



Case series

Less radical surgery for women with early stage cervical cancer: Our experience on radical vaginal trachelectomy and laparoscopic pelvic lymphadenectomy



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ABSTRACT

We report the use of radical vaginal trachelectomy (RVT) with pelvic laparoscopic lymphadenectomy (LPL) in patients with early stages cervical cancer (FIGO stage IA2-IB1). This is a case series prospectively collected over a 6-year period (2011–2017) at the Ipswich hospital, UK. Cases were compared to a group of women with a similar stage of cervical cancer, but treated with radical hysterectomy (RH) and pelvic lymphadenectomy (PL). A total of 19 patients (group 1) underwent RVT and LPL, and 51 (group 2) had RH and PL. We included: 5/19 (26%) stage IA2 and 14/19 (74%) stage IB1. Among those, we had: 12/19 (63%) cases of squamous cell carcinoma (SCC), 7/19 (37%) of adenocarcinoma. Mean hospital stay was 2.7 days (range 2–4) in group 1 versus 4.8 days (range 3–8) group 2 (p -value = 0.173). The complication rate was not statistically different between the two groups 4/19 (21%) and 7/51 (14%) (p -value 0.169). The mean follow-up period was 47.3 months (range 7–78) in both groups. There were no cases of recurrence in group 1 and 2/51 (4%) cases in group 2, but the difference was not significant (p -value = 0.497). In our experience RVT in well-selected patients is a safe treatment option with similar oncological outcomes when compared to patients undergoing more extensive surgery for the same early stage cervical cancer.

1. Introduction

Cervical cancer (CC) affects over half a million women worldwide yearly (Fidler et al., 2017). It is estimated that 25% of women are diagnosed before 40 years of age and among them 45% have a surgically treatable stage of CC at presentation (Kong et al., 2014). This has posed new challenges in the management of this disease and over the last 3 decades there has been a widespread use and demand for fertility-sparing surgery (FSS). CC spreads laterally to the parametrial tissue, inferiorly to the vagina and rarely superiorly to the uterine body or the fundus (Matsuo et al., 2017). Because of this, it is possible to maintain the fundus and adnexa in most small size cancers confined to the cervix and thus keep the possibility of future childbearing. The standard surgical treatment for early stage CC (Stage IA2-IB1) is radical hysterectomy (RH), which has good results, but inevitably renders the women infertile (Brucker and Ulrich, 2016). In 1987, Daniel Dargent et al. advocated a method of radical trachelectomy (RT) combined to pelvic lymphadenectomy (PL) to treat selected cases of early CC and reported 95 patients having the procedure with an overall recurrence rate of 4% and 3% death rate (Dargent et al., 1994; Dargent, 2000). Since then

there have been published > 900 cases with a recurrence rate between 1 and 7% and a death rate between 1 and 3%, which are comparable to RH (Macdonald and Tidy, 2016).

We are in an era where surgical treatment for gynecologic cancers emphasizes: minimal invasiveness, reduction of postoperative morbidity and preservation of function. In light of this, we question why the surgical management of selected patients with early stage CC could not also be an example of a less extensive surgical philosophy. We therefore want to add weight to the evidence regarding the safety of less radical surgery in early stage CC by using the oncological outcomes from our cohort.

2. Materials and methods

We report our case series of patients who underwent RVT with PL from October 2011 to December 2017 at the Gynecologic Oncology department of the Ipswich hospital. Data have been recorded prospectively. Eligible criteria to perform the procedure were: women with early-stage CC (Stage A2-IB), absence of radiologic evidence of lymph node metastasis and a strong desire to preserve fertility. Stage of disease

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and grading were assessed using the International Federation of Obstetrics and Gynaecology (FIGO) system, and histological subtypes were reported according to the World Health Organization system. Patients with adenosquamous histology were grouped with the adenocarcinomas. Lymphovascular space involvement was defined as the presence of malignant cells in endothelial lined spaces seen on histologic examination of the radical trachelectomy specimen or cone biopsy or large excision of transformation zone (LLETZ). Post-operative complications included were graded using the Clavien-Dindo classification (Katayama et al., 2016). This group of patients who underwent RVT + LPL was called “group 1” and were compared with “group 2” which included women with stage IA/IB and negative pelvic lymph nodes who had RH and PL (this procedure was performed by laparotomy in all the patients). At the preoperative assessment, we include: careful counseling, formal staging by examination under anaesthetic (EUA), magnetic resonance imaging (MRI) of the pelvis and review of the slides from either a diagnostic cone biopsy or a LLETZ before the procedure. The length of the cervix and the depth of the uterine cavity were measured carefully both at EUA and MRI to ensure that the correct amount of tissue was removed at surgery.

We performed RVT and LPL as described by Sheperd's group (Shepherd et al., 1998; Shepherd and Oram, 2001). Post-operatively, we leave a size 12 Foley's catheter in the isthmus with the balloon inflated for retention with 3mls of water. This catheter is left in situ for 2 days to prevent synechiae and isthmus stenosis. After surgery, women were reviewed in colposcopy clinic at 6 and 18 months and with a pelvic MRI scan at 6, 12 and 24 months. At each follow-up appointment, complications were recorded, and vaginal vault and isthmic smears were taken using a spatula and endocervical brush. Women were asked to use contraception for 6 months after the surgery.

Patients' characteristics were reported with descriptive statistics and Fisher's exact test by using PrismV5 was used to compare group 1 and 2. Statistical significance was defined as $P < 0.05$. Consent to publish surgical outcomes was obtained by the patients prospectively.

3. Results

We included 19 patients with early stage CC (stage IA2-IB1), who underwent RVT and LPL to preserve fertility. Mean age was 28.5 (range 24–35). Among those 5/19 (26%) were stage IA2 and 14/19 (74%) were stage IB1. We had 12/19 (63%) cases of squamous cell carcinoma (SCC), and 7/19 (37%) with adenocarcinoma. We had 5/19 (26%) with grade 1, 6/19 (32%) patients with grade 2 and 8/19 (42%) with grade 3 cervical cancer. No patients were found with positive pelvic lymph nodes, and 3/19 (16%) patients had a lymph-vascular invasion. The tumour was ≤ 2 cm in 18/19 (95%) patients. Demographic and histological characteristics for group 1 and group 2 are summarized in Table 1. No residual disease at the specimen after the RVT was found in 18/19 (95%) patients. The average hospital stay was 2.7 (range 2–4 days). The mean estimated blood loss was 181.6 (range 100–300). Mean follow-up period was 47.3 months (range 7–78). There were no cases of recurrence in the 15/19 (78%) patients among the all cohort, who have been followed-up for 3 years. There were no intraoperative complications. Post-operative complications were present in 4/19 (21%) patients: 1/19 had a vesico-vaginal fistula, 1/19 complained of dyspareunia and developed vaginal infection 12 days after the operation, 1/19 stenosis of the isthmus which caused hematometra seven months post-surgery and 1/19 had the cervical stitch interfering with intercourse. Additional surgical procedures were, therefore, necessary in 2/19 cases, one because stenosis of the cervix, which was treated successfully by dilatation, another patient had a vesicovaginal fistula, which was successfully repaired surgically. Only 1/19 (5%) conceived after in-vitro fertilization treatment (IVF), 3/19 (25%) patients are undergoing IVF and the others are trying to conceive by spontaneous conception.

In group 2 we had 51 patients with similar early CC (Stage IA2-IB1)

Table 1
Demographic and histological characteristics patients in group 1.

	RVT+ LPL	RH
Age, Mean (range)	28.5 (24–35)	29.5 (25–40)
Histological type, n (%)		
Squamous	12/19 (63%)	40/51 (78%)
Adenocarcinoma	7/19 (37%)	10/51 (20%)
Others [†]	none	1/51 (2%) [†]
Stage, n (%)		
IA2	5/19 (26%)	17/51 (33%)
IB1	14/19 (74%)	34/51 (67%)
Grade, n (%)		
Well (Grade 1)	5/19 (26%)	10/51 (20%)
Moderate (Grade 2)	6/19 (31%)	22/51 (43%)
Poor (Grade 3)	8/19 (42%)	19/51 (37%)
LVSI [#]		
Yes	3/19 (16%)	12/51 (23%)
No	16/19 (84%)	39/51 (76%)
Tumour dimension		
≤ 2 cms	18/19 (95%)	15/51 (29%)
≥ 2 cms	1/19 (5%)	36/51 (71%)

RVT = Radical Vaginal Trachelectomy. RH = Radical hysterectomy.

LPL = laparoscopic pelvic lymphadenectomy #LVSI = Lymphovascular space invasion +Others: basaloid cervical cancer.

to group 1, but treated with RH and PL. We had 40/51 (78%) with SCC, 10/51 (20%) adenocarcinomas and 1/51 (2%) basaloid cervical cancer. LVSI was present in 12/51 (23%) patients. All characteristics for group 2 are reported in Table 1. Mean EBL was 547.9 (range 300–2000), which was more than the one found in group 1, however, the difference was not statistically significant (p -value 0.296). Mean in-patients hospital stay was 4.8 days (range 3–8 days). We had 1/51 (2%) patient who had ureter damage intra-operatively and 6/51 (12%) postoperative complications including: 2/51 (4%) had dyspareunia, 2/51 (4%) temporary leg numbness, 1/51 (2%) supra-pubic chronic pain and 1/51 (2%) vesico-vaginal fistula. However, the difference in complications rate between the two groups was not statistically significant (p -value 0.413). A residual tumour in the final specimen was present in 34/51 (67%) (see Table 2).

4. Discussion

Our data supports the consideration of less radical surgery in selected patients with early stage CC desiring FSS. In some cases after a large diagnostic cone biopsy or LLETZ, no residual tumour can be found in the final specimen and it could be argued that a hysterectomy may be an over-treatment. It has been reported about 31% (Lee et al., 2018) of patients with stage IA2-IB with parametrial involvement and therefore potentially 70% of patients are exposed to more extensive surgery with no therapeutic advantage. Thus, it is time to re-evaluate the need to remove the whole uterus for early stage CC and to define algorithms including clinical and pathological characteristics to help in patient selection for less radical surgery. It is also challenging to organise randomized trials in this context due to a small population of women eligible to undergo this type of FSS. In addition, there are few surgeons trained to perform this procedure and as consequence a lack of large

Table 2
Differences in surgical outcomes between group 1 and group 2.

	RVT + LPL	RH + PL	P-Value
Total complications rate	4/19 (21%)	7/51 (14%)	0.413
Mean EBL (mls) (range)	181.6 (100–300)	547.9 (300–2000)	0.296
Mean inpatient hospital stay (Days) (range)	2.7 (2–4)	4.8 (3–8)	0.173
Residual tumour after surgery	18/19 (95%)	34/51 (67%)	0.500
Recurrence rate	0/19 (0%)	2/51 (4%)	0.497

series to identify differences in recurrence. We do not exclude patients with tumour size more than 2cms. We agree with authors reporting that the incidence of parametrial involvement in women with a tumour size of < 2 cm is 0.6%, but it increases with larger cancer size (Boyras et al., 2016). Other clinicians have also suggested that infiltration of less than half of the cervical stroma is the limit for a safe trachelectomy (Bentivegna et al., 2016). However, deep stromal invasion and LVSI may not be reliably obtained pre-operatively, and this is one of the reasons why RH is still considered the gold standard. We, therefore, advocate a careful histopathological review of the sample obtained before planning the surgery to be able to assess as accurately as possible histology type of CC, depth of invasion and LVSI. During the surgical procedure, we aim to transect the cervix about 1 cm above the endocervical tumour margin and a maximum of 1 cm caudally from the internal cervical os, and we recommend the use of adjuvant therapy or more radical surgery if free margins are < 8–10 mm (Shepherd and Oram, 2001).

We had no intraoperative complications in our RVT, and this is less when compared to other centres reporting complication rates of 4%. However, we had a similar to other centres post-operative complication rate of 14% (Bentivegna et al., 2016; Churchill et al., 2015). We reported a higher EBL and inpatient stay in group 2, which was however not statistically significant when compared to group 1 (p -value 0.173 and 0.296 respectively). We had one patient in group 1, who presented with severe pain six months post-operatively and on pelvic ultrasound scan demonstrated a haematometra, which required dilatation of a stenotic isthmus under general anaesthesia. The problem of complete isthmic stenosis has already been previously reported. Our findings are in agreement with other authors (Shepherd and Oram, 2001), and we do not advocate hysterectomy following completion of a family. We did not have any recurrences or deaths in group 1 over a mean period follow-up of 47.3 (range 7–78). We acknowledge that in our cohort we had a higher percentage of residual tumour in the specimen in group 2 when compared to group 1 (p -value = 0.500), which may suggest strict criteria of inclusion in our centre for FSS. However, with more cases of FSS and from different centres, it will become easier to have more statistically significant data and longer follow-up to support the use of less invasive surgery for early stages CC and to define criteria of inclusion for this surgery.

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Authors' contributions

IR performed data collection, analysis and wrote the first draft of the manuscript. WM, RN, MN, BR contributed to the editing and approval of the final version of the manuscript.

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