



# ART Outcomes After Hysteroscopic Proximal Tubal Occlusion Versus Laparoscopic Salpingectomy for Hydrosalpinx Management in Endometriosis Patients

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## Abstract

The objective of this paper is to compare assisted reproductive technology (ART) cumulative live birth rates after hysteroscopic proximal tubal occlusion and laparoscopic salpingectomy in endometriosis patients, for management of hydrosalpinx. This is an observational cohort study at a university hospital, including all endometriosis patients with hydrosalpinges undergoing ART, between January 2013 and December 2018. The patients underwent either laparoscopic salpingectomy or hysteroscopic proximal tubal occlusion with Essure® when laparoscopy was not an option (extensive pelvic adhesions at exploratory laparoscopy or a history of multiple abdominal surgeries with frozen pelvis). The diagnosis of endometriosis was based on published imaging criteria using transvaginal sonography (TVUS) and magnetic resonance imaging (MRI). Endometriosis patients with hydrosalpinges diagnosed by hysterosalpingography and/or TVUS and/or MRI were included. The primary outcome was the cumulative live birth rate. A total of 104 patients were included in the study; 74 underwent laparoscopic salpingectomy and 30 underwent proximal tubal occlusion with Essure®. The Essure® group had longer infertility durations ( $58.9 \pm 30.0$  months vs.  $39.5 \pm 19.1$  months,  $p = 0.002$ ) and a higher incidence of associated adenomyosis (76.7% vs. 39.1%,  $p < 0.001$ ) than the salpingectomy group. The cumulative live birth rate was 56.6% after 44 ART cycles in the Essure® group and 40.5% after 99 ART cycles in the salpingectomy group ( $p = 0.13$ ). In a population of endometriosis patients undergoing ART, women treated by Essure® for management of hydrosalpinx have similar cumulative live birth rates as women treated by laparoscopic salpingectomy.

**Keywords** Assisted reproductive technology · Cumulative live birth · Endometriosis · Essure® · Hydrosalpinx

## Introduction

Endometriosis is a benign chronic gynecological disorder defined by the presence of endometrial tissue outside the uterine cavity [1]. The disease is heterogeneous, with lesions exhibiting three distinct phenotypes: (i) superficial peritoneal endometriosis, (ii) ovarian endometrioma, and (iii) deeply infiltrating endometriosis [2]. It is widely accepted that endometriosis alters fertility due to multiple pathophysiological mechanisms, including tubal alterations [2].

Assisted reproductive technology (ART) is one of the therapeutic options commonly offered to infertile endometriosis patients [3]. Of note, hydrosalpinx, one of the most severe manifestations of tubal diseases, is associated with a 50% decrease in ART pregnancy rates and a two-fold increase in the miscarriage rate compared to women without hydrosalpinx [4]. The mechanisms by which hydrosalpinx

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negatively affects ART outcomes are still unclear, but it may be due to several factors including the embryotoxic properties of the tubal fluid, the mechanical flushing of the embryo from the uterus, and a decrease in endometrial receptivity, mediated in part by an inflammatory endometrial response [5–8]. Surgical procedures that interrupt the communication between the tube and the uterine cavity, such as laparoscopic salpingectomy, result in improved ART outcomes [9]. However, these interventions entail surgical risks, especially in patients with dense pelvic adhesions such as those often encountered in endometriosis. Therefore, minimally invasive alternative therapies such as hysteroscopic proximal tubal occlusion devices, like Essure® microinserts, could provide significant benefits.

However, few studies to date have compared the ART results in patients with hydrosalpinx treated with laparoscopic salpingectomy versus Essure® microinserts [10–14]. Furthermore, no studies have focused on the specific population of endometriosis patients. Therefore, the aim of the present study was to evaluate, for the first time, cumulative live birth rates after tubal occlusion by Essure® devices versus after laparoscopic salpingectomy in endometriosis patients with hydrosalpinges who were undergoing ART.

## Materials and Methods

### Ethics Approval

This study was approved for publication by the Ethics Review Committee of the Cochin University Hospital (CLEP) (n° AAA-2020-08043) and all of the participants provided written informed consent.

### Study Protocol

The study population consisted of all the endometriosis patients with hydrosalpinges who underwent in vitro fertilization (IVF) or intra-cytoplasmic sperm injection (ICSI) at a tertiary care center between January 2013 and December 2018. Patients were followed up until they were pregnant, or until the last frozen embryo (resulting of the most recent ART attempt studied for each patient) was transferred, if no pregnancy occurred. The inclusion criteria for this study were the following: (i) endometriosis-related infertility as the main indication for ART (infertility being defined as at least 12 months of unprotected intercourse not resulting in pregnancy [15]); (ii) uni- or bilateral hydrosalpinges diagnosed by hysterosalpingography (HSG) and/or transvaginal sonography (TVS) and/or magnetic resonance imaging (MRI) [16]; and (iii) age  $\leq$  43 years. The exclusion criteria were vitrified oocyte procedures and patients already included in another ART research protocol.

All of the patients underwent an ad hoc work-up to accurately diagnose and stage the endometriosis, based on previously published imaging criteria using TVS and MRI (104 patients (100%) phenotyped by the two imaging techniques) [17, 18]. The MRI examinations were performed by experienced radiologists who are referring practitioners for image-based diagnosis of endometriosis [19]. In addition, for women with a previous history of surgery for endometriosis, the diagnosis was confirmed histologically, particularly in case of superficial endometriosis lesions, which may be difficult to diagnose using imaging criteria. As different endometriosis phenotypes frequently occur in combination, the patients were arbitrarily assigned to a group according to the most severe lesion according to a previously published classification process [20], from the least to the most severe: superficial endometriosis, ovarian endometrioma, and deeply infiltrating endometriosis (DE). In the case of DE, the severity was assessed based on two parameters, namely the number and the anatomic location of the DE lesions. In cases involving multiple DE sites, the patients were classified according to the worst finding (least to most severe: uterosacral ligament(s), vagina, bladder, intestine, and ureter) [3]. Associated adenomyosis was diagnosed using imaging criteria based on TVS and MRI [21].

### Surgical Procedure

The procedure was conducted before the ART and it involved one or both fallopian tubes, depending on whether uni- or bilateral hydrosalpinges were present.

#### Laparoscopic Salpingectomy

No conversions to laparotomy to perform the salpingectomy were carried out. Salpingectomy involved stepwise desiccation at the mesosalpinx with bipolar electrocoagulation, and subsequent incision from the mesosalpinx to the tubal isthmus using scissors. All of the tube, from 1 to 1.5 cm from the uterine cornua, was excised. Proximal tubal ligation was carried out as an alternative procedure to salpingectomy in women with unexpected extensive adnexal adhesions that precluded total salpingectomy. Proximal tubal ligation was performed by bipolar diathermy applied at two separate sites on the isthmus segment of the hydrosalpinges, located at 1 and 1.5 cm from the cornual section of the fallopian tube, followed by section. The excluded hydrosalpinges were left in situ [12].

#### Hysteroscopic Proximal Tubal Occlusion with Essure® Intratubal Devices

Patients were offered placement of Essure® devices (Bayer HealthCare Pharmaceuticals, Inc., Whippany, NJ, USA) when a laparoscopic procedure was not feasible (i.e., extensive pelvic adhesions found at exploratory laparoscopy that made

laparoscopic tubal salpingectomy or proximal occlusion impossible, or patients with a history of multiple abdominal surgeries and a previous laparoscopy indicating a frozen pelvis). The devices were placed in an ambulatory setting and the insertion of the hysteroscope (5.5-mm rigid hysteroscope with a 5-Fr working channel; Olympus Nederland B.V., Netherlands) was performed according to the method of Bettocchi [22]. The Essure® microinserts were placed into the proximal end of the fallopian tube using a special delivery system. The Essure® devices were placed with up to four coils protruding into the uterine cavity [14]. Twelve weeks after the placement, a pelvic X-ray was carried out to check the position of the Essure® devices [23]. Adverse events [24] were recorded during the study period.

### General Characteristics

The study analysis used a prospectively managed database. For each patient, the personal history data and the results of fertility investigations were collected before the ART treatment. The following data were recorded: age; height; weight; body mass index (BMI); smoking habits; parity; gravidity; duration of infertility; cycle day-3 levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), and anti-Müllerian hormone (AMH), as well as the antral follicle count (AFC) score; and the presence of an associated male infertility. A previous history of surgery for endometriosis was recorded for each patient, classified as excision of superficial lesions, deep lesion excision, bowel resection, or ovarian cystectomy.

### IVF-ICSI: Clinical and Laboratory Procedures

The women were monitored and managed according to our institutional clinical protocols. Thus, all of the patients were synchronized using timed administration of an oral contraceptive containing 0.03 mg of ethinyl E2 and 0.15 mg of levonorgestrel (Minidril®; Pfizer Holding, Paris, France), as described previously. Various controlled ovarian stimulation (COS) protocols were used, with 150 to 450 IU/day of recombinant follicle-stimulating hormone (FSH; Bemfola®; Gedeon Richter, France) and human menopausal gonadotropin (hMG; Menopur®; Ferring Pharmaceuticals, France): (i) a gonadotropin-releasing hormone (GnRH) antagonist protocol, (ii) a long agonist protocol, and (iii) a short agonist protocol. The gonadotropin doses and the type of controlled ovarian stimulation protocol were determined according to the individual patient characteristics [25].

Final oocyte maturation was triggered when  $\geq 3$  ovarian follicles of  $\geq 17$  mm were visible by ultrasound and when the E2 levels were  $\geq 1000$  pg/mL. In case of a deferred embryo transfer (ET), the final oocyte maturation was achieved using either a single injection of 0.2 mg of GnRH agonist

(triptorelin, Decapeptyl®; Ipsen, France) or by 250 mg of recombinant human chorionic gonadotrophin (rhCG; Ovitrelle®; Serono, France), according to the COS protocol. In case of a fresh ET, the final oocyte maturation was achieved by triggering with rhCG, irrespective of the stimulation protocol. The decision whether or not to defer the ET was based on a mutual decision by the patient and the doctor [26]. Oocyte retrieval (OR) was performed 35 to 36 h later by transvaginal aspiration under ultrasound guidance. Oocyte insemination, embryo culture, cryopreservation, and thawing were carried out according to our laboratory procedures, as detailed previously [25].

The ET was performed on day 2 or at the blastocyst stage. In fresh cycles, vaginal progesterone (a 200-mg vaginal capsule three times a day, Utrogestan®; Besins International, Montrouge, France) was initiated on the day of the OR and continued for the entire first trimester of pregnancy, and E2 was delivered transdermally (0.2 mg/day, simultaneously through two Vivelledot® 100 systems; Novartis Pharma SA, Rueil-Malmaison, France) or orally (8 mg/day, Provames®; Sanofi-Aventis, Paris, France) 4 days after the OR and continued for the first month of pregnancy. In frozen cycles, the women received hormone replacement therapy (HRT), which consisted of transdermal (0.2 mg/day, simultaneously through two Vivelledot® 100 systems; Novartis Pharma SA, Rueil-Malmaison, France) or oral (8 mg/day, Provames®; Sanofi-Aventis, Paris, France) E2 and subsequently vaginal progesterone 600 mg daily (a 200-mg vaginal capsule three times a day, Utrogestan®; Besins International, Montrouge, France), continued for the entire first trimester of pregnancy.

### ART Outcomes

The ART results were assessed by analysis of the following outcomes: (i) clinical pregnancies [15]; (ii) live births [15]; and (iii) early miscarriages [27]. The main outcome measure was the cumulative live birth rate (LBR), defined as the proportion of patients who had at least one live birth, whether from the first transfer attempt or subsequent transfers of frozen-thawed supernumerary embryos. Once a woman obtained a live birth from IVF/ICSI, she no longer contributed to the cumulative rates [28].

The following perinatal outcomes were also studied: preterm birth (PTB) (< 37 weeks of gestation) and low birthweight (LBW) (< 2500 g regardless of gestational age) [15].

### Statistical Analysis

The data were analyzed using SPSS® version 12.0 software (SPSS Inc. Headquarters, Chicago, IL, USA). A *p* value < 0.05 was considered to be statistically significant. The continuous data were presented as means and the standard

deviations; the categorical data as numbers and percentages. To compare the two study groups, the Mann–Whitney  $U$  test was used for the non-normally distributed continuous outcomes, and Pearson's chi-square or Fisher's exact test was used for the categorical variables.

The cumulative probability of the first birth during the study period was estimated by the Kaplan–Meier method, according to the IVF/ICSI cycle number. The log-rank test was used to compare the survival curves, with R version 3.6.3.

To identify potential confounding variables that could be independently associated with the live birth rate, we performed a logistic regression analysis. Confounding factors were tested by univariate analysis and were added in a multiple logistic regression model. The variables included in the multiple regression model were those that were significant by univariate analysis at  $p$  value  $< 0.10$  and those clinically relevant (i.e., the hydrosalpinx management method, an associated male factor, and the embryo transfer strategy). In case of significant differences, odds ratios (ORs) and their 95% confidence intervals (95% CIs) were calculated.

## Results

### Study Population

Between January 2013 and December 2018, 104 endometriosis patients with hydrosalpinges underwent 143 ART cycles at our tertiary care center, as displayed in Supplementary Figure 1. Management of the hydrosalpinges prior to the ART was by means of Essure® placement for 30 patients (28.8%), while 74 patients (71.2%) underwent a laparoscopic salpingectomy. Among the Essure® group, 15 patients had no history of prior surgery for endometriosis, but either had a history of multiple abdominal surgeries with indication of a frozen pelvis in the surgical reports ( $n=6$ ) or had an exploratory laparoscopy showing extensive pelvic adhesions preventing from performing tubal proximal occlusion ( $n=9$ ). No postoperative complications or adverse events occurred for any of the patients in the Essure® group, and the postoperative X-ray confirmed appropriate placement of the device(s). The demographic data, the clinical characteristics of the study population, and the ART cycle characteristics are summarized in Tables 1 and 2. The two groups were overall comparable in terms of the distribution of the endometriosis phenotypes, the history of previous surgery for endometriosis, the ovarian reserve parameters, and the ART cycle characteristics, except for three parameters. The Essure® group had longer infertility durations ( $58.9 \pm 30.0$  months vs.  $39.5 \pm 19.1$  months,  $p=0.002$ ) and a higher incidence of associated adenomyosis (76.7% vs. 39.1%,  $p<0.001$ ) than the salpingectomy group. Moreover, the patients in the Essure® group had a higher proportion of frozen-thawed ET compared to those in the salpingectomy group (96.7% vs. 80.9%,  $p = 0.004$ ).

### ART Outcomes

In total, 143 ART cycles were analyzed: 44 in the Essure® group and 99 in the salpingectomy group, associated with 61 and 110 ET (including fresh and frozen-thawed embryo transfers), respectively. Neither the ART cycle outcomes nor the perinatal outcomes studied were statistically different between the groups, as shown in Table 3. The cumulative live birth rates after four ART cycles did not differ significantly between the two study groups (14/30 patients in the Essure® group versus 22/74 in the salpingectomy group), reaching 56.6% in the Essure® group and 40.5% in the salpingectomy group ( $p = 0.13$ ), as shown in Fig. 1. Supplemental Table 1 displays the results of the multivariate analysis comparing patients who had a live birth and those who had not. Only the ART cycle rank and the number of oocytes retrieved remained significantly associated with the live birth rate ( $p = 0.04$  and  $p = 0.008$ , respectively), confirming that the hydrosalpinx management method did not significantly impact ART outcomes ( $p = 0.16$ ).

## Discussion

This study on infertile endometriosis patients showed that management of hydrosalpinges with hysteroscopic tubal occlusion prior to ART results in a similar cumulative LBR as laparoscopic salpingectomy.

The strength of this study lies in the following points: (i) this is the first study to assess the effectiveness of hysteroscopic proximal tubal occlusion compared to laparoscopic salpingectomy in endometriosis patients. These patients often have extensive intra-abdominal adhesions that make use of Essure® devices particularly relevant; (ii) the diagnosis of endometriosis was based on stringent imaging criteria performed by senior dedicated radiologists [19]. Thus, the endometriosis phenotype was accurately defined; (iii) numerous variables were prospectively collected using a standardized questionnaire before the ART [3]; (iv) finally, we chose the cumulative LBR as the primary outcome, which is currently the best outcome for assessment of the efficacy of ART cycles [29].

However, our study suffers from certain limitations: (i) this was a non-randomized study, as the choice of hydrosalpinx management with Essure® was based on proven or expected high surgical risk. Therefore, the Essure® group was expected to have a less favorable ART prognosis due to more severe forms of endometriosis, as suggested by the higher infertility durations and the higher proportion of associated adenomyosis. Yet, we found similar cumulative LBR in both groups, which underlines the value of having a hysteroscopic proximal tubal occlusion device in this specific population who have particularly unfavorable fertility prognoses.

**Table 1** Baseline characteristics of the study population

| Characteristics <sup>a</sup>                | Essure® (n = 30) | Salpingectomy (n = 74) | p value             |
|---|------------------|------------------------|---------------------|
| Age (years)                                 | 33.3 ± 3.2       | 31.9 ± 4.1             | 0.081 <sup>u</sup>  |
| Smoking habits                              | 5 (16.7%)        | 9 (12.2%)              | 0.752 <sup>k</sup>  |
| BMI (kg/m <sup>2</sup> )                    | 23.8 ± 4.5       | 22.9 ± 3.8             | 0.398 <sup>u</sup>  |
| Duration of infertility (months)            | 58.9 ± 30.0      | 39.5 ± 19.1            | 0.002 <sup>u</sup>  |
| Type of infertility                         |                  |                        | 0.338 <sup>k</sup>  |
| Primary                                     | 28 (93.3%)       | 63 (85.1%)             |                     |
| Secondary                                   | 2 (6.7%)         | 11 (14.9%)             |                     |
| Associated male factor                      | 3 (10%)          | 15 (20.3%)             | 0.263 <sup>k</sup>  |
| Hydrosalpinx                                |                  |                        | 0.122 <sup>k</sup>  |
| Unilateral                                  | 14 (46.7%)       | 48 (64.9%)             |                     |
| Bilateral                                   | 16 (53.3%)       | 26 (35.1%)             |                     |
| Ovarian reserve parameters                  |                  |                        |                     |
| Day-3 FSH (IU/L)                            | 8.0 ± 2.3        | 8.1 ± 4.3              | 0.427 <sup>u</sup>  |
| Day-3 LH (IU/L)                             | 4.8 ± 2.6        | 5.1 ± 3.8              | 0.784 <sup>u</sup>  |
| Day-3 Estradiol (pg/mL)                     | 49.3 ± 22.8      | 50.9 ± 36.0            | 0.599 <sup>u</sup>  |
| AFC   | 12.1 ± 5.0       | 10.5 ± 7.2             | 0.061 <sup>u</sup>  |
| AMH (ng/mL)                                 | 2.0 ± 1.1        | 2.5 ± 2.1              | 0.492 <sup>u</sup>  |
| Endometriosis phenotype                     |                  |                        | 0.405 <sup>k</sup>  |
| SUP   | 0 (0%)           | 2 (2.7%)               |                     |
| OMA   | 3 (10%)          | 3 (4%)                 |                     |
| DE  | 27 (90%)         | 69 (93.3%)             |                     |
| Associated OMA                              | 19 (85.2)        | 46 (66.7%)             | 0.862 <sup>k</sup>  |
| Associated adenomyosis                      | 23 (76.7%)       | 29 (39.1%)             | <0.001 <sup>k</sup> |
| Number of prior surgeries for endometriosis |                  |                        | 0.432 <sup>k</sup>  |
| 0   | 15 (50%)         | 43 (58.1%)             |                     |
| 1   | 12 (40%)         | 28 (37.8%)             |                     |
| ≥ 2   | 3 (10%)          | 3 (4.1%)               |                     |

BMI body mass index, FSH follicle-stimulating hormone, LH luteinizing hormone, AFC antral follicle count, AMH anti-Müllerian hormone, SUP superficial endometriosis, OMA ovarian endometrioma, DE deeply infiltrating endometriosis

<sup>a</sup> The continuous data are presented as means ± standard deviation; the categorical data are presented as numbers (percentages)

<sup>u</sup> Mann–Whitney *U* test

<sup>k</sup> Pearson’s chi-square test or Fisher’s exact test

Moreover, we performed a multiple logistic regression analysis to allow adjustment for relevant confounders, which confirmed that the hydrosalpinx management method did not significantly impact the ART live birth rate; (ii) the two groups differed significantly in terms of the embryo transfer strategy. Indeed, the proportion of frozen-thawed embryo transfers (FET) was higher in the Essure® group. This was probably due to a more frequent deferred embryo transfer policy, which is thought to improve ART outcomes in severe forms of endometriosis and adenomyosis [26]. In fact, a subgroup analysis comparing the live birth rates between the two study groups according to the timing of the first embryo transfer, i.e., fresh or first FET after a freeze-all cycle, found no significant differences neither in the fresh embryo transfer group

(Essure®: 2/2 (100%) versus salpingectomy: 6/16 (37.5%), *p*=0.183) nor in the FET group (Essure®: 4/25 (16%) versus salpingectomy: 10/43 (23.3%), *p*=0.755), though numbers are very low to draw firm conclusions. Furthermore, the multivariate analysis comparing patients who had a live birth with those who had not did not highlight an impact of the embryo transfer strategy on the live birth rate, thereby alleviating the influence of this in-between group difference on our results; (iii) the analysis of ART outcomes by pooling the results of different embryo transfer methods or various ovarian stimulation protocols could also be seen as a limitation. Yet, cleavage-stage versus blastocyst-stage embryo transfers appear to result in similar cumulative LBR [30, 31], as well as single versus double embryo transfers [32, 33]. Moreover,

**Table 2** ART cycle characteristics

| Characteristics <sup>a</sup>                      | Essure® (n=30)  | Salpingectomy (n=74) | p value            |
|---|-----------------|----------------------|--------------------|
| Total number of ART cycles                        | 44              | 99                   |                    |
| ART cycle distribution                            |                 |                      | 0.546 <sup>k</sup> |
| 1 cycle   | 30              | 74                   |                    |
| 2 cycles  | 10              | 15                   |                    |
| ≥ 3 cycles  | 4               | 10                   |                    |
| Number of ART cycles per patient                  | 1.5 ± 0.8       | 1.3 ± 0.8            | 0.092 <sup>u</sup> |
| Stimulation protocols for intra-couple ART cycles | 42 (95.5%)      | 93 (93.9%)           | 0.141 <sup>k</sup> |
| Long agonist                                      | 1 (2.4%)        | 12 (12.9%)           |                    |
| Short agonist                                     | 9 (21.4%)       | 21 (22.6%)           |                    |
| Antagonist  | 32 (76.2%)      | 60 (64.5%)           |                    |
| Natural cycles                                    | 1 (2.2%)        | 3 (3%)               | 0.640 <sup>k</sup> |
| Oocyte donation cycles                            | 1 (2.2%)        | 3 (3%)               | 0.640 <sup>k</sup> |
| Total dose of injected gonadotropins (IU)         | 3102.3 ± 982.9  | 2999.7 ± 904.1       | 0.541 <sup>u</sup> |
| Duration of ovarian stimulation (days)            | 10.9 ± 1.8      | 10.9 ± 1.7           | 0.998 <sup>u</sup> |
| Peak estradiol levels at triggering (pg/mL)       | 1611.8 ± 1038.8 | 1480.5 ± 968.4       | 0.900 <sup>u</sup> |
| Number of oocytes retrieved                       | 6.7 ± 3.8       | 6.8 ± 5.7            | 0.448 <sup>u</sup> |
| Cancelation rate per cycle                        | 8 (17.8%)       | 22 (22.2%)           | 0.543 <sup>k</sup> |
| Transferred embryos                               |                 |                      | 0.004 <sup>k</sup> |
| Fresh embryos                                     | 2 (3.3%)        | 21 (19.1%)           |                    |
| Frozen-thawed embryos                             | 59 (96.7%)      | 89 (80.9%)           |                    |
| Embryo stage                                      |                 |                      | 0.062 <sup>k</sup> |
| Cleavage stage                                    | 9 (14.8%)       | 30 (27.3%)           |                    |
| Blastocyst stage                                  | 52 (85.2%)      | 80 (72.7%)           |                    |
| Embryo transfer                                   |                 |                      | 0.102 <sup>k</sup> |
| SET   | 56 (91.8%)      | 91 (82.7%)           |                    |
| DET   | 5 (8.2%)        | 19 (17.3%)           |                    |

ART assisted reproductive technology, SET single embryo transfer, DET double embryo transfer

<sup>a</sup> The continuous data are presented as means ± standard deviation; the categorical data are presented as numbers (percentages)

<sup>k</sup> Pearson's chi-square test or Fisher's exact test

<sup>u</sup> Mann–Whitney *U* test

GnRH agonist and antagonist protocols appear to be equally effective in endometriosis patients [34, 35]. Therefore, it is unlikely that this bias impacted the assessment of cumulative LBR.

Our results provide new insights regarding the complex management of hydrosalpinx in this group of patients who frequently have extensive pelvic adhesions that make laparoscopic salpingectomy of high surgical risk. Indeed, most studies to date have reported lower ART outcomes after hysteroscopic tubal occlusion compared to laparoscopic surgery [11, 12]. In these studies, the lower pregnancy outcomes following Essure® management of hydrosalpinx were mainly explained by a difference in the implantation rate, which may be caused by the device itself causing a lower endometrial receptivity [12].

Conversely, in our study, neither the cumulative LBR nor the miscarriage rates were statistically different

between the two groups of patients. Several hypotheses can be put forward to account for the disparities with the existing literature. First, Essure® were inserted by skilled clinicians used to well-positioning the devices, which may have minimized the potential deleterious impact of the devices on endometrial receptivity [36], thereby contributing to improved ART outcomes. Secondly, the 33% miscarriage rate in the salpingectomy group of our study is quite high compared to the 15% miscarriage rate described in a recent meta-analysis by Barbosa et al. [13]. This difference is likely to be due to the increased basal incidence of miscarriage in endometriosis patients [37], thereby masking the relative difference between the Essure® group and the salpingectomy group.

Safety concerns have recently been raised regarding Essure® devices [24] leading to them being withdrawn from

**Table 3** ART outcomes

| ART outcomes <sup>a</sup>           | Essure® (n=30) | Salpingectomy (n=74) | p value            |
|-------------------------------------|----------------|----------------------|--------------------|
| Implantation rate <sup>b</sup>      | 24/66 (36.4%)  | 33/129 (25.6%)       | 0.118 <sup>k</sup> |
| Clinical pregnancy rate             |                |                      |                    |
| Per cycle                           | 22/44 (50%)    | 33/99 (33.3%)        | 0.058 <sup>k</sup> |
| Per ET                              | 22/61 (36.1%)  | 33/110 (30%)         | 0.417 <sup>k</sup> |
| Miscarriage rate <sup>c</sup>       | 7/22 (31.8%)   | 11/33 (33.3%)        | 0.920 <sup>k</sup> |
| Ectopic pregnancy rate <sup>d</sup> | 1/22 (4.5%)    | 0/33 (0%)            | 0.400 <sup>k</sup> |
| Live birth rate                     |                |                      |                    |
| Per cycle                           | 14/44 (31.8%)  | 22/99 (22.2%)        | 0.222 <sup>k</sup> |
| Per ET                              | 14/61 (23%)    | 22/110 (20%)         | 0.647 <sup>k</sup> |
| Perinatal outcomes                  |                |                      |                    |
| Preterm birth <sup>e</sup>          | 2/14 (14.3%)   | 0/22 (0%)            | 0.144 <sup>k</sup> |
| Low birthweight <sup>f</sup>        | 1/14 (7.1%)    | 2/22 (9.1%)          | 0.668 <sup>k</sup> |

ET embryo transfer

<sup>a</sup> The data are presented as numerator/denominator (%)

<sup>k</sup> Pearson’s chi-square test or Fisher’s exact test

<sup>b</sup> Implantation rate = number of gestational sacs/number of embryos transferred

<sup>c</sup> Miscarriage rate = number of miscarriages/numbers of clinical pregnancies

<sup>d</sup> Ectopic pregnancy rate = number of ectopic pregnancy/numbers of clinical pregnancies

<sup>e</sup> Preterm birth = birth <37 weeks of gestation

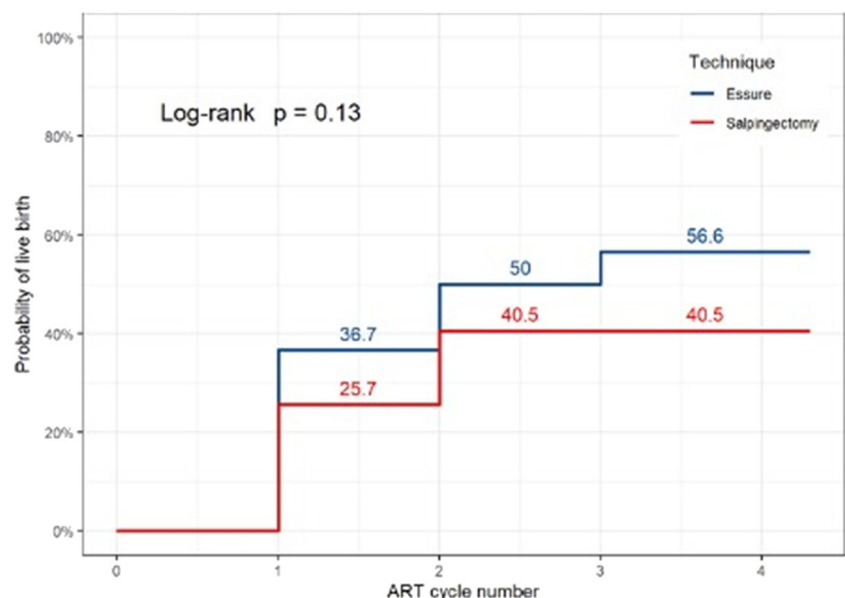
<sup>f</sup> Low birthweight = birthweight < 2500 g irrespective of the gestational age

the market. There is, therefore, a need for alternative methods for proximal tubal occlusion. One of the newly described procedures consists of radiologically guided tubal occlusion with embolization microcoils [38]. Another strategy relies on hysteroscopic placement of platinum microinserts, and this has also yielded promising ART outcomes in small non-comparative studies [39, 40]. Further studies are urgently

needed, however, to find a suitable alternative to Essure® devices in patients with a history of dense pelvic adhesions and for further evaluating the ART live birth rates after performing these procedures.

Overall, our study suggests that hysteroscopic proximal tubal occlusion is a reasonable alternative to laparoscopic salpingectomy in endometriosis patients with hydrosalpinges,

**Fig. 1** Kaplan-Meier curves of the cumulative live birth rates in the Essure® and the salpingectomy group, according to the ART cycle number



as it results in a similar cumulative ART live birth rate. Finding a replacement for Essure® devices, especially in this population with patients at high surgical risk, could be of great therapeutic interest.

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**Author Contribution** PS and CC conceived of and designed the study. CM, MB, MC, JPS, AM, LM, and PS collected the data. CM, MB, JPS, AM, and PS developed the statistical analyses. CM, MC, JPS, AM, and PS authored the manuscript. All of the authors read and approved the final version of the manuscript.

**Data availability** NA

**Code Availability** NA

## Declarations

**Ethics Approval** This study was approved for publication by the Ethics Review Committee of the Cochin University Hospital (CLEP) (n° AAA-2020-08043).

**Consent to Participate** All the participants provided written informed consent.

**Consent for Publication** All the participants provided written informed consent.

**Conflict of Interest** The authors declare no competing interests.

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