchet IB, Lortie K. Confirmation of Essure microinsert tubal coil placement with conventional and volume-contrast imaging three-dimensional ultrasound. Fertil Steril. 2005;84:504-8.
46. Emanuel MH, Exalto N. Ultrasound Obstet Gynecol. 2011;37:498
47. Emanuel MH, van Vliet M, Weber M, Exalto NFirst experiences with hysterosalpingo-foam sonography (HyFoSy) for office tubal patency testing. Hum Reprod. 2012;27:114-7
48. Van Schoubroeck D, Van den Bosch T, Meuleman C, Tomassetti C, D'Hooghe T, Timmerman D. The use of a new gel foam for the evaluation of tubal patency. Gynecol Obstet Invest. 2013;75:152-6

11a

English Summary

Summary

Chapter 1 gives an overview and historical perspective of sterilisation methods and describes the outline of this thesis.

In **chapter 2** we conducted a systematic review to evaluate the feasibility, reliability and safety of modern hysteroscopic sterilisation methods. All longitudinal studies addressing hysteroscopic tubal sterilisation were considered for inclusion, both prospective and retrospective. Studies were included if they investigated reliability or safety of sterilisation techniques, risk factors for failure of hysteroscopic sterilisation. Only original studies were included with > 20 patients were included. Descriptive articles, case-series (non-consecutively), reviews, surveys, technical reports were excluded. A total of 45 articles were included: 7 articles concerned Ovabloc, 36 Essure, and 2 Adiana sterilisation.

The Ovabloc Intratubal Device methode is an office procedure which can be done using local anaesthesia. A catheter is installed into the ostium and a silicon mixture solidifies with in 5 min into a soft rubber plug. The procedure is repeated on the contra lateral side. A post-procedure x-ray is captured. If after three month a second x-ray shows that the position of the devices has not altered, the patient can rely on Ovabloc for sterilisation.

The Essure is an 4 cm expanding spring device made of a nitinol outer coil and stainless steel innercoil with PET fibers. The microinsert is placed in the proximal section of the fallopian tube under. The PET fibres cause localised tissue ingrowth from the surrounding tube , thereby achieving mechanical occlusion of the tube and anchoring of the device. Different diagnostic tests (hysterosalpingography, x-ray and ultrasound) are described to confirm adequate position and bilateral tubal occlusion after three months.

The Adiana System is a combination of the 60-second application of radiofrequency (F) to the mucosa of the fallopian tube, followed by deployment of a porous silicon 3.5 mm matrix in to the thermal lesion. The procedure is than repeated on the other side. The matrix provides a substrate for tissue ingrowth, leading to tubal occlusion. A three-months hysterosalpingography is indicated to confirm bilateral tubal occlusion. The devices are not radiopaque.

All hysteroscopic sterilisation technique offers distinct advantages over laparoscopic sterilisation or mini-laparotomy with reduced need for anaesthesia and decreased risk for injury to intra-abdominal organs. It can be performed in an office setting with local or no anaesthesia. Patient tolerability and satisfaction was high in all studies despite the large difference in settings and pain management protocols that were used (no anaesthetics, para-cervical block, intravenous sedation and general anaesthesia). The Ovabloc system had a higher placement failure rate, because of higher numbers of unsatisfactory position at the three months control, due to migration or expulsions of the plugs. Also the number of unsuccessful procedures was higher but we have to realise that procedures were performed with larger (8 mm)

single flow instruments, initially with Hyskon or carbon dioxide as distension medium. Long-term data were spare. At least 12 patients, of a group of 1588 patients who relied on, conceived after a satisfactory three months x ray. In 2009 the method was stopped.

The bilateral placement reliance represents the number of women who were ultimately instructed to that they could rely on the sterilisation divided by the number of intention to treat was similar for both techniques. The three years cumulative pregnancy rate for Adiana was 15/1000, while we calculated a 1/1000 pregnancy rate for commercial use of Essure. Since March 2012 the Essure method is the only available method on the market.

Chapter 3 describes a study to compare the test characteristics of two diagnostic tests for Essure confirmation. The pelvic- x rays, transvaginal ultrasound and HSG imaging was performed in 150 women with successful bilateral placement. The results of transvaginal ultrasound as compared with the results of HSG as the "reference test" showed a sensitivity of 50% and a specificity of 95%. One patient with correct position of the microinserts but with tubal patency on one side could not be identified by ultrasound or x-ray. A second patient with an expulsion of one microinsert was well diagnosed by both ultrasound and x ray. When we compared diagnostic characteristics of the ultrasound with pelvic X-ray as the reference test (accepting the case with tubal patency as satisfactory) the sensitivity and specificity were 100% and 95%, respectively. In only 8 patients with a satisfactory pelvic x ray it was not possible to confirm the satisfactory position of the devices with ultrasound. The predictive value of a satisfactory transvaginal ultrasound result is than 99% and the predictive value of an unsatisfactory result is 11%.

In this cohort of 150 women there was no case of perforation of a microinsert. Therefore we developed a new study to estimate the diagnostic accuracy and interobserver reproducibility of pelvic x-rays in the diagnosis of bilateral sterilisation with Essure.

In **Chapter 4** six observers evaluated x-rays from 47 patients, including one case with a complete perforation of one device, one case of proximal position and tubal patency on HSG and one abnormal x ray from the patient with complete expulsion of one device and tubal patency on HSG. Three gynaecologists with experience in Essure sterilisation and x-ray reading and 3 radiologists with specific training in confirmation of Essure sterilisation with x-ray were involved. After evaluation of the results it seemed that the test characteristics of pelvic x-ray as the imaging technique to assess the position of the microinserts were poor, as was the reproducibility. The sensitivity and specificity for x-rays read by gynaecologists was 0.67 (95% CI,0.29–0.96) and 0.79 (95% CI, 0.58–1.00) and for radiologists 1.0 and 0.5 (95% CI, 0.36–0.64). The interobserver agreement in reliability (Fleiss's k-statistics) of pelvic x-ray of hysteroscopic sterilisation assessment with Essure ranged from slight (**k**-value: 0.09) for gynaecologists to moderate (**k**-value: 0.52) for radiologists. *Because of the limitations of x-ray compared to ultrasound and the non-superior diagnostic characteristics and poor interobserver agreement, we do not recommend the routine use of pelvic x-ray for the assessment of the positioning of microinserts after hysteroscopic sterilisation. Only if expulsion or perforation of a device is suspected and ultrasound examination is not confirmative a x-ray can be helpful.*

In **chapter 5** we describe three different types of incorrect position of Essure microinserts detected at 3 months' follow-up and their appearance on x ray and by ultrasound. In a series of hundred patients who underwent hysteroscopic sterilisation with Essure three cases were identified with an abnormal position of a microinsert. In case A, both inserts were not clearly visible with vaginal ultrasound while on pelvic X ray an abnormal configuration of one insert was seen. HSG showed tubal patency. The perforated microinsert was laparoscopically removed. Retrospectively, the patient had experienced abdominal pain for several weeks after the procedure. In Patient B one device was missing which was recognised with all confirmation-tests. Patient had not noticed an expulsion. In a second attempt a new microinsert was placed successfully. In the third patient who had a difficult bilateral placement due to adhesions in the uterine cavity one device was expulsed to the uterine cavity. With ultrasound examination one device could not be made clearly visible. X pelvis showed an abnormal configuration of one device and on HSG there was tubal patency. After hysteroscopic removal of the microinsert a second device was correctly placed. Complications after Essure placement can be detected during the procedure itself or at follow-up. When, during the procedure, there is doubt about the position of a microinsert, a transvaginal ultrasound can be performed at that time. But one should realise that in case of perforation and expulsion, most incorrectly placed microinserts will migrate in the period after the procedure. A majority of cases will not be detected during or directly after the procedure. *We advise screening patients with apparent successful bilateral placement but with difficult placement procedures, other suboptimal conditions during the procedure, or abdominal pain earlier than 3 months after the procedure. Initially this can be done with transvaginal ultrasound after the patient's first period or withdrawal bleeding (approximately 4 weeks), and when in doubt, a pelvic X-ray can be performed.*

Because hysteroscopic sterilisation is a rather new method, it is important that all pregnancies are reported and that the cases are reviewed to determine the cause of the unintended pregnancy. Some of the causes might be preventable. Understanding these causes can be helpful to improve the follow-up protocols and reduce the number of failures in the future. In **chapter 6** we describe a retrospective analysis of 10 unintended pregnancies after Essure sterilisation in the Netherlands from August 2002 till May 2008. In one case pregnancy already occurred before the procedure (luteal pregnancy). In three cases single placement was followed by HSG after three months and bilateral tubal occlusion was concluded. In the other six cases an abnormal position of a microinsert was recognised after termination of pregnancy although from 1 case data were lacking. In these 5 cases there was non-compliance to the protocol. *A procedure with only a single device placement in a patient without a history of salpingectomy of the contra-lateral tube should be considered as unsuccessful and an HSG should not be performed.*

With the information we collected from our earlier in the Netherlands. We developed a revised protocol for the follow-up after Essure sterilisation. Objectives were to reduce the need for radiologic confirmation (x-ray examination and HSG), without compromising the effectiveness of Essure. In January 2005, this new protocol for follow-up of Essure sterilisation was introduced in the Netherlands. With the new Dutch protocol, transvaginal ultrasound is used for the 3-month confirmation of tubo-cornual location of the microinserts after an uncomplicated successful bilateral

placement. The criteria for a normal successful bilateral procedure include procedure time of 15 minutes or less, microinsert visible after placement, fewer than 9 coils protruding into the uterine cavity, and no unusual events during the procedure. In all other cases, HSG is still indicated. A procedure with only a single device placement in a patient without a history of salpingectomy of the contra-lateral tube should be considered unsuccessful, and HSG should be abandoned, because of a high risk of false positive confirmation of occlusion of the contra-lateral tube. When findings at ultrasound examination are inconclusive or abnormal location of a microinsert is suspected, HSG is indicated.

In a multicentre study, described in **chapter 7** we evaluated the revised protocol based on first-line confirmation using transvaginal ultrasound at 3 months after uncomplicated successful Essure sterilisation and analysed the rate of success of placement and effectiveness of the method. Data of 1145 consecutive cases from 5 clinics were collected and analysed. The overall successful placement rate was 93.6% (1072 of 1145 intentions to treat). In 6% of patients with intention to treat, Essure sterilisation was successfully completed; however, the procedure was not considered straightforward. According to the Dutch protocol, TVU was scheduled at 4 weeks after the procedure, and HSG at 3 months. In 4.5%, the ‘‘standard‘‘ 3-month TVU was inconclusive; thus, HSG was scheduled as outlined in the protocol. In 50 of these 52 patients, HSG confirmed bilateral occlusion with normal position of the devices. Only in 2 of these patients there was an abnormal positioning of 1 device: 1 expulsion and 1 perforation. Including patients with a successful second attempt and successful single placement. Overall 14.3% of patients (164 of 1145) with intention to treat underwent HSG. In 9 patients, HSG showed evidence of an abnormal position of 1 or 2 devices (2 expulsions and 7 perforations). Finally 1037 patients were instructed to rely on the sterilisation. The 24-months cumulative pregnancy rate was 3.86 per 1000 (4/1037). None of these pregnancies was related to failure of the sterilisation method. Two patients conceived with only one device in situ, one after bilateral placement and ultrasound confirmation and one with bilateral tubal occlusion on HSG after single placement. In two cases there was a perforation of one device after a complicated procedure.

When the device was properly placed; in 1 case the device was absent or incorrectly positioned, and in three cases there was noncompliance with the protocol. *The Dutch protocol for confirmation of Essure sterilisation, with transvaginal ultrasound as first-line test, reduced the number of HSGs, thus reducing costs, inconvenience, and discomfort without influencing the effectiveness of the sterilisation. Compared with the FDA protocol, the Dutch control protocol is associated with high patient compliance. In cases of difficult placement, the extra TVU confirmation at 4 weeks did not reduce the number of HSGs. Thus, the need for routine TVU after a difficult hysteroscopic procedure should be abandoned, with sole reliance on the 3-month HSG as a confirmatory test.*

After the success of occlusion of the fallopian tubes with microinserts for contraceptive use, a new indication was presented in 2005 to obstruct hydrosalpinges of subfertile woman to improve the results of IVF treatment as an alternative for salpingectomy to improve the chance of ongoing pregnancies in IVF-programs.

Chapter 8 provides a prospective study to investigate the success-rate of proximal tubal occlusion with Essure devices in subfertile women with hydrosalpinges and to observe the results of subsequent treatment with IVF. Ten patients had successful placement of the Essure devices without any complications. Proximal tubal occlusion was confirmed by hysterosalpingography in 9 out of 10 patients. A 40% ongoing pregnancy rate was achieved with 20% life births after one IVF cycle and/or frozen embryo transfer. *Our case series shows good pregnancy rates with IVF-ET following Essure placement, and is consistent with others found after laparoscopic salpingectomy.*

A significant concern for women with unintended pregnancies and subfertile women wishing to conceive with microinserts in situ, is the trailing of Essure coils into the uterine cavity and its possible effects on implantation as well as on pregnancy. Therefore we collected data of 50 pregnancies in 43 patients in the Netherlands who became pregnant with 1 or 2 Essure microinserts in situ.

In **Chapter 9** we analysed the obstetric outcomes of 50 pregnancies in 43 women with 1 or 2 Essure microinserts in place and found a good outcome for ongoing pregnancies. Of 26 unintended pregnancies after hysteroscopic sterilisation with Essure 17 (65.4%) were electively terminated, and 9 (34.6%) resulted in the birth of a healthy baby. Each of the 2 patients with sterilisation regret treated via IVF/ET conceived after the first single embryo transfer. Both delivered a healthy baby. In the IVF-group with pre-procedure closure of hydrosalpinges15 of 23 pregnancies (65%) were ongoing. Only 2 patients had a microinsert with 5 coils in the uterine cavity. In 1 of these patients, pregnancy ended in miscarriage. In the other patient, pregnancy ended with stillbirth. After removal of the microinserts, dramatically her next pregnancy ended with a second still birth. The number of miscarriages (35%) in the group who underwent IVF/ET after proximal closure of hydrosalpinges is not unexpectedly high and reflects findings reported in the literature. The number of ongoing pregnancies in this group is encouraging and congruent with the literature on pre-IVF salpingectomy or tubal occlusion. *It is unlikely that the presence of Essure microinserts interferes with implantation and the developing amniotic sac and foetus*.

Chapter 10 is a general discussion on the findings of this thesis and provides the answers to the research questions posed in the outline of this thesis**.** Furthermore some future perspectives are discussed, including the introduction of new hysteroscopic sterilisation devices and alternative non-ionising confirmation tests.

A recommendation is made to register all data of patients seeking for sterilisation in the Patient Outcome Measurement Tool that has recently been introduced in the Netherlands.

11b

Nederlandse samenvatting

Nederlandse samenvatting

Wereldwijd vertrouwen meer dan 100 miljoen vrouwen op sterilisatie als definitieve vorm van anticonceptie. Al meer dan 100 jaar worden vrouwen gesteriliseerd. Met de komst van de laparoscopische sterilisatie heeft deze techniek in veel Westerse landen lange tijd de voorkeur gehad, boven de meer invasieve technieken waarvoor een (min) laparotomie noodzakelijk was. Drie hysteroscopische sterilisaties technieken zijn afgelopen decennia met in Nederland geïntroduceerd. De Ovabloc Intratubal Device methode (1980) met injectie van een vloeistof met siliconen, waardoor zich een rubber plug vormt in de tuba. Waarbij controle plaats vindt door middel van twee röntgenfoto's, direct na de ingreep en na drie maanden. De Essure methode (2002), waarbij veertjes met polyester vezels in de eileiders worden geplaatst , waarna afluiting ten gevolge van weefsel ingroei gecontroleerd wordt door middel vane een röntgenopname of Hysterosalpingogram na 3 maanden. Als laatste de Adiana Permanent Contraception Method (2009), waarbij een thermisch beschadiging wordt veroorzaakt van de mucosa van de tuba, waar na een poreuze silicone matrix ter hoogte van de laesie wordt achtergelaten. Na 3 maanden dient afsluiting van de tubae bevestigd te worden door middel van een HSG. Sinds maart 2012 is na het verdwijnen van Ovabloc en Adiana alleen de Essure methode nog maar beschikbaar in Nederland.

Hoofdstuk 1 geeft een historisch overzicht van de verschillende methoden van sterilisatie van de vrouw en beschrijft de doelstellingen en vraagstellingen van dit proefschrift.

Hoofdstuk 2 beschrijft een systematisch literatuuroverzicht van cohortstudies over hysteroscopische sterilisatie bij de vrouw. Er werd gekeken naar de effectiviteit, betrouwbaarheid en veiligheid van de drie verschillende hysteroscopische sterilisatie methoden die in Nederland werden toegepast.

In **Hoofdstuk 3** worden een drietal casus beschreven, met abnormale positie van een Essure device. Bij een patiënte trad een perforatie op van het device, bij de tweede trad een expulsie naar het cavum uteri op en bij de derde trad complete expulsie van het device op. De röntgenfoto van de eerste patiënten toonde een abnormale positie en configuratie van het device op met deviatie van de het proximale einde van de buitenste veer (4th marker)

Hoofdstuk 4 beschrijft de resultaten van een studie, waarbij de betrouwbaarheid van de interpretatie en de interobserver variabiliteit van de beoordeling van een röntgen bekkenfoto na Essure sterilisatie door 6 onderzoekers. In totaal werden 47 foto's beoordeeld door 3 gynaecologen met ruime ervaring van Essure plaatsing en drie radiologen met specifieke training in het lezen van röntgenfoto's na Essure sterilisatie. Op basis van eerdere HSG's waren drie foto's afkomstig van patiënten waarbij de sterilisatie als onbetrouwbaar moest worden beoordeeld (1 perforatie, 1 expulsie en 1 proximale positie). De testkarakteristieken en de reproduceerbaarheid van de beoordeling van de röntgenfoto's ter bepaling van de correctheid van de positie van de micro-inserts was slecht. De interobserver agreement met behulp van Fleis's statistiek

(schaal 0,0 - 1,0) voor de gynaecologen was gering (k = 0,09) en matig voor de radiologen (k = 0,52). De negatief voorspellende waarden voor beide groepen was hoog (resp. 98% en 100%) hetgeen wil zeggen, dat een als betrouwbaar uitgeboekte foto overeenkomt met een betrouwbare sterilisatie. Echter de positief voorspellende waarde was laag (resp. 43% en 13 %) hetgeen betekent dat het niet kunnen bevestigen van een betrouwbare sterilisatie, niet wil zeggen dat deze ook onbetrouwbaar is. De radiologen beoordeelden correct de drie foto's van patiënten met onbetrouwbare sterilisatie, echter in een groot aantal van de betrouwbare sterilisaties, was er minimaal 1 radioloog die een aanvullend HSG adviseerde. Twee gynaecologen beoordeelde de foto met perforatie als betrouwbaar en door 1 gynaecoloog werd de abnormale (proximale) positie van het device in het cavum uteri niet herkend.
Door alle zes de onderzoekers werd de foto van een patiënt met complete expulsie correct beoordeeld. Geconcludeerd wordt dat het niet is aan te bevelen een rontgen foto van het bekken als eerst test te verrichten na Essure sterilisatie. Slechts indien er verdenking is op expulsie of perforatie van een microinsert, en de echo is niet conclusief , is een x pelvis een nuttige aanvulling.

In **Hoofdstuk 5** worden de resultaten besproken van een studie, waarbij de testkarakterieken van twee verschillende confirmatietesten werden bepaald en werden vergeleken. Bij 150 patiënten met succesvolle dubbelzijdige plaatsing van Essure, werd drie maanden na de procedure een vaginale echo (transvaginale ultrasound, TVU) en HSG gemaakt. De eerste blanco opname van het HSG werd gelijk gesteld aan een X bekken. Transvaginale Ultrasound heeft een sensitiviteit van 50% en een specificiteit van 95% ten opzichte van de gouden standaard, het HSG. Voor het X bekken waren sensitiviteit en specificiteit respectievelijk 100% en 99%. De voorspellende waarde van de transvaginale ultrasound dat de micro-insert niet goed gepositioneerd is bedroeg 11%, terwijl de voorspellende waarde van een goed gepositioneerde micro-insert 99% was.

Hoofdstuk 6 betreft een retrospectieve analyse van 10 ongewenste zwangerschappen na Essure sterilisaties in Nederland, die zijn ontstaan sinds de introductie in augustus 2002 tot mei 2008. In 1 geval bleek achteraf, dat patiënte al zwanger was ten tijde van de sterilisatie. In 3 gevallen was een dubbelzijdige plaatsing mislukt en toonde het HSG geen toe- en doorgankelijkheid van de eileiders en werd de sterilisatie als betrouwbaar beoordeeld. Van de overige 6 patiënten betrof het in 5 gevallen een abnormale positie van het device, terwijl van 1 patiënt geen gegevens bekend zijn. In alle gevallen, behoudens de ene casus waarvan de gegevens ontbreken, was er sprake van verkeerde beoordeling van de confirmatietest of afwijking van het protocol. Geconcludeerd wordt dat bij patiënten zonder voorgeschiedenis van de verwijdering van een eileider, een enkelzijdige plaatsing geduid moet worden als mislukte sterilisatie en niet gevolgd moet gaan door een HSG.

Hoofdstuk 7 beschrijft de resultaten van een prospectieve multicentre cohort studie, waarbij een nieuw protocol met echoscopische controle na ongecompliceerde hysteroscopische sterilisatie door middel van Essure wordt geëvalueerd. Bij 90,3% (1034/1045) van de procedures was er sprake van een

probleemloze dubbelzijdige plaatsing tijdens een eerste procedure. Bij 887 patiënten met een ongecompliceerde procedure kon na 3 maanden met echo (transvaginal ultrasound) worden geconcludeerd dat patiënten konden vertrouwen op de sterilisatie. Uiteindelijk, na een eventuele tweede procedure en/of HSG controle konden 1037 vrouwen vertrouwen op de sterilisatie. In totaal werd bij 14,3% van de vrouwen een HSG gemaakt. Bij 7 vrouwen bleek er sprake te zijn een perforatie en bij 2 werd een expulsie vastgesteld. In de eerste 24 maanden na de confirmatie traden 4 zwangerschappen op. Het 2 jaar cumulatieve zwangerschapscijfer bedroeg 3,86 /1000, terwijl er geen method-failures waren. Het vernieuwde Nederlands protocol met transvaginale ultrasound als eerste keuze voor confirmatietest vermindert het aantal noodzakelijke HSG's en daarmede de kosten. Het is vriendelijker voor de patiënt en vermijd ioniserende straling, zonder dat het de betrouwbaarheid van de sterilisatie nadelig beïnvloed. In vergelijking met de Verenigde Staten, waar een HSG verplicht is, gaat het Nederlands protocol gepaard met een hoge therapietrouw ("patiënt compliance").

Hoofdstuk 8 beschrijft de resultaten van een studie waarbij patiënten met tubaire infertiliteit een IVF behandeling ondergingen na afsluiting van 1 of 2 hydrosalpingen door middel van Essure. Het onderzoek betrof 10 patiënten met 1 of 2 hydrosalpingen en een contra-indicatie voor laparoscopische tubectomie. In alle gevallen kon een micro-insert in de aangedane eileider worden geplaatst en bij allen op één na werd met HSG bevestigd dat de hydrosalpinx proximaal werd afgesloten door de micro-insert. Na 40% van de embryo-transfers trad een doorgaande zwangerschap op en het percentage levend geboren kinderen was 20% per behandelingscyclus.

In **Hoofdstuk 9** worden de uitkomsten besproken van zwangerschappen bij vrouwen met 1 of 2 micro-inserts in situ. De gegevens werden verkregen door middel van een enquête onder Nederlandse gynaecologen, die Essure sterilisaties verrichten. In totaal werden gegevens verzameld van 50 zwangerschappen bij 43 vrouwen. Bij 26 vrouwen trad de zwangerschap op na Essure sterilisatie en 21 zwangerschappen ontstonden na IVF behandeling bij 15 vrouwen met hydrosalpingen, die waren afgesloten door middel van micro-inserts. Van de ongeplande zwangerschappen eindigde er 17 door middel van zwangerschapsafbreking. Van de 9 doorgaande zwangerschappen eindigde er 8 met de geboorte van een gezond kind, terwijl van 1 zwangerschap de gegevens ontbreken. Van de 22 zwangerschappen na IVF vooraf gegaan doorafsluiting hydrosalpingen met micro-inserts eindigde er 8 in een miskraam en waren er 14 doorgaand. Twee zwangerschappen eindigde met een partus immatures, Deze twee casus worden besproken. Beide vrouwen werden opnieuw zwanger na een volgende IVF behandeling. De overige 12 zwangerschappen leidde tot de geboorte van 13 gezonde kinderen, waaronder een tweeling geboren bij 34 weken. Bij 2 vrouwen betrof het een zwangerschap na IVF na spijt van de sterilisatie. Beide vrouw baarden een gezond kind.
De resultaten van de studie komen overeen met eerdere bevindingen dat het onwaarschijnlijk is dat de aanwezigheid van micro-inserts een negatieve invloed heeft op de implantatie en ontwikkeling van vruchtvliezen en foetus.

In **Hoofdstuk 10** worden algemene conclusies, resultaten en tekortkomingen van dit proefschrift beschreven. Nieuwe ontwikkelingen op het gebied van hysteroscopische

sterilisatietechnieken en alternatieven confirmatietesten worden besproken. Toekomstig onderzoek dient zich te richten op een analyse van de oorzaak van mislukte sterilisaties en de noodzaak van een eventuele confirmatietest. Een aanbeveling wordt gedaan voor een landelijke registratie van alle uitgevoerde sterilisaties en de opgetreden complicaties, inclusief zwangerschappen in POMT (Patient Outcome Measurement Tool).