

# Assisted conception following radical trachelectomy

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**BACKGROUND:** Radical trachelectomy (RT) has been established as a valuable fertility-preserving treatment in women with early stage cervical cancer. A number of these women will require assisted conception which may bring certain challenges to those managing treatment. An awareness of those challenges is essential to maximize outcome in terms of live birth rates.

**METHODS:** All women who had undergone assisted conception following RT were assessed with respect to treatment management and pregnancy outcome.

**RESULTS:** Pregnancy rates were good, with nine pregnancies in seven women treated. Difficulties in treatment were essentially related to isthmic stenosis. There was a clear need for trial embryo transfer (ET) prior to treatment and dilatation of the isthmus where necessary. The premature delivery rate was high (75% at <37 weeks), highlighting the importance of single ET to avoid multiple pregnancy.

**CONCLUSIONS:** Assisted conception following RT is associated with a good pregnancy rate, although there is a high miscarriage and premature delivery rate. Treatment outcome should be maximized by careful patient preparation in terms of assessing the need for isthmic dilatation, and ET should be performed by an experienced operator.

**Key words:** radical trachelectomy / embryo transfer / isthmic dilatation / cervical cancer / IVF

## Introduction

Childbearing remains one of the most important goals and accomplishments in life. Radical trachelectomy (RT) is a fertility preservation procedure for early stage cervical cancer which has been performed for over 20 years since first described by French gynaecologist Dargent in 1987. The procedure commences with a laparoscopic pelvic lymphadenectomy. In radical vaginal trachelectomy, a 1–2 cm vaginal cuff together with paracervical tissue is removed and the cervix is amputated at the level of the internal os. A non-absorbable monofilament suture such as nylon is inserted around the isthmus as a cerclage and then isthmovaginal anastomosis is performed (Shepherd *et al.*, 2006). Abdominal approach of RT has also been described.

RT has been shown to be a valuable fertility-preserving option in the management of early stage cervical cancer (Boss *et al.*, 2005; Plante *et al.*, 2005; Shepherd *et al.*, 2006). Many women can anticipate conceiving spontaneously following RT (Boss *et al.*, 2005; Plante *et al.*, 2005; Shepherd *et al.*, 2006; Aust *et al.*, 2007). Shepherd *et al.* (2006) followed up 123 women who had RT, 63 attempted pregnancies and there were 55 pregnancies in 26 women. The 5 year cumulative

pregnancy rate among women trying to conceive was 52.8% (Shepherd *et al.*, 2006). However, in a minority of women, assisted conception may be required (Aust *et al.*, 2007). Plante *et al.* (2005) followed up 72 women who had had RT with 50 spontaneous pregnancies in 31 women but 10% had subfertility problems requiring assisted conception. Subfertility can either be pre-existing prior to RT or following the surgery itself. Isthmic stenosis with adhesion formation, lack of cervical mucus to aid sperm migration and possible vascular compromise may be the contributing factors following RT.

Women requiring assisted conception who have had a RT, however, bring a different set of challenges for the reproductive medicine specialist and it is essential that such women are appropriately managed throughout their treatment to maximize a good outcome. The objective of this review of all patients treated who had previously undergone an RT was to assess the problems faced when managing treatment and the outcome following treatment.

## Materials and Methods

Since 1997, our unit has received 11 referrals for assisted conception in women who had previously undergone RT and has treated eight patients.

Three patients decided not to proceed with treatment. The fertility unit has close links with the gynaecology department which is one of the largest centres performing RT and contains one of the largest cohorts of RT patients in the country. These patients are seen easily and quickly for consultation and their fertility treatment thereafter.

Of these eight patients, two had intrauterine insemination (IUI), four had IVF, one had ICSI and one surrogacy (Table I). The patient who required surrogacy due to failure of canalization of the stenosed isthmus was excluded from the analysis for the purpose of this study. The age of the eight patients ranged from 22 to 40 years. Four cases suffered from primary subfertility and four were secondary. The time from RT to assisted conception ranged from 2 to 5 years and 2 months. The aetiology for these patients included endometriosis in two patients, tubal factor in one patient, tubal and endometriosis in one patient, male factor in one patient and three had unexplained subfertility. All women underwent routine fertility investigations and the decision for assisted conception was made in compliance with the usual criteria used in our unit and in accordance with the patients' history. Stimulation protocols used were the same as per our unit protocols as expected for age and hormonal profile. Prior to IUI or embryos transfer (ET), all women underwent a 'trial' embryo transfer (trial ET) to assess the ability to enter the uterine cavity and to measure the uterine depth. A Wallace soft catheter was used initially for this and if entry into the cavity was not possible, a stiffer Frydman catheter was used.

## Results

Both IUI patients required isthmus dilatation prior to their treatment with one patient needing to have a further dilatation prior to IUI cycle number 3 (Table I). Both required mild sedation for the IUI due to hypersensitivity of the vaginal mucosa at the point of entry into the uterine cavity. Of the five patients who had IVF/ICSI treatment, there were no difficulties in proceeding with oocyte retrieval. Two patients underwent isthmus recanalization prior to treatment. One patient had already had recanalization twice for haematometra and stenosed isthmus prior to being referred to our fertility centre. A trial ET on this patient under ultrasound guidance was unsuccessful and therefore a transmyometrial ET was planned but fortunately, on the day of ET, it was possible to pass a Frydman catheter under ultrasound guidance into the uterine cavity with sedation. Another patient also had isthmus dilatation prior to her treatment at another private fertility unit. She underwent trial ET with a Wallace soft catheter without difficulty. Out of these five patients, two patients had difficulty with ET at the time and required a Frydman catheter under ultrasound guidance and three patients had an easy transfer with a soft Wallace catheter. The process of ET involved positioning the patient in the lithotomy position and ausco bivalve speculum was passed into the vagina to identify the isthmus opening. The isthmus was cleaned with a cotton bud stick and the type of catheter used was dependent on the prior trial ET.

Of the seven women treated, there were nine pregnancies. Three pregnancies were achieved in two women who had undergone IUI cycles. Six pregnancies were achieved in five women who had undergone IVF/ICSI cycles.

There were four newborns, of which three were preterm at 25, 27 and 30 weeks gestation and they were all in good health. All were delivered by classical Caesarean section. There were also three first trimester miscarriages and two mid-trimester miscarriages at 20 and

22 weeks gestation with spontaneous vaginal delivery. Only one patient underwent an evacuation of retained product of conception (ERPC) in the first trimester miscarriage and the procedure was uneventful. Only one patient so far has not achieved a pregnancy and is seeking further treatment.

## Discussion

RT offers women with early stage cervical cancer the opportunity to preserve their reproductive potential, although other causes of subfertility may be present, either pre-existing or following RT, with a subsequent need for assisted conception. Other possible contributing factors, such as dyspareunia following RT with scar formation and psychological fear of cancer recurrence, may deter some to try naturally.

Although RT is a fertility-sparing procedure, patients should be counselled that neither pregnancy nor live birth can be guaranteed. Patients should also be informed and counselled regarding the obstetric risks following RT including mid-trimester miscarriage, preterm premature rupture of membrane and subsequent preterm labour (Boss *et al.*, 2005; Plante *et al.*, 2005; Shepherd *et al.*, 2006; Aust *et al.*, 2007). Shepherd *et al.* (2006) reported that 71.4% of deliveries were <37 weeks in his series of 123 women following RT. In our study, the preterm delivery rate at <37 weeks was 75%. Because of the high risk nature of the pregnancy, the involvement of high risk obstetricians in the care of these women is paramount to ensure the optimal outcome.

Patients should be made aware of the difficulties surrounding IUI and ET during the initial assisted conception consultation. Isthmus stenosis is reported to occur in ~15% of RT patients (Boss *et al.*, 2005). This remains a challenge for the reproductive physician as to the problem of cannulating the isthmus for ET or IUI. Isthmus stenosis is also associated with haematometra and menstrual disorders. Isthmus dilatation is the solution for this problem prior to treatment and this procedure may need to be repeated in-between treatments. In this study, two IUI and two IVF patients had to undergo isthmus dilatation prior to and during treatment. The timing of the isthmus dilatation in relation to IUI and ET in this study was variable ranging from during the treatment cycle up to 5 years prior to treatment. This complication should be anticipated in all RT patients and a trial IUI or ET should be performed before treatment is started to ensure that access into the uterine cavity is possible.

ET remains one of the most important stages in IVF treatment and the ease of transfer is one of the factors associated with good IVF outcome (Abou-Setta *et al.*, 2007). In this study, two out of five IVF/ICSI patients had difficult ETs, although one of these patients had had several isthmus dilatations prior to treatment. Others have attempted using a Malecot catheter as a stent to maintain the isthmovaginal opening but did not result in pregnancy (Aust *et al.*, 2005).

Uterine cavity length should also be measured prior to treatment either during the trial ET procedure or during the hysteroscopy procedure for isthmus dilatation. In this study, the uterine cavity lengths in all patients were between 4 and 5 cm only. Routine use of ultrasound-guided transfer is useful as it helps to judge the place of deposition of the embryos and also to prevent creating a false passage for the transfer. The isthmus can be difficult to locate

**Table I** Summary of patients' treatment following RT

Case	Method	Age (year)	Aetiology	Time of RT to treatment	Dilatation of isthmus	Embryo transfer catheter type	Ease of embryo transfer	Number of embryo transfer	Pregnancy outcome	Singleton/twin	Outcome:live birth/miscarriage
1	IUI	39	Endometriosis (primary)	25 months	Yes	Wallace	Easy (sedation required)	N/A	Yes:1st cycle	Singleton	Live birth at 38 weeks by classical C/S
2	IUI	26	Unexplained (secondary)	32 months	Yes, repeated prior to cycle 3	Frydman	Difficult (sedation required)	N/A	Yes:1st cycle Yes:9th cycle	Singleton Twin but 1 twin demised at 10 weeks	Miscarriage at 6 weeks (ERPC) Live birth at 30 weeks by classical C/S
3	IVF	31	Tubal/ endometriosis (primary)	24 months	Yes, twice prior to treatment	Frydman	Difficult (sedation required)	2	Yes:1st cycle Yes:1st FET cycle	Singleton Singleton	Spontaneous miscarriage at 12 weeks Spontaneous miscarriage at 20 weeks
4	IVF	31	Endometriosis (primary)	28 months	No	Wallace	Easy	2 1	Yes:1st cycle Yes:1st FET cycle	Singleton Singleton	Live birth at 25 weeks by classical C/S Live birth at 27 weeks by classical C/S
5	IVF	40	Tubal (primary)	5 years 2 months	Yes	Wallace	Easy	2	Yes:1st cycle	Singleton	Spontaneous miscarriage at 8 weeks
6	IVF/ICSI	39	Male/PCOS (secondary)	5 years	No	Frdyman	Difficult (sedation required)	1	No		
7	IVF	27	Unexplained (secondary)	3 years	No	Wallace	Easy	2	Yes:2nd cycle	Twin	Spontaneous miscarriage at 22 weeks

FET, frozen embryo transfer; C/S, Caesarean section; N/A, non-applicable; ERPC, evacuation of retained product of conception; RT, radical trachelectomy; IUI, intrauterine insemination.

after RT as this procedure causes scarring and distortion of the normal anatomy. An experienced fertility clinician should carry out the ET as the procedure can be very difficult. In one of our IVF patients, the initial plan of transmyometrial transfer was narrowly avoided as an experienced clinician was able to pass a Frydman catheter on the day of ET. This patient in fact had undergone isthmic recanalization twice prior to treatment.

The option of single ET should be offered to all these patients due to the high obstetric risks of premature preterm rupture of membranes leading to preterm labour. Therefore, the risk of a multiple pregnancy should be reduced by transferring a single embryo. In this study, only two patients agreed to single ET, despite extensive counselling. There is one twin pregnancy following IVF with the transfer of two embryos in this study, but she miscarried at 22 weeks gestation. One of the IUI patients also had a twin pregnancy, but one twin demised at 10 weeks gestation and she had a live birth at 30 weeks gestation.

## Conclusion

The valuable lessons learnt from our experiences are that assisted conception is normally associated with a good pregnancy rate in these patients but women need to be counselled regarding the risk of difficulty in cannulating the isthmus, the potential need for isthmic dilatation and the high risk of preterm delivery. Single ET should be the norm for RT patients to avoid multiple pregnancy in an already high-risk pregnancy.

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