

# The management of pregnancy after trachelectomy for early cervical cancer

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## Key content

- Cervical cancer continues to affect many women in the UK with over half under the age of 45 years at the time of diagnosis; with a trend towards starting families later in life this raises fertility concerns.
- While the standard treatment for stage IA2 or IB1 cervical cancer is a radical hysterectomy, radical trachelectomy has been shown to have equivalent 5-year survival and is a surgical option if there is a wish to preserve fertility.
- Although trachelectomies are performed by gynaecological oncologists, the management of any subsequent pregnancies falls under the remit of obstetricians who therefore require a sound knowledge of the procedure and potential obstetric sequelae.
- Pregnancies following trachelectomy are high risk because of the increased rate of mid-trimester miscarriage and preterm delivery, often as a consequence of preterm prelabour rupture of membranes.

- Delivery is by caesarean section, traditionally by classical section as a permanent isthmic suture is placed at the time of trachelectomy, but nowadays a transverse incision may be used to reduce morbidity and the implications on future fertility.

## Learning objectives

- Management of a pregnancy following radical trachelectomy.
- Intrapartum care of post-radical trachelectomy pregnancy and complication risks.
- Impact of trachelectomy and subsequent pregnancy on the woman.

## Ethical issues

- Informed consent surrounding trachelectomy and future pregnancies.

**Keywords:** cerclage / cervical cancer / fertility-sparing / pregnancy / trachelectomy

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## Introduction

There are over 3000 women diagnosed with cervical cancer every year in the UK, making it the 12<sup>th</sup> most common cancer in women in the country.<sup>1</sup> Worldwide, cervical cancer still remains the fourth most common cancer in women, with over 60% of women surviving the disease for 10 years or more, reflecting the improved survival rates.<sup>1</sup>

Approximately 52% of women with cervical cancer in England and Wales are under the age of 45 years, as per UK Cancer Research statistics in 2012.<sup>1</sup> With increasing numbers of young women surviving the disease, the option for treatment with fertility preservation becomes a priority and a key factor in quality of life.<sup>2,3</sup> Fertility-sparing surgery for early cervical cancer includes knife biopsy with or without

laparoscopic lymphadenectomy for stage IA1 disease and trachelectomy for stage IA2–IB1.<sup>4</sup>

Trachelectomy, as first described by Dargent in 1994,<sup>5</sup> has revolutionised care for women of childbearing age with small-volume, early-stage cervical cancer. The **basic concept of a trachelectomy is to remove the cervix with surrounding tissue (parametrium and upper vagina)** in order to achieve oncological clearance of the central tumour, while retaining the uterus (uterus-sparing). **The uterine isthmus and vagina are re-anastomosed and a permanent suture is inserted in the isthmic part of the uterus to mechanically tighten the lower opening of the uterus, thus creating a ‘neo-cervix’** (Figure 1). Depending on pre-trachelectomy histological parameters, it may be oncologically appropriate to preserve a small portion of the proximal cervix at the internal os: this is thought to

reduce some of the potential obstetric complications following trachelectomy.

The **oncological results** of a **radical trachelectomy (removal of cervix, upper portion of the vagina and the parametrium) with pelvic lymphadenectomy are comparable to a radical hysterectomy with pelvic lymphadenectomy, with a 5-year survival of 95–98%** according to Cancer Research UK data.<sup>1</sup> **Recurrence rates appear to be the same** irrespective of whether the trachelectomy is performed by the vaginal, abdominal, laparoscopic or robotic approach.<sup>5</sup>

With the earlier detection of cervical cancer and an increase in the number of women undergoing fertility-sparing surgery, women with post-trachelectomy pregnancies are increasingly encountered in obstetric practice. It is important that clinicians are familiar with the potential **complications** in this group of women, such as **preterm labour, preterm prelabour rupture of membranes (PPROM) and miscarriage**. This article aims to provide guidance using the current literature and expert opinion.

## Systematic review

A search of the following databases was performed: Embase, MEDLINE, PsycINFO, AMED, CINAHL and LILACS from inception to January 2016. Grey literature was searched through SIGLE (1990–2015). There were no language restrictions. MeSH headings and keywords for ‘cervical cancer’ or ‘trachelectomy’ were used combined using the Boolean operator ‘and’ with the terms ‘pregnancy or ‘preterm labour’ or ‘miscarriage’ or ‘cerclage’. A hand search of bibliographies from relevant articles was performed to identify articles not electronically cited. All types of trachelectomy surgery were included and the results were pooled for pregnancy outcomes. Observational studies with more than five pregnant women were included. The data were independently extracted by two reviewers using a

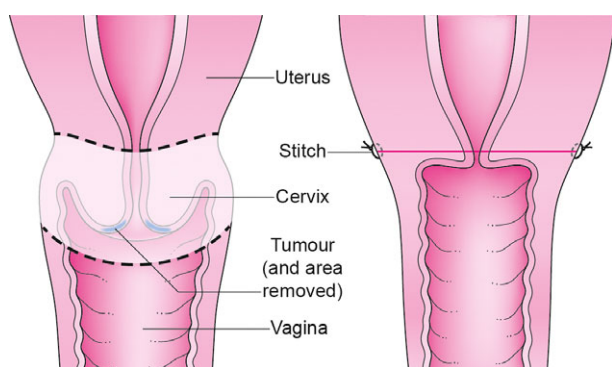
pre-designed data collection form. A total of 1079 abstracts were identified from 1664 citations after removing duplicates. Of these, 33 full text papers were reviewed and 25 suitable studies were identified (Figure 2), which described 752 pregnancies.<sup>2,6–30</sup> Unfortunately, the data pertaining to pregnancy outcomes are inconsistently reported and quite limited.

Data on the spontaneous conception rate suggest that up to 61% (151/248) of women who conceived following a trachelectomy required assisted reproduction techniques to achieve a pregnancy, which is a higher rate when compared with the population who have not had a trachelectomy, although underlying fertility causes were not always documented.<sup>8,11,12,14,16,18,21,22,25,28</sup> The mean time from surgery to conception was 31 months, with the mean surgical follow-up period of 47 months. The pooled live birth rate of women pregnant following trachelectomy was 62.8% (404/643), with several studies published before all pregnant women had completed their pregnancies.<sup>2,10,12,16,17,20,24,30</sup> The rate of first-trimester miscarriage was 16% and second-trimester miscarriage was 7%. The percentage of women who delivered at term was 54.8%. Women were advised to deliver by caesarean section, although whether by lower segment or upper segment (classical) was not consistently documented.

## Obstetric care

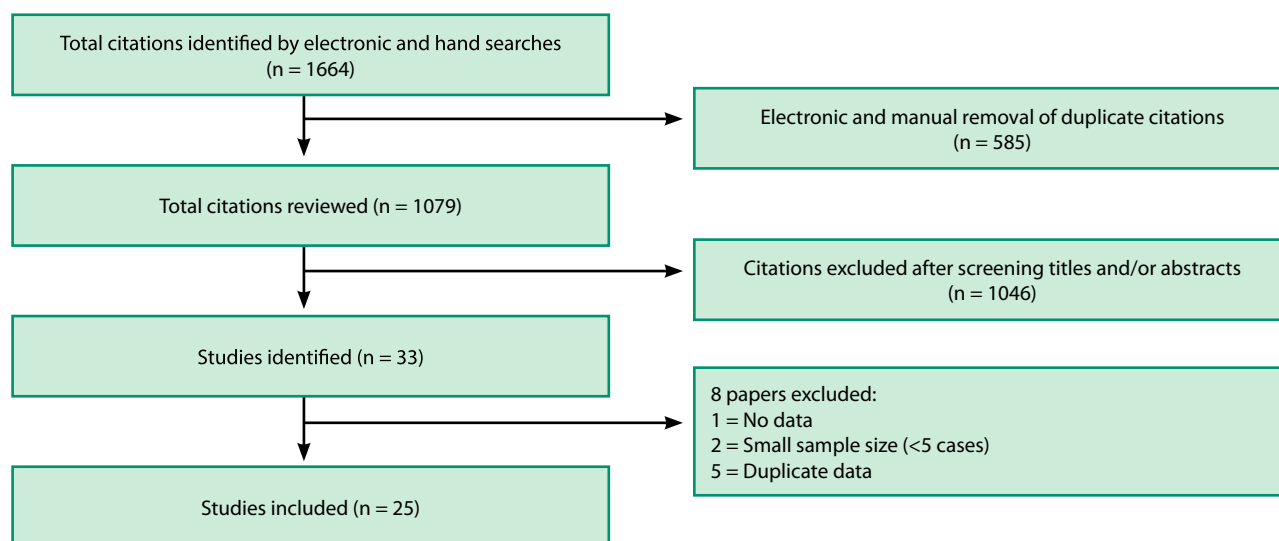
In the absence of national or international guidance on the management of women with post-trachelectomy pregnancies, there tends to be a limited awareness of the potential obstetric problems in this group of women. While the need for evidence-based management strategies is recognised, the paucity of robust evidence remains a problem. Until such time that new evidence emerges, peer recommended best practice is the best alternative.<sup>31</sup>

Central to the understanding of the management of these women is the knowledge of the implications of the altered anatomy following removal of the cervix. It is postulated that in pregnancy the **cervical length, the internal os and the endocervical mucus plug play an important role in maintaining cervical competence and preventing ascending infection**. A **shortened cervix (or neo-cervix in women following trachelectomy)** is thought to lead to a loss of **mechanical, cellular, biochemical and immunological barriers resulting in cervical (isthmic) incompetence, ascending infection, higher risk of second-trimester miscarriages, prematurity, PPROM and chorioamnionitis**.<sup>12,32</sup> Detection of labour may be difficult to assess as there may be painless progressive dilatation of the neo-cervix leading to mid-trimester miscarriages and preterm labour (25–28%).<sup>15,31</sup> Women should be made aware of these risks prior to and early in pregnancy, and should be managed as high risk.<sup>11</sup>



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**Figure 1.** A diagram showing trachelectomy surgery and the position of a permanent suture. Reproduced with permission from Jo's Cervical Cancer Trust (<https://www.jostrust.org.uk/>).



**Figure 2.** Study selection for a systematic review of the pregnancy outcomes following trachelectomy surgery.

Fertility units should avoid transferring more than one embryo to avoid the possibility of multiple pregnancies.

These women require a multidisciplinary team approach with early input from the oncology team, counselling support services, clinicians specialised in transvaginal ultrasound scans of post-trachelectomy women, consultant obstetricians and neonatal teams. To maximise all possibilities of a favourable outcome, it is vital that care providers have appropriate obstetric management pathways in place.

The systematic review showed that the rate of first-trimester miscarriage is 16%, which is similar to the rate among the general population of 15–20%. However, the rate of second-trimester miscarriage is 7% (as high as 8.6–11% in some studies), which is higher than the general population rate of 4%. Most of the second-trimester miscarriages are caused by infection and PPRM.<sup>33</sup> In the event of a first-trimester miscarriage, medical management is recommended without having to remove the cerclage. Surgical evacuation can be performed through the isthmic cerclage with neo-cervical dilatation to Hegar size 7 if required, preferably under ultrasound guidance.<sup>34</sup> This should be undertaken by a senior clinician, as locating the neo-cervix may be difficult with an increased risk of perforation.<sup>35</sup> When managing second-trimester miscarriages, the cerclage may need to be removed before the prostaglandin regimen is commenced. The role of hysterotomy remains contentious, depending on the gestation.<sup>36,37</sup>

The high risk of preterm labour associated with trachelectomy can be extrapolated from the data available on women who have had knife cone treatment or large loop excision of the transformation zone. Kyrgious et al.'s<sup>38</sup> meta-analysis of 27 studies has demonstrated that preterm labour is directly correlated to the excision of a core depth of more

than 10 mm of cervical tissue (relative risk –2.59, 95% CI 1.80–3.72). Based on these data, the risk of preterm labour in women post-trachelectomy can be projected to be similarly high if not more, as trachelectomy involves excision of a larger volume, or all of the cervix, compared to a cervical conisation procedure. Risk of preterm delivery post-trachelectomy is quoted to vary between 20% and 30%; the current review found this figure to be 45%. Overall, 55% of women delivered in the third trimester.

Serial isthmic or neo-cervical length scans to monitor isthmic shortening and funnelling along with simultaneous active screening for genital infections are recommended.<sup>27,31</sup> There is no evidence to recommend consideration of insertion of an additional suture, which can be technically difficult. In order to reliably detect the sonographic changes of early isthmic shortening and dilatation, it would be ideal for the clinician performing the transvaginal ultrasound to be familiar with the sonographic appearance of an attenuated neo-cervix of women following a trachelectomy, although sonographic training may be difficult to arrange considering the infrequent presentation of these cases.<sup>39</sup>

It has been speculated that the isthmic suture itself may be a cause of infection, and prophylactic antibiotics and fortnightly infection screening from 16 weeks may be beneficial.<sup>27,40</sup> Conversely, the Society of Obstetricians and Gynaecologists of Canada<sup>41</sup> recommends only that urine be tested for culture and sensitivity and vaginal cultures for bacterial vaginosis at the first obstetric visit, and any infections be treated in women at high risk of preterm labour. However, these guidelines are specifically for women with a history of cervical insufficiency rather than trachelectomy patients who may not have a cervix. For this reason, in the authors' practice the stitch is buried under the

vaginal epithelium during the vaginal–isthmic anastomosis, in order to reduce the theoretical risk in relation to the foreign body of the cerclage in the vagina. Some clinicians advise women to use condoms during sexual intercourse and avoid spas and swimming pools to minimise the risk of infection during pregnancy. Vaginal progesterone pessaries have been shown to decrease the rate of preterm labour in non-treated asymptomatic women with a short cervix (with particular reference to spontaneous delivery before 34 weeks) from 34% to 19% in the treated group, although not specifically in those who have had a trachelectomy.<sup>42</sup> More recently, in 2016 the OPTIMUM trial<sup>43</sup> showed no evidence that vaginal progesterone pessaries reduce the risk of preterm delivery.

There is no evidence to support routine antenatal administration of prophylactic steroids versus administering steroids once preterm labour commences. Considering the high reported incidence of early preterm labour and PPRM, the authors recommend consideration of prophylactic steroids from 24 weeks if preterm labour appears imminent.<sup>44</sup> Limitation of activity in the second half of pregnancy is postulated to prevent mechanical strain on the isthmic region, although a randomised controlled trial of bed rest versus no intervention in women at high risk of preterm labour showed no benefit in bed rest. Bed rest is preferably avoided unless there is vaginal bleeding or a suspicion of early threatened labour.<sup>45,46</sup> Thromboprophylaxis in the form of thrombo-deterrent stockings is recommended, with low-molecular-weight heparin being reserved for women with additional risk factors for venous thromboembolic disease. Elective dental work is to be avoided in pregnancy because of the known association between periodontitis and adverse pregnancy outcomes, such as low birthweight and preterm labour.<sup>47</sup> Sexual intercourse may be a source of infection; patients may be advised to consider avoiding coitus from 20–36 weeks of gestation.<sup>48</sup>

There is consensus in the literature that the mode of delivery should be by a planned or prelabour caesarean section, as there is a risk of uterine rupture and severe haemorrhage if contractions commence. The main problem during a caesarean section is the absent or poorly formed lower segment caused by severe distortion following cervical amputation, with the risk of an extension of the transverse lower segment uterine incision into the uterine arteries causing catastrophic haemorrhage.<sup>12</sup> Traditionally, a classical caesarean section with a midline vertical upper segment incision was recommended;<sup>45</sup> nowadays there is growing evidence on the safety of a transverse incision by lower segment or high transverse incision to reduce morbidity and risks of future fertility issues, such as repeat caesarean section and placental implantation problems.<sup>27,49,50</sup> A transverse incision may be considered if the lower segment is sufficiently well developed. Technical difficulty in obtaining adequate exposure at surgery and haemorrhage should be anticipated,

and the presence of a senior clinician at surgery is recommended. In view of the anticipated difficulties at delivery, timing of the procedure is recommended by 37 weeks to avoid the woman going into spontaneous labour and requiring an emergency caesarean section.

## Contraception counselling

Patients should be carefully counselled about contraceptive options. Contraception is advised for 6 months after trachelectomy, extrapolating Himes and Simhan's data that conceiving within 2–3 months of the conisation procedure was associated with a high risk of preterm labour.<sup>31,51</sup> It is reasonable to counsel women to avoid pregnancy for at least 6 months after trachelectomy, both in view of the large volume or totality of cervix removed and to enable confirmatory evidence of absence of early recurrent disease. Confirmation of no early recurrence is with a negative colposcopic assessment, vaginal vault and isthmic smear, and pelvic magnetic resonance imaging scan.<sup>36</sup>

There does not appear to be an increased risk of cervical cancer among users of oral hormone contraception.<sup>52</sup> The use of combined hormone methods, subdermal implants and progesterone implants are given UK Medical Eligibility Criteria for Contraceptive Use (UKMEC) advisory status 2, that is, the advantages of using contraception outweigh the theoretical or proven risks.<sup>53</sup> Progesterone-only pills have been given a rating of UKMEC 1, that is, there is no restriction on the use of this contraceptive method. However, since the cervix is removed, the progesterone-only pill, which relies on the action of cervical mucus, which is lost, may be ineffective as a method of contraception. Insertion of an intrauterine system may be technically challenging because of difficulty locating the isthmic os and isthmic stenosis. In order to reduce this complication, some surgeons insert a urinary catheter through the isthmus during the trachelectomy and leave it in place for three days post-surgery.<sup>12</sup> Intrauterine system insertion should be attempted by an experienced clinician.

## Women's experiences in pregnancy following trachelectomy

Women who have a trachelectomy are not only coping with the impact of a cancer diagnosis, but also with the potential effects of surgery on their reproductive health. All women should have access to a clinical nurse specialist in gynaecological oncology who can provide them with information, advice and support, and be a key contact during treatment and their decision-making process. These women may also benefit from psychological counselling and contact with peer support groups. Beaver and Booth<sup>54</sup> described how patients need adequate information such as



likelihood of cure, spread of disease and treatment options in order to make a decision. In relation to trachelectomy, specific long-term reproductive risks and the role of the womb in relation to their feminine identity should also feature in the decision-making consultation.

In a qualitative interview study of 12 women, some of whom had been pregnant after trachelectomy, it was reported that while some women experienced joy and confidence during pregnancy, many felt worried and experienced an expectation of difficulty or a sense of foreboding during the pregnancy.<sup>55</sup> A few women reported emotional detachment from their pregnancy, such as not buying items or making preparations. Coping behaviour, such as altering activities or detachment, was similar to other studies on behaviour in a subsequent pregnancy after experiencing a previous pregnancy loss.<sup>56</sup> For those who had experienced pregnancy loss after a trachelectomy, some reported a sense of regret, because of not raising their concerns at the hospital or not maintaining communication channels with the original hospital that had performed the surgery, while some reported feeling that they had reached their emotional and physical limitations.<sup>55</sup> Many women, particularly those who had experienced a pregnancy loss, commented on the lack of consistent information about pregnancy management after a trachelectomy. Overall, they felt that there were inconsistencies in antenatal advice and obstetricians' knowledge, with variable advice ranging from decreasing daily activities, avoiding baths and sex, to use of pessaries or antibiotics. They expressed the need for consistent information, such as pregnancy statistics, experiences of other women and care during pregnancy. The general feeling was captured by one participant's statement: *'I wanted the combined wisdom of everybody who had been through the trachelectomy'*.

## The potential reduction in the number of women having a trachelectomy

For the foreseeable future, trachelectomy will continue to be the standard management for women with stage IA2 or IB1 cervical cancer wanting fertility preservation. However, in light of growing observational, non-randomised evidence that the risk of parametrial involvement for women with low-volume, low pathological risk tumours is less than 1%,<sup>57</sup> a number of groups have now published case series on less radical surgery for such women, for example, knife cone with laparoscopic bilateral pelvic lymph node dissection.<sup>58,59</sup> However, it is imperative that a change to less radical surgery, fertility-preserving or not, is only done without a detrimental impact on oncological outcome. As highlighted in the 2014 Cochrane meta-analysis,<sup>60</sup> the outcome of three large continuing international randomised controlled trials should be awaited before standard practice is changed. The authors therefore do not anticipate any significant reduction

in the number of women requiring obstetric care post-trachelectomy in the near future.

## Conclusion

It is imperative that pregnant women are able to access appropriate and consistent obstetric information as well as emotional support during their pregnancy. Obstetricians will need to be aware of the evidence base for the management of pregnancy after a trachelectomy. Involvement of national epidemiological bodies like the UK Obstetric Surveillance System in reviewing the management of post-trachelectomy pregnancies would help gather information as to how these women are managed across the country, thus providing much needed data. Until such a time, maintaining communication channels between the obstetrician and the

### Box 1. Recommendations for antenatal care

- Every woman who becomes pregnant after a trachelectomy should be considered high risk with early referral for consultant-led obstetric care with multidisciplinary input (grading of recommendation: C)
- Vaginal progesterone pessaries may be considered from 12 weeks (200 mg twice a day) until 36 weeks<sup>42</sup> (grading of recommendation: B)
- Serial fortnightly isthmic length scans<sup>31</sup> (grading of recommendation: C)
- Urine should be tested for culture and sensitivity and vaginal cultures for bacterial vaginosis at the first obstetric visit, and any infections should be treated.<sup>41</sup> Additionally, consider prophylactic antibiotics if clinically indicated at 16 and 24 weeks (grading of recommendation: C)
- Consider a course of two doses of prophylactic steroids from 24 weeks of gestation if there are signs of preterm labour or delivery appears imminent<sup>44</sup> (grading of recommendation: A)
- Avoid unnecessary vaginal digital examinations (grading of recommendation: C)
- Consider avoiding sexual intercourse from 20 weeks onwards as this may be a source of infection<sup>48</sup> (grading of recommendation: C)
- Consider avoiding strenuous activities such as heavy lifting, exercise or prolonged periods of standing in the second trimester onwards<sup>41</sup> (grading of recommendation: C)
- Avoid elective dental work during pregnancy to minimise risks of infection and preterm birth resulting from periodontitis<sup>47</sup> (grading of recommendation: B)
- Commence antibiotics and prophylactic steroids if premature rupture of membranes occurs with a view to deliver as soon as possible, as per Royal College of Obstetricians and Gynaecologists' guidance<sup>44,61</sup> (grading of recommendation: A)
- Aim to deliver by elective caesarean section around 37 weeks, but maintain a low threshold for delivery in case of preterm prelabour rupture of membranes as there is a high risk of subclinical chorioamnionitis (grading of recommendation: C)

Grading of evidence is as per Royal College of Obstetricians and Gynaecologists' Green-top Guideline grades of recommendation. Because of a lack of evidence on antenatal management, many recommendations are based on expert opinion (grading of recommendation C)

gynaecological oncologist with the creation of individualised antenatal care plans would help to ensure a holistic team approach.

Box 1 summarises the recommendations for antenatal care for women following a trachelectomy.

### Disclosure of interests

AT has written the RCOG Green-top Guideline number 70 on the management of bladder pain syndrome. EB is a member of the RCOG Scientific Advisory Committee. The authors report no conflict of interest.

### Contribution of authorship

AT performed literature searches, extracted data, researched, drafted and revised the paper. FW performed data extraction, drafted and revised the manuscript. PL, EB and AJ drafted and revised the manuscript. KR conceived the idea, drafted and revised the manuscript. All authors approved the final version.

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