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Cervical cancer

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Keywords: invasive cervical cancer young women uterine conservation radical trachelectomy Standard treatment for invasive cervical cancer involves either radical surgery or radiotherapy. Childbearing is therefore impossible after either of these treatments. A fertility-sparing option, however, by radical trachelectomy has been shown to be effective, provided that strict criteria for selection are followed. Fertility rates are high, whereas recurrence is low, indicating that a more conservative approach to dealing with early small cervical tumours is feasible. Careful preoperative assessment by magnetic resonance imaging scans allows accurate measurement of the tumour with precise definition to plan surgery. This will ensure an adequate clear margin by wide excision of the tumour excising the cervix by radical vaginal trachelectomy with surrounding para-cervical and upper vaginal tissues. An isthmic cerclage is inserted to provide competence at the level of the internal orifice. A primary vagino-isthmic anastomosis is conducted to restore continuity of the lower genital tract. Subsequent pregnancies require careful monitoring in view of the high risk of spontaneous premature rupture of the membranes. Delivery by classical caesarean section is necessary at the onset of labour or electively before term. Over 1100 such procedures have been carried out vaginally or abdominally, resulting in 240 live births. Radical vaginal trachelectomy with a laparoscopic pelvic-node dissection offers the least morbid and invasive route for surgery, provided that adequate surgical skills have been obtained. © 2012 Elsevier Ltd. All rights reserved.

Introduction

Cervical cancer is the second most common malignancy to affect women, with over half a million cases occurring worldwide each year. Of these cases, more than 350,000 will die from their disease because most cases occur in under-developed countries and present at an advanced incurable stage.

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In Europe, about 38,000 cases are diagnosed each year, more than two-thirds of which would be expected to be cured and survive. Success rates will vary from country to country, depending on the facilities for treatment available and, more importantly, whether a screening programme has been established. Such programmes will detect early stage disease and are aimed at preventing the development of invasive cancer by treating pre-malignant cervical intraepithelial neoplasia before a truly invasive and malignant tumour develops.

Screening by cytology with the use of Papanicolaou cervical smears was first introduced on a population basis in British Columbia in the 1970s. A dramatic decrease in the incidents of cervical cancer and subsequent death rate was reported. These studies were subsequently confirmed with programmes in Scandinavia and then England and Wales. Although opinions differ on what age screening should commence, most authorities agree that as the age of coitarche varies from country to country depending on social and religious principles, the pre-malignant process will have commenced in the most cases by the age of 20 years, and therefore screening should commence at that age.

In developed countries with established screening programmes, the incidence of invasive cancer has continuously decreased, with a proportional increase in the number of early lesions and more particularly an increase in the number of pre-malignant intraepithelial neoplasias. These premalignant cases may be successfully treated with excellent results by conisation procedures, usually loop excision with diathermy (the large loop excision of the transformation zone or loop electrosurgical excision procedure).

Cone biopsy remains an integral part of diagnostic and therapeutic management and may be enough of an excisional procedure to treat superficially invasive (micro-invasive) carcinoma. Women with established invasive cancer will be treated either by radiotherapy or radical surgery, depending on stage. These two methods of treatment have withstood the test of time for the past 120 years. Early stage IB tumours have excellent cure rates with radical abdominal hysterectomy and bilateral pelvicnode dissection. This procedure was originally described by Wertheim, although various modifications by either the abdominal or vaginal route (the Schauta operation) have been described, and more recently by the use of laparoscopic and minimally invasive surgery. Cure rates of between 80 and 85% are expected. At the same time, although radiotherapy may offer similar cure rates for early stage disease, it is generally accepted that more advanced stage IIB and above disease should be treated by this method with sensitising chemotherapy usually in the form of weekly cisplatin. Improving cure rates for even more advanced disease have been achieved without the need for surgery. Should recurrence occur, however, then a small number of women may be salvaged by ultra-radical excenterative procedures with or without some form of diversion and reconstruction.

Because of social and professional circumstances, women are delaying childbirth into their midand late 30s and even early 40s. As a result, a significant number will present with early invasive cervical cancers having not completed their families or indeed even having started them. There is, therefore, an increasing need for consideration of fertility sparing surgery in suitable cases.

The concept of a vaginal cervicectomy (trachelectomy, from the Greek 'trachelos'- cervix) was first conceived by Franz Novak in Ljubljana in 1948.¹ In fact, he thought he was treating carcinoma *in situ*, but a number of invasive cervical cancers were included. Aburel² described an abdominal approach for removing the cervix in 1956. Neither of these procedures gained support. In the 1970s, however, Burghardt and Holzer³ realised that it was not necessary to remove the corpus uteri in all cases of small early invasive cancer.

Uterine conservation was re-introduced by Dargent et al.⁴ in the early 1990s. They excised the cervix with para-cervical and upper vaginal tissues from the vaginal route, and at the same time carried out a laparoscopic pelvic-node dissection. Shepherd et al.⁵ and Roy and Plant⁶ modified this technique and reported that successful outcomes (pregnancy and cure rates) were possible after such surgical treatment. Ungar et al.⁷ in 2005 re-introduced the abdominal approach in combination with a pelvic-node dissection, showing that this was feasible, particularly for those surgeons not comfortable with carrying out radical vaginal surgery. Other investigators have supported this.

Imaging techniques, especially with magnetic resonance imaging (MRI), have now been developed for more precise identification and localisation of cervical tumours. Better selection is therefore possible. This allows radical local excision of the cervix and of tumour but with conservation of the corpus uteri and, on occasion, part of the upper proximal cervix at the internal orifice while at the same time obtaining adequate clear margins. As yet, accurate identification of involved lymph nodes, especially with microscopic disease, is not possible. Developments have been made in positron emission tomography and computerised axial tomography. The identification of potential sentinel nodes using radio-nucleotide techniques will also lead to a reduction in the need for routine pelvic-node dissection.⁸ This is necessary so that microscopic occult and overt macroscopic lymph-node disease can be identified, and women requiring adjunctive treatment after surgery targeted.

The principles of surgery follow Halstead's principles⁹ to achieve an adequate wide local excision of the primary tumour with surrounding normal para-cervical vaginal tissues. This is for the first or lower part of a Schauta radical vaginal hysterectomy¹⁰ or the lower and distal part of a Wertheim's radical abdominal hysterectomy¹¹ with upper partial colpectomy. At the same time, the pelvic lymph nodes draining the cervix are removed either by an extraperitoneal or transabdominal approach, which may be by either laparoscopy or traditional open surgery.

Patient selection

Screening procedures in programmes are becoming increasingly established throughout the world, and many early and small cervical cancers are being detected through abnormal cervical smears. Alternatively, abnormal post-coital or intermenstrual bleeding may result in a clinical examination showing a cervical tumour. Subsequent colposcopy with a biopsy will lead to diagnosis with or without cone biopsy. The extent of the tumour may be assessed clinically with the existence of co-existing intraepithelial neoplasia. Cone biopsy, either by cold knife or diathermy, excision (a large loop excision of the transformation zone or loop electrosurgical excision procedure) is the established method for most accurately assessing the stage and size of a cervical tumour. The depth and diameter of the lesion with a three-dimensional measurement will thus give a volume. For small, superficially invasive tumours, stage IAI and some IAII tumours (i.e. cone biopsy) may be therapeutic and therefore no further treatment is required (see Table 1 for International Federation of Gynecology and Obstetrics staging of early cervical cancer). The margins of excision must be clear of both invasive and high-grade pre-invasive intraepithelial neoplasia. Fertility conservation may therefore be achieved without hysterectomy and without removal of the whole cervix. Although there is a risk of cervical incompetence, depending on how high the excision has been carried and whether the internal orifice has been compromised, a cervical suture may be necessary in any ensuing pregnancy to try and achieve cervical competence and avoid premature labour. Any woman who has had a cone biopsy should report this to her obstetrician during any subsequent pregnancy so that clinical and ultrasound assessment of the cervix may be carried out throughout pregnancy.

Table 1

The International Federation of Gynecology and Obstetrics staging 2009: early stage cervical carcinoma.

Stage 1	The carcinoma is strictly confined to the cervix (extension to the corpus should be disregarded).
IA	Invasive carcinoma, which may be diagnosed only by microscopy with deepest invasion 5 mm
	or less and largest extension 7 mm or more.
IAI	Measured stromal invasion of 3 mm or less in depth and extension of 7 mm or less.
IA2	Measured stromal invasion of greater than 3 mm and not greater than 5 mm with an extension
	of not greater than 7 mm.
IB	Clinically visible lesions limited to the cervix uteri or pre-clinical cancers greater than stage IA. ^a
IBI	Clinically visible lesion 4 cm or less in greatest dimension.
IBII	Clinically visible lesion greater than 4 cm in greatest dimension.
Stage II	Cervical carcinoma invades beyond the uterus, but not to the pelvic side wall or to the lower
	third of the vagina.
IIA	Without parametrial invasion.
IIAI	Clinically visible lesion 4 cm or less in greatest dimension.
IIA2	Clinically visible lesion greater than 4 cm in greatest dimension.
IIB	With obvious parametrial invasion.

^a All macroscopically visible lesions, even with superficial invasion, are allowed to stage IB carcinomas. Invasion is limited to a measured stromal invasion with a maximum depth of 5 mm and a horizontal extension of greater than 7 mm. Depth of invasion should not be greater than 5 mm taken from the base of the epithelium of the original tissue – superficial or glandular. The depth of invasion should always be reported in mm, even in those cases with 'early (minimal) stromal invasion' (about 1 mm).

It is generally accepted that skip lesions may occur with glandular intraepithelial neoplasia and involve any crypt or gland throughout the endocervical canal up to the level of the internal orifice. It is now recognised that this may also occur on occasions with squamous cell lesions in crypts that have undergone metaplasia within the transformation zone, although this does not usually extend as far up the endocervical canal as for glandular lesions. Glandular intraepithelial neoplasia, therefore, does require removal of the upper and proximal endocervical canal as well as the ectocervix and transformation zone. It is wise to carry out a fraction of a uterine curettage at the same time as a cone biopsy to be as certain as possible that no other abnormal crypts or glands exist beyond the depth of a conisation procedure.

Given that the incidents of lymph-node involvement with superficially invasive Stage IAI cervical cancer is less than 1% and with IAII superficially invasive cancer generally between 3 and 5%, routine lymph-node dissection may be avoided. If, however, there is extensive lymphovascular space invasion or the lesion is one of the larger sized stage IAII tumours approaching the diameter and depth of invasion of a stage IBI lesion, then it is necessary and wise to carry out a simultaneous pelvic-node dissection with the cone biopsy.

If fertility sparing, however, is not an issue because of the age of the women or she has completed her family, then a hysterectomy is an entirely reasonable option to offer; the radicality and need for pelvic-node dissection will depend on the arguments presented above.

Once the tumour has become a truly invasive stage IB lesion, with a depth of more than 5 mm, the incidence of lymph-node involvement significantly increases. Pelvic-node dissection with a more radical excision of the primary tumour and cervix is then indicated. When fertility preservation is not required, radical hysterectomy should be advised. This will remove the cervix and primary tumour with a surrounding cuff of between 1 and 2 cm of normal tissue, including the para-cervical, paravaginal and upper vaginal tissues themselves en bloc with the uterus and parametrial tissues. The ovaries and fallopian tubes may be conserved, depending on the age and wishes of the patient. Glandular lesions do have an incidence of about 5 and 10% secondary involvement of the ovaries, which does need to be taken into consideration. A simultaneous en-bloc dissection of the pelvic lymph nodes takes place up to, and including, the common iliac lymph nodes.

Women considering fertility preservation are usually self selected, but will then need to decide after formal assessment and staging whether they should undergo the procedure. Although all women should be advised of current accepted standard methods of treatment, some are not able to take the responsibility before deciding on a more conservative approach, especially when the subsequent potential risks of prematurity are explained. As a general rule, tumours 2 cm or less are suitable for a more conservative approach, such as by trachelectomy, but larger tumours are treated by the more traditional radical hysterectomy or, depending on other circumstances, chemoradiotherapy. All centres, however, carrying out fertility preservation will have individual cases with tumours larger than 2 cm, which after careful assessment have been deemed suitable for a radical wide local excision but with uterine conservation. This, however, is the exception. In our study,⁵ three women had stage IIA lesions, six women had lesions larger than 2 cm, and one woman had lesions up to 5 cm in diameter. These are the exceptions and not the rule. In general, the small number of reported cases, however, have occurred in lesions larger than 2 or 3 cm in diameter.

Staging of the tumour

Cervical cancer is most accurately staged by MRI. This will specifically identify and define a cervical tumour and should preferably be carried out before any form of diagnostic cone biopsy.¹² This is not always possible if the conisation is necessary for diagnosis of invasive disease. The MRI will also allow assessment of pelvic lymph nodes, and an abdominal scan (computed tomography or MRI) will allow assessment of the upper retroperitoneal and para-aortic nodes. The size of the tumour may be measured as well as its location and distance from the isthmus (Figs. 1 and 2). The length of the endocervical canal and uterine cavity may be assessed. More accurate measurement is now available using an endovaginal coil with MRI imaging to obtain better definition of the tumour and involvement of the cervix with the inner portion of the paracervical and paravaginal tissues.¹³ Axial and sagittal views may be taken and are useful in planning surgery and for reference during the surgical procedure itself.



Fig. 1. Magnetic resonance imaging axial view showing tumour in posterior lip of cervix. Published with permission from Gyn Onc. Peltecue GL and Trope CG (eds). Bucharest Publishing House. Romanian Academy 2010. Chapter 13D, pp. 319, 320, 321, 323.

Pelvic-node dissection

Pelvic-node dissection is currently necessary in order to determine which women have microscopic occult metastases from a primary cervical carcinoma. If lymph nodes are obviously or suspiciously enlarged on an MRI scan, then these women will need treatment by chemoradiotherapy. Arguments may be presented for a staging laparoscopic node dissection with these women, or alternatively a positronemission tomogrphy scan to determine the existence of higher para-aortic nodes. Those decisions will be determined by individual practice and multi-disciplinary discussion between radiologists, radio-therapists and gynaecological cancer surgeons at their respective cancer centres. Reported incidents of nodal involvement with superficially invasive lesions is low, but quoted as 1% for stage IAI, and up to 7.8% with stage IAII. Stage IB tumours have a 16–18% incidence of pelvic-node involvement.¹⁴

Women undergoing pelvic-node dissection with fertility-sparing radical trachelectomy may have this carried out either as part of a formal staging procedure (i.e. examination under anaesthesia with cystoscopy and sigmoidoscopy before a second procedure when the trachelectomy is carried out). The alternative is to assess by colposcopy with or without anaesthesia and staging then to carry out the trachelectomy and pelvic-node dissection at one operative sitting. In our centre, it is our preference to carry out a formal examination under anaesthesia with colposcopy in order to assess fully the tumour, its mobility and accessibility through the vagina and, at the same time, proceed to a laparoscopic pelvic-node dissection, carried out trans-abdominally. Between 1 and 2 weeks later, if the lymph nodes are negative, and no other adverse features are apparent taking the MRI staging scan into account, then radical vaginal trachelectomy is carried out. Thus far, no complications have occurred with postoperative induration, fibrosis or sepsis resulting from the lymphadenectomy. Care is taken not to disturb the para-cervical tissues during this initial procedure, as otherwise ureteric complications could be encountered with the second vaginal operation.



Fig. 2. Magnetic resonance imaging, sagital view with endocervical coil demonstrating tumour. Published with permission from Gyn Onc. Peltecue GL and Trope CG (eds). Bucharest Publishing House. Romanian Academy 2010. Chapter 13D, pp. 319, 320, 321, 323.

Pre-operative counselling

In our centre, all women and their partners are fully informed of their options for treatment, the risks of surgery (which are much the same as for a radical hysterectomy) as well as the success and failure rate.¹⁵ The two important end results to emphasise are recurrence, and therefore the potential death rate, but also the 5-year survival and expected cure rate. It is also important to raise the issue of fertility rates and the risk of premature labour. It is emphasised that spontaneous rupture of the membranes with subsequent premature birth is a risk in up to 20% of cases owing to ascending chorio-amniotis resulting from the lack of a cervical mucus plug once the cervix has been removed. In our centre, with squamous cell lesions, we try and conserve up to 0.5 cm of the proximal cervix at the isthmus and internal orifice in all squamous lesions, providing that a good 1 cm clearance may be obtained from the tumour. On occasions, it is possible to conserve up to 1 cm. This, however, does not apply to glandular lesions when the whole end cervical canal needs to be removed. Women are informed that, anatomically and physiologically, the cervix is necessary to conceive a pregnancy, hold a pregnancy and retain it within the uterus as well as to subsequently aid in the delivery of the baby near or at term. Removal of the cervix, therefore, is defying nature and this does need to be fully appreciated with precautions taken and understood to prevent a tragic obstetric outcome.

An important caveat is that are any adverse prognostic factors are determined once the final pathology is reported, then completion treatment either by radical surgery or more usually chemo-radiotherapy is essentially indicated.

All women are also advised that they should not conceive for at least 6 months after fertility-sparing surgery in order to allow adequate healing for the anatomises between the vagina and isthmus. Six to twelve months also allows sufficient time for early recurrence to have manifested in most cases. Clinical follow up by examination, colposcopy and cytology, as well as MRI imaging, is explained.

Finally, it is emphasised that any subsequent pregnancy must be carefully supervised in a high-risk feto-maternal unit, with adequate supporting neonatal facilities to manage a potential premature baby. Delivery must be by a classical caesarean section using a low vertical incision into the uterus, as

the lower segment is not present. The temptation to carry out a transverse incision into what seems to be the lower segment may be fraught with danger. This area is significantly fibrosed, and the lower segment either absent or extremely narrow even if a small cuff of proximal upper end cervix has been conserved. The incision may extend laterally and tear through the uterine vessels causing major haemorrhage. This occurred once in our study⁵ when the obstetrician concerned would not accept what seemed to be common sense advice.

Various measures have been proposed to prevent ascending infection either by carrying out a Würm suture occluding the isthmic os or alternatively a Saling procedure to cover the os by mobilising adjacent vaginal epithelium. This, however, is not straightforward because the trachelectomy will have removed the upper 1–2 cm of the vagina. The subsequent anastomosis results in scarring, fibrosis and puckering. Should premature rupture occur, then appropriate antibiotic treatment is necessary and obstetric advice should be given about when the delivery and evacuation of the uterus should most suitably take place.

Radical trachelectomy

Radical trachelectomy may be carried out either vaginally or abdominally. Traditional gynaecological surgery training has emphasised the vaginal approach for dealing with pathology within the lower genital tract requiring repair, reconstruction or other vaginal procedures such as hysterectomy. Gynae-cological pelvic cancer surgeons will have familiarised themselves with the anatomical relationships within the pelvis from the perineal and vaginal route, and will understand the physiological workings of the pelvis and potential ramifications of surgical intervention. Those that are familiar with vaginal surgery and feel comfortable with mobilisation of relevant structures, including the bladder and ureters by this approach, can ensure that an adequate vaginal cuff, with surrounding para-vaginal and paracervical tissues, may be obtained around the primary tumour.

Others surgeons may feel more comfortable, depending on their experience, with an abdominal approach either by open surgery or by laparoscopy.^{16,17} Although the vaginal approach may seem more challenging, it has less morbidity and a quicker recovery time, especially when associated with a laparoscopic pelvic-node dissection. Potential complications may be similar to the abdominal procedure; however, as with other laparoscopic and minimally invasive techniques, it requires less hospital stay and women can return to work earlier, causing less inconvenience to the woman, her family and society. Therefore, this is the more favoured approach.

Radical vaginal trachelectomy & laparoscopic pelvic node dissection

Pelvic-node dissection is either carried out as part of the staging procedure or trachelectomy. An extraperitoneal approach may be taken but it is preferable to carry out the lymphadenectomy laparoscopically, and in our experience, transperitoneally. Four portals are used with the laparoscope and umbilical portal inserted by the Hasson direct entry technique. A sub-umbilical incision is used to identify the peritoneal cavity. A carbon dioxide pneumoperitoneum is introduced, and the three further portals inserted under direct vision. The abdominal cavity is inspected; the upper abdomen is assessed first followed by the pelvis. A thorough inspection of the liver, omentum, paracolic gutters and subdiaphragmatic peritoneum followed by the ovaries, fallopian tubes, pelvic peritoneum and Pouch of Douglas is carried out. The uterus and its mobility is assessed. Other pathology, such as endometriosis or chronic pelvic sepsis with adhesions, is looked for.

The peritoneum overlying the external iliac vessels is incised, exposing the pelvic side walls proximal to the round ligaments. The infundibulo-pelvic ligament and gonadal vessels are identified, care being taken to avoid and preserve them. The ureter is located overlying the bifurcation of the common iliac vessels, deep to the infundibulo-pelvic ligament. The obturator fossa is opened by dissection along the medial and inferior aspect of the external iliac vein, thus exposing the obturator nerve. Above this, in the areola tissue on the medial aspect of the posterior parietal peritoneum, is the obliterated hypo-gastric artery, which is the terminal branch of the internal iliac artery. This is not to be confused with either the obturator nerve or the ureter. Clear anatomical differentiation may be confirmed by identification proximally (i.e. cranially before these structures delve deeper into the

pelvis). Tugging gently on the obliterated hypogastric artery will move and pucker the lateral umbilical ligament, thus confirming its identification. This is seen well on the posterior aspect of the anterior abdominal wall distally at the limit of view within the pelvis.

The obliterated hypogastric artery is elevated with the round ligament in order to open up and identify the paravesical space and the rest of the pelvic side wall laterally. An aberrant obturator vein is looked for. This seems to be more common than quoted in the anatomical text books and may lead to troublesome haemorrhage.

With complete pelvic lymphadenectomy, obturator nodes are removed initially, followed by the internal iliac and external iliac nodes. Any blood or haemorrhage that occurs may be removed from the pelvis by carrying out the deep dissection first and so not obstructing satisfactory visualisation caused by blood tracking down from the more superficial or anterior dissection. The distal common iliac nodes are removed, care being taken to avoid traumatising the ovarian vessels.

A similar procedure is carried out on the contra-lateral side. A mixture of sharp and blunt dissection is used, with haemostasis being achieved using bipolar diathermy. Other electrosurgical modalities may be used depending on the facilities available (at increased cost) in any particular unit.

The pelvis is irrigated and a tonsil swab inserted into the pelvic side walls for haemostasis. This is removed at the end of the procedure and replaced with fibrin tissue gauze to encourage haemostasis and absorb any leaking lymphatic fluid in order to limit lymphocele formation.

Trachelectomy is then carried out if it is to be part of the same procedure. Once the vaginal operation is completed, the abdomen is then inspected once more laparoscopically before removing the portals under direct vision. Haemostasis is confirmed, and any further fluid collected is removed. Carbon dioxide gas is extracted and the four portals closed using a number 1 suture material such as Ethicon Vicryl (polyglactin) to the rectal sheath (for the larger 8 and 10 mm portals) followed by 3/ 0 monocryl or vicryl sutures to close the skin incisions.

Radical vaginal trachelectomy

The extended lithotomy position is used to obtain adequate exposure to the cervix through the vagina. Two assistants are necessary in order to obtain lateral retraction of the vaginal walls using deep vaginal side wall retractors. These should be insulated to prevent diathermy burns to the rest of the vagina and lower genital tract (Figs. 3 and 4).

The cervix is grasped with a vulsellum, care being taken to avoid traumatising the tumour as much as possible. Infiltration with 1 in 200,000 adrenalin and 0.25% bupivicaine as a four-quadrant paracervical block is carried out to limit bleeding in an otherwise vascular field and also to open up tissue planes and give further postoperative analgesia. An incision is made circumscribing the cervix, including a 2-cm cuff of vagina. The bladder and therefore isthmus is carefully identified, with the likely position of the internal os beneath this. Similarly, posteriorally, the reflection of the peritoneum from the Pouch of Douglas in the posterior fornix identifies the posterior aspect of the internal os and therefore upper limit and margin of the cervix. The vaginal cuff is mobilised using cutting diathermy followed by sharp dissection. The bladder is further mobilised anteriorally using gauze pledgelets. The bladder pillars are visualised and the paravesical spaces opened on both sides lateral to these. The incision is continued posteriorally cutting through and identifying the uterosacral ligaments and thus opening up the rectovaginal septum.

Once an adequate cuff of vagina has been mobilised around the cervix, this may then be drawn distally over the cervix itself and grasped within the blades and teeth of heavy forceps (Cropaks), or alternatively the vaginal cuff may be closed using interrupted sutures, which are then grasped for traction. The cervix itself, therefore, is covered, having inverted the vaginal epithelium over it. The sharp dissection around the upper cervix and isthmus is deepened using the harmonic scalpel (Ethicon Ultracision Endoscopy). This allows adequate dissection with haemostasis and division of the tissue. It also avoids the need for using further clamps and transfixion sutures. The bladder pillar is transected and the descending branch of the uterine artery (the cervical branch) is identified. It is clamped within the harmonic scalpel, cauterised and divided. The ureteric tunnel is thus identified and the ureter may be palpated to the side of the uterus as a cord, which becomes evident as the specimen is pulled on by traction and then released. The ureter is rolled and reflected out of the surgical field crainially by blunt



Fig. 3. Tissue to be excised: cervix and upper vagina with a surrounding 1–2 cm cuff of paracervical tissue. The descending branch of the uterine artery (cervical branch) is divided below the ureter. Published with permission Gyn Onc. Peltecue GL and Trope CG (eds). Bucharest Publishing House. Romanian Academy 2010. Chapter 13D, pp. 319, 320, 321, 323.

dissection and preserved safely. Dissection using the harmonic scalpel is then continued laterally to include between 1 and 2 cm of the lateral ligament in the para-cervical and lower parametrial tissues. The uterosacral ligament is divided deeply, again with 1–2 cm margins. The rectovaginal septum is reflected, if possible by avoiding perforation or opening of the peritoneum within the pouch of Douglas. Our preference is not to open this cavity in order to limit the possibility of pelvic infection occurring. There is often free fluid within the pouch of Douglas after pelvic-node dissection, either as blood stained if the lymphadenectomy has just been carried out as part of the same procedure or as clear serous fluid if it has been carried out 1–2 weeks earlier. Any opening or hole that is made into the pelvic peritoneum may be closed using a 2-0 vicryl suture. Depending on how much cervix is present (and often a considerable amount has been removed beforehand at the time of a cone biopsy), then it is relatively straightforward to reflect and mobilise the peritoneum and utero-vesical ligament anteriorally as well as the rectovaginal septum and pouch of Douglas posteriorally without having to open it.

Once the specimen is fully mobilised, the uterine cavity is once more sounded to measure the length and estimate the position of the tumour within the cervix itself. Taking into account the cuff of vagina, the distance from the external orifice and cervico-vaginal margin to be removed is confirmed by measurement using a metal rule. An extra centimetre is included above the tumour in order to ensure adequate clearance as measured on the MRI. Cutting diathermy is used then to mark the estimated excision line.

An Hegar dilator is placed into the endocervical canal with the cervix dilated up to Hegar 6. The dilator is left in the canal in order to facilitate identification. Cutting diathermy is then used to divide the cervical stroma at the chosen incision line either at the isthmus, or if possible (and a certain amount of cervical tissue may be conserved), 0.5–1 cm distal to this (Fig. 5). The cervix is thus amputated from the body of the uterus and removed. A suture is inserted for orientation into the specimen anterior on the vaginal margin at 12 O'clock. If there is any question of margin involvement, then frozen section analysis may be requested or alternatively further excision carried out either of the endocervical canal or vaginal margins.

Isthmic cerclage and vagino-isthmic anastomosis

Once haemostasis has been confirmed, an isthmic cerclage using non-absorbable number 1 nylon or prolene is inserted with four bites through the stroma of the isthmus or upper cervix. The Hegar 6 dilator remains *in situ* in order to avoid occluding the isthmic os. A knot is tied anteriorally at 12 O'clock around the dilator, thus ensuring that the os itself is not closed or stenosed, and an adequate passage may be maintained for menstrual flow and also spontaneous miscarriage should this occur. This size of



Fig. 4. Specimen mobilised with vaginal cuff before dividing the isthmus. Published with permission from Gyn Onc. Peltecue GL and Trope CG (eds). Bucharest Publishing House. Romanian Academy 2010. Chapter 13D, pp. 319, 320, 321, 323.

dilator will also allow insertion of a number 8 uterine catheter or cannula for evacuation of retained products, should this be necessary in the future (Fig. 5).

The suture is grasped for gentle traction and the vaginal margins identified. Four mattress sutures of number 1 Ethicon Vicryl (polyglatcin) are inserted anteriorally, posteriorally and on both lateral sides, care being taken to commence from the vaginal incision carrying the suture through the stroma of the cervix and then re-inserting through the os before extracting the suture from the vaginal margin once more. The Hegar dilator remains within the os in order to prevent stenosis or suturing closed the os itself. Two further angle sutures are inserted, one on each side laterally, to close the lateral incisions which otherwise would form a pocket, although this would close in time.

A number 12 Foley catheter is inserted through the isthmus into the uterine cavity having removed the Hegar dilator. The balloon is distended using 3 cc of fluid in order to retain this within the cavity. This catheter is left for 72 h in order to prevent synechiae formation and an isthmic stenosis. A bladder catheter (number 14 Foley) is inserted and left for 5 days to encourage bladder emptying. During this



Fig. 5. Vagino-isthmic anastamosis and isthmic cerclage with knot tied anteriorally. Published with permission Gyn Onc. Peltecue GL and Trope CG (eds). Bucharest Publishing House. Romanian Academy 2010. Chapter 13D, pp. 319, 320, 321, 323.

time, pelvic floor exercises may be commenced. When the catheter is removed, a residual urine volume is checked to ensure adequate and complete voiding. Rarely, this is unsatisfactory and recatheterisation has to be carried out for a further 48–72 h. If voiding is still not possible, then selfcatheterisation is necessary for 3–4 weeks. This has occurred in only about 5% of women and, in no case thus far, has this problem continued beyond 6 weeks.

A vaginal pack is inserted and this is removed after 24 h. Prophylactic broad-spectrum antibiotics are used to cover the procedure. The estimated blood loss expected is less than 100 cc.

Abdominal radical trachelectomy

The abdominal approach may be taken either using an open lower transverse incision for the laparotomy or alternatively a laparoscopic minimal access technique. The procedure will comprise the lower part of a radical abdominal hysterectomy. It has been advocated that the vaginal route should be reserved for tumours less than 2 cm, but it may be possible to extend this limit under certain circumstances for larger tumours to be removed via the abdominal route. Those experienced in radical vaginal surgery, however, would contend that it is possible for such larger tumours to be removed safely and under direct vision with adequate clearance by either route.

The abdominal approach involves opening the para-vesical spaces once the lymph-node dissection has been completed. The uterine vessels are identified and the ureters reflected laterally. Cervical branches of the descending uterine artery are identified and divided. As for a radical hysterectomy, the para-rectal spaces are opened by blunt dissection, so identifying adequate para-cervical and paravaginal tissues for excision with a 2-cm cuff of vagina mobilised, reflecting the bladder anteriorally and the rectum posteriorally. The uterosacral ligaments and lateral (cardinal) ligaments are divided, with a 1–2 cm inclusion in the specimen as for the vaginal approach. Once the specimen itself has been removed, a vagino–isthmic anastomosis is carried out under direct vision abdominally.

Division of the uterine vessels in order to simplify excision of the cervix and para-cervical tissue before re-anastomosis of the uterine vessels has been proposed. Most authorities would contend that this is unnecessary given that there is a good blood supply to the uterus bilaterally and from other sources, including the infundibulo– pelvic (ovarian) vessels. It is also unnecessary to divide the uterine vessels in order to carry out the trachelectomy and cervical excision. It is the descending branches of the uterine artery that require division, not the main artery itself, which may be conserved. It is unlikely, therefore, that compromise of the blood supply to the endometrium will ensue.

Continuous bladder drainage after surgery will be established by catheterisation as for a radical hysterectomy or the radical vaginal procedure.

The choice of approach will depend on whichever route a particular surgeon feels most comfortable with. As for any surgery, for whatever indication, compromising the chance of cure by selecting an inappropriate procedure, either to conform with patient demand or unrealistic surgical ambitions, should not be permitted to prevail. Careful patient selection and counselling is essential.

Trachelectomy during pregnancy

Invasive surgery such as trachelectomy during pregnancy is not advised, although there are exceptions to even the most stringent of rules and guidelines. In our study, four women underwent the procedure during pregnancy. Three of these took place early in the first trimester before the pregnancies had been diagnosed. One spontaneously miscarried as a late heavy period, and the other two continued until 34 and 36 weeks before being delivered by caesarean section. Calculation of dates indicated that certainly two of these women had not missed a period, and all three must have conceived shortly before being admitted for surgery but after the cancer had been diagnosed.

The fourth women was 13 weeks when she was diagnosed with her cancer before undergoing a large loop diathermy excision with further investigations. In retrospect, piecing the biopsy material and ultimate specimens together, her tumour measured 5 cm in diameter but was exophytic. She declined all conventional treatment, advice and a radical vaginal trachelectomy was carried out at 15 weeks of pregnancy. A prior pelvic-node dissection had been carried out laparoscopically. Margins of excision were clear, and all lymph nodes negative. A healthy live infant was delivered at 28 weeks after spontaneous rupture of the membranes. Both mother and child are well with no evidence of recurrence, some 3 years later.

This is not to advocate and promote such management but to emphasise the need for individualisation. It is also essential to warn women that they must use contraception before undergoing such radical or indeed any surgery for cervical and other cancers. From our experience, pregnancy tests should be carried out on all women even if they declare that they have not missed a period before undergoing surgery.

Neo-adjuvant chemotherapy during pregnancy

Cervical cancer is rarely treated primarily by chemotherapy; however, a substantial body of evidence (albeit anecdotal) indicates that neo-adjuvant chemotherapy is effective.¹⁸ Lesions that are larger than 2 cm need to be substantially reduced in size to make surgery with conservation of the body of the uterus feasible. The upper endocervical canal must not be involved. Although lesions cannot be 'downstaged', they can be 'downsized'. Stage IIA and even early stage IIB lesions, therefore, may be considered for a management in this way before undergoing planned elective radical vaginal trache-lectomy after adequate pelvic node dissection. A two-stage surgical approach, therefore, is important to

ensure that there is no evidence of locoregional or distal spread. The same stringent criteria are necessary for selection and a decision about completing treatment, once the final histopathology has been reviewed.

On an individual basis, neo-adjuvant chemotherapy is also given during pregnancy, in the second trimester, when delivery may be delayed until fetal maturity at 34 weeks. After this, either radical hysterectomy is carried out (at the same time as caesarean section) or a delayed vaginal traehelectomy postpartum. It is important to consider the risk of tumour spread and metastases occurring after calculating the doubling time from the size of the volume of the tumour that is present. All such cases, however, require careful individual consideration, and there is no substitute for advising standard treatment with common sense. Some flexibility, however, is to be encouraged.

Follow up

Women are discharged home once all packs and catheters have been removed and spontaneous voiding has been achieved. In our practice, this is on the fifth postoperative day. Under some circumstances, especially if patients live locally (which is often not the case), then discharge home with the catheter remaining *in situ* maybe encouraged. Careful follow up with a strict protocol is essential given that trachelectomy is a relatively new procedure and expectations for patients are high. Once the pathology has been reviewed, the woman is seen after 2 weeks to discuss the results. If these are satisfactory, with no adverse prognostic factors indicating the need for further treatment by either chemoradiotherapy (in the case of unexpected positive lymph nodes) or completion of radical hysterectomy (in the case of an unexpected positive central margin), then contraception is advocated for at least 6 months. If recurrence is not evident at this time, then fertility and conception should be encouraged sooner rather than later in case of other fertility problems, either co-incidentally or consequent to the surgery.

Follow up continues every 3 months for a year and then every 4 months for another year. Subsequently, 6-monthly visits continued up to 5 years, then yearly for a further 5 years (i.e. up to 10 years). At each visit, a clinical examination is carried out with colposcopy at 6 months and 1 year. Vaginal vault and isthmic smears are taken at each visit. An MRI scan is carried out at 6, 12 and 24 months.

After 10 years, women may return to the screening programme if there is one established, or alternatively most will wish to continue with a yearly smear. This is entirely reasonable given the circumstances but may need to be undertaken by a gynaecologist rather than an inexperienced general or nursing practitioner.

Interpretation of the isthmic and vaginal vault smears may be difficult owing to the potential for misinterpreting endometrial cells.¹⁹ Thirteen per cent of these may be absent but 41% of smears will contain squamous cells only. These should be reported as unsatisfactory in the first 2 years and only negative after this, although the absence of glandular cells should always be reported. If a smear is reported as abnormal, then a careful case review should be undertaken with a further colposcopic and clinical examination. Careful palpation of the vaginal vault and then review of the MRI scan will be necessary.

Clinical experience

In our clinical experience, over 200 women (208, as of October 2011) have undergone radical vaginal trachelectomy with a laparoscopic pelvic-lymph node dissection, with a mean age of 30.6 years. Most were for stage IBI tumours, with a small number of stage IAII and stage IIA lesions (see Table 2 for results).

These are carefully selected on an individual basis, with one young woman aged 18 years, having a clear-cell carcinoma of the vagina, which extended onto the cervix.²⁰ Lymphovascular space invasion was present in 33% (68 cases).

Two-thirds of the women (133 cases) had squamous cell lesions, but one-third had glandular tumours of one form or another. This relatively increased proportion of glandular tumours indicates the screening out with early detection of squamous cell carcinoma at an early stage and also identifying intra-epithelial lesions before they become malignant.

or 200 Women who elected for futurear trachelectomy.	
Age – Mean years (standard deviation)	30.6 (4.3)
Stage Ia1	1
Ia2	3
Ib1	202
Ib2	1
2a1	1
Number of lymphovascular space invasion (%)	68 (33%)

Experience at St Bartholomew's and The Royal Marsden Hospitals: demographic details of 208 women who elected for radical trachelectomy

Twenty-four women (11.5%) required completion treatment in view of high-risk adverse prognostic factors on the final histopathology. Elective completion hysterectomy once childbearing has been achieved and completed is not carried out. Two women have undergone hysterectomy for benign purposes because of menorrhagia. Both had two caesarean sections and the surgical procedure (hysterectomy) was not straightforward owing to extensive adhesions and scarring that had inevitably occurred with the trachelectomy and also subsequent caesarean sections. One of these women had a trial of a Mirena intrauterine progestogen containing device. Insertion of the coil was also difficult owing to the isthmic stenosis and short uterine cavity.

Sixty other women have been referred for consideration of fertility-sparing surgery but have been deemed unsuitable for a variety of reasons. These include (1) too far advanced disease or stage especially with large tumours; (2) lesser radicality with cone biopsy with or without lymph-node dissection deemed as adequate treatment (this applies especially to Stage IAI or IAII disease and very small superficial IBI lesions); (3) unrealistic expectations about fertility; and (4) individual patient decision (not being able to decide on novel treatment).

Complications

Thirteen women (6%) developed an isthmic stenosis requiring either dilation or ultrasound-guided hysteroscopy and dilatation as part of further treatment for infertility. Eleven women either rejected the cerclage or had to have this removed because of cutting out (5%). Five women had temporary retention of urine but subsequently voided satisfactorily to completion and with normal sensation. Three women developed amenorrhea and two dyspareunia. Ten women developed lymphocysts managed conservatively, but only four had mild lymphodema that was troublesome. Three women suffered from dyspareunia.

Most operative complications occurred during the early development period of the procedure. These included three women suffering ureteric damage and fistula, one women stained a bladder perforation, and one had damage to the external iliac artery requiring repair. Two further women required open surgery to deal with pelvic side wall haemorrhage.

Recurrent disease

Disease in eight women have thus far recurred, and five women have died. Most recurrences are expected within the first 12–18 months, but with this procedure recurrence varies between 4 and 90 months. Recurrences have been local at the vaginal vault, locoregional in the pelvic para-cervical or side wall tissues, or distal in the para-aortic region. One patient developed recurrence of an adenocarcinoma in a retained ovary, 9 years after radical trachelectomy. None of the recurrences had adverse prognostic factors requiring completion of treatment at the original time of surgery. All recurrences were treated with chemo-radiotherapy after diagnosis. The ovarian recurrence was excised by oophorectomy (Table 3).

Pregnancy outcome

A total of 120 women have become pregnant, and 69 live births have taken place. One woman had a stillbirth, which may have been prevented if earlier delivery after premature rupture to the

Table 2

Table 3

Complications of radical vaginal trachelectomy with a laparoscopic pelvic-lymph node dissection, including recurrence.

Recurrence and time detected	Eight women had disease recurrence: five of those had squamous cell carcimona (occurring at 4, 7, 18, 21 and 26 months) and three women had adenocarcinoma (occurring at 36, 51 and 90 months).
Isthmic stenosis	10
Temporary parasthesia	5
Retention of urine	6
Cerclage cut or expelled	10
Lymphocyst	10
Secondary haemorrhage	2
Ureteric damage or fistula	3
Uterine perforation	3
Laparotomy for pelvic haemorrhage	3
Bladder perforation	1

membranes had been advised. As far as it is known, 27 first-trimester spontaneous miscarriages have occurred, with 16 taking place in the second trimester. Two terminations have taken place, one for social reasons and the other for a congenital abnormality. One ectopic pregnancy has been reported (Table 4).

Delivery and risk of prematurity

All deliveries have been by planned classical caesarean section apart from one. As mentioned, this single case suffered from a near catastrophic haemorrhage owing to a transverse incision in the lower uterine tissues extending through the uterine vessels. It is mandatory that a vertical incision is undertaken to avoid this risk, which could be fatal.

A total of 26 women experienced spontaneous premature rupture of the membranes owing to ascending chorio-amniotis. Of these, 12 were significantly premature, less than 32 weeks. Most other pregnancies reached adequate fetal viability and underwent an elective caesarean section at 36–38 weeks. Thus far, all reported births, apart from the stillbirth, have resulted in normal developing children.

All women should be cautioned against the development of potential infection during pregnancy. Consideration should be given to either giving prophylactic antibiotics at 16 and 24 weeks of pregnancy, which seems to be the most vulnerable times for a membrane rupture or alternatively regular sterile swabs should be taken for culture.

Overall experience with trachelectomy

From my assessment of the literature and personal contact with other surgeons carrying out fertility-sparing surgery, about 900 radical vaginal tracheletomy procedures have been carried out,

Table 4

Pregnancy outcome: pregnancies among 208 women who were selected for radical trachelectomy.

Live births	69 in 50 women
Stillbirths	1 in 1 woman
Neonatal deaths	0 in 0 women
Miscarriages (occurring before 14 weeks)	27 in 21 women
Miscarriages (occurring at 14 weeks or after)	17 in 12 women
Terminations	2 in 2 women
Ectopic pregnancy	1 woman
Ongoing pregnancy	1 woman
Surrogate live birth	2 women
Total pregnancies	120

with 370 pregnancies and 215 live births; 15% of these pregnancies have been premature. Disease in 37 women has recurred, and 18 women have died. This represents a similar recurrence and death rate to our experience as discussed above.

About 200 abdominal trachelectomy procedures have been reported with fewer pregnancies (n = 35), resulting in 21 live births. Only one has been reported as having been significantly premature. Two had disease recurrence, but these data are most probably incomplete as they were not fully reported.

Although experience, therefore, is greater with the vaginal procedure, figures for the abdominal operation are too small to make satisfactory comparisons.

Conclusion

With earlier detection of invasive cervical cancer, fertility preservation is increasingly needed, especially with childbearing being postponed at a time in many women's lives when cervical cancer is developing and becoming more common. Fertility preservation with conservation of the uterus after a radical trachelectomy seems to be a safe and realistic option for well-motivated women adamant that they wish to maintain their fertility options. Careful selection with MRI scanning for staging and sizing the tumour is essential. Small squamous cell lesions at the squamocolumnar junction may be excised, with adequate clear margins retained if possible between 0.5 and 1 cm of a proximal endocervical stroma. This will reduce the risk of premature labour owing to spontaneous rupture of the membranes. Although individualisation is essential, as a general rule, tumours 2 cm or less are suitable for this procedure; however, under exceptional circumstances, larger tumours may be considered.

Recurrence rates are acceptably low, with no apparent difference between histological types or grade. Conception rates are pleasingly high, with infertility problems apparently not arising from the trachelectomy procedure itself. For women requiring assisted reproduction (other than those who develop a cervical stenosis), some have had causes coincidental to the cervical cancer and surgery has been required.

The isthmic cerclage does seem to be efficient, allowing most women to reach fetal viability and maturity. Delivery has to be by a low vertical classical caesarean section either at the onset of labour or electively at 36–38 weeks of pregnancy.

Those women who are not anxious to conserve their fertility but are unfortunate enough to develop a cervical cancer, are advised to undergo standard treatment by either radical hysterectomy, pelvicnode dissection or chemo-radiotherapy. In time, it is anticipated that an even more conservative approach may be taken to small-volume tumours but with lesser surgery and local excision by conisation, providing accurate and careful imaging is possible. When it is also feasible to image and assess microscopic lymph-node spread, then lymphadenectomy will be avoided.

Practice points

- Radical vaginal trachelectomy offers a realistic alternative to young women with early invasive cervical cancer who wish to conserve fertility.
- Careful selection for radical vaginal trachelectomy results in acceptable low recurrence rates while allowing high pregnancy rates.
- In considering fertility sparing surgery, careful localisation of the cervical tumour by MRI allows measurement of the tumour and likely clearance from the isthmus.
- Radical vaginal trachelectomy risks premature labour as a result of ascending chorioamnionitis and spontaneous rupture of membranes.
- After radical vaginal trachelectomy, delivery should be by a classical caesarian section at the onset of labour or electively at 36–38 weeks.

Research agenda

- Reducing radicality of surgery for small cervical tumours.
- The localisation of cervical tumours by endovaginal MRI.
- The avoidance of lymphadenectomy in early stage localised cervical cancer.
- The prediction and avoidance of premature rupture of the membranes after radical vaginal trachelectomy.
- The development of conservative sub-total trachelectomy may conserve the upper cervix and permit subsequent vaginal delivery.

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