*Case Series*

Oncologic and Fertility Outcomes Following Radical Trachelectomy in Early-Stage Cervical Cancer: Insights from a Single-Institution in Malaysia

ABSTRACT

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| **Aims:** Radical trachelectomy is a fertility-preserving surgical option for early-stage cervical cancer. It remains an uncommon choice among women, with limited cases reported in Malaysia. This case series explores the fertility and oncologic outcomes of radical trachelectomy in managing early cervical cancer among women of reproductive age in our institution.**Study design:** We retrospectively evaluated five patients who underwent abdominal radical trachelectomy in National Cancer Institute, Putrajaya for a median follow-up period of 3 years. **Place and Duration of Study:** Department of Gynecology Oncology at National Cancer Institute, Putrajaya Malaysia between January 2016 and December 2023. **Methodology:** The medical records of all patients who underwent abdominal radical trachelectomy at National Cancer Institute, Putrajaya Malaysia were reviewed. Data were obtained from medical and pathologic records. Data collected included age, parity, stage, preoperative tissue diagnosis, tumor size, evidence of lymph vascular space invasion, estimated blood loss, margin, final histopathology report, surgical complication, obstetric outcome and additional chemoradiotherapy treatment. **Results:** A total of 104 new patients were diagnosed with early cervical cancer. During this period, 99 radical hysterectomies and five radical trachelectomies were performed. The patients’ ages ranged from 27 to 40 years old. The median estimated blood loss was 400mL, median surgical time was 320 min and median length of hospitalization was 5 days. The oncological outcomes varied among the patients. Four out of five patients survived and remain disease-free, while one experienced recurrence, requiring debulking surgery and additional chemoradiation therapy. Reported complications included cervical stenosis, pseudocyst formation and wound breakdown, all of which were manageable without long-term effects. Notably, three patients achieved pregnancy, although only one resulted in a live birth.  |

*Keywords: Cervical Cancer, radical trachelectomy, fertility*

1. INTRODUCTION

Cervical cancer ranks as the sixth most common cancer among females in Malaysia based on the Summary of the Malaysian National Cancer Registry report 2017 to 2021 (National Cancer Registry Department, 2024). The age-standardized incidence rate (ASR) of cervical cancer in Malaysia from 2017 to 2021 was 6.0, showing only a slight decrease compared to the rate of 6.2 in the previous years (2012-2016), despite the presence of available national screening programmes (National Cancer Registry Department, 2024). Several women diagnosed with cervical cancer have not completed their childbearing (Pareja et al, 2008). The number of women seeking fertility-preserving treatment options is steadily arising, driven by the increasing average of childbirth-age in Malaysia (Vital Statistics, 2022). In Malaysia, the age- standardized incidence rate (ASR) for individuals of reproductive age diagnosed with cervical cancer ranges between 0.1 to 5.9 (National Cancer Registry Department, 2024).

Early detection greatly improves the 5-year survival rate for cervical cancer. Various preventive strategies and treatment protocols were implemented to eliminate cervical cancer, and all countries must reach and maintain an incidence rate below 4 per 100 000 women as recommended by World Health Organization (WHO) (Noor et al, 2024). In Malaysia effective screening methods, such as HPV testing, cytology, and colposcopy, have been part of the national health program since 1969 and play a vital role in the early detection of cervical cancer (Noor et al, 2024). Early cervical cancer traditionally managed surgically by radical hysterectomy and pelvic lymphadenectomy. Increasing evidence in the literature suggests that radical trachelectomy is another viable option with satisfactory oncologic and obstetrical outcomes for women who wish to preserve their fertility (Yoshino et al, 2020; Smith et al, 2020; Chen et al, 2022; Siegler et al, 2024). Radical trachelectomy can be performed through a vaginal, abdominal, laparoscopic, or robotic approach and combined with open or laparoscopic pelvic lymph node dissection (Wu et al,2017).

The first report of radical vaginal trachelectomy was documented by Daniel Dargent in 1994 (Vo et al, 2024). Currently the National Comprehensive Cancer Network guidelines suggest that radical trachelectomy is a treatment option for selected women with early-stage cervical cancers (Stage 1A2 to 1B2) (NCCN, 2024). Surgeon should adhered with strict patient selection criteria to balance surgical safety with potential risk of morbidity to the patient.

The oncological outcomes following radical trachelectomy in early cervical cancer are good (Kohler et al, 2024). Majority of centres showed low recurrence and death rates ranging from 0-6.8% and 0-5.2% respectively (Kohler et al, 2024). Given the low recurrence and death rate, there is substantial potential for women of childbearing age to conceive. Studies showed that radical trachelectomy is associated with a favourable pregnancy rate and live birth rate, making it an important consideration for young women diagnosed with early cervical cancer (Kohler et al, 2024).

The option of fertility preservation for women with operable cervical cancer remains uncommon, with no reported cases in Malaysia. The availability of opportunities and skilled surgeons is another significant challenge, as cases of radical trachelectomy are rare and there are limited numbers of surgeons with the required expertise. The goal of this study was to explore the fertility and oncologic outcomes in a series of patients who underwent radical trachelectomy for early-stage cervical cancer at National Cancer Institute, Putrajaya, Malaysia.

2. Methodology

**2.1 Study population**

The medical records of all patients who underwent abdominal radical trachelectomy at National Cancer Institute, Putrajaya Malaysia between January 2016 and December 2023, were reviewed. Approval from the institutional review board was obtained prior to data collection. Data were obtained from medical and pathologic records. Data collected included age, parity, stage, preoperative tissue diagnosis, tumour size, evidence of lymph vascular space invasion, estimated blood loss, margin, final histopathology report, complication, obstetric outcome and additional chemoradiotherapy treatment.

**2.2 Eligibility Criteria**

Patient were considered eligible if they met the criteria for radical trachelectomy. These included a confirmed diagnosis of cervical cancer and desire for future fertility preservation. Patients were informed that radical hysterectomy remains the standard treatment for women with early cervical cancer.

**2.3 Surgical techniques for Abdominal Radical trachelectomy**

The radical trachelectomy procedure was similar in part to abdominal radical hysterectomy. A midline laparotomy was performed. Uterus was exposed and bilateral pelvic lymph nodes was dissected first. After the development of pararectal and paravesical spaces, bilateral parametria were exposed. The ureters are then dissected bilaterally until insertion in the bladder with lateral mobilization. The uterine arteries were kept intact bilaterally. The rectovaginal space was exposed, cardinal and the uterosacral ligaments were resected. The cervix was cut at the level of isthmus including 2 cm of upper vagina. The specimen is sent for frozen section evaluation to ensure at least 5mm margin is free of tumour. If the evaluation revealed a positive margin, patients would proceed with radical hysterectomy. A cerclage was place in all patients using a permanent sutured tied in the posterior aspect of the uterus. Intrauterine Copper Device was inserted in all patients except one (Table 1, patient 1). Finally, the vaginal cuff sutured with the lower uterine segment with 1-0 synthetic absorbable surgical suture. The abdominal wall is then closed after hemostatic secured.

**2.4 Follow-up**

Postoperative follow-up was conducted 2 weeks after surgery. The complete histopathological report was reviewed during this visit. Concurrent chemoradiotherapy was offered to patients with lymph vascular invasion, positive lymph nodes, high-grade tumour or positive surgical margin. Follow-up visits were then scheduled every three months for the first 2 years and every 6 months for the subsequent 5 years. These follow-ups included pelvic examinations, pelvic ultrasounds and smear. Each patient was allowed to attempt to become pregnant if there was no evidence of residual or recurrent disease after 12 months follow-up.

3. results

 Between January 2016 and December 2023, a total of 104 new patients were diagnosed with early cervical cancer and underwent operation at the National Cancer Institute Putrajaya. During this period, 99 radical hysterectomies and five radical trachelectomies were performed. In our case series, Table 1 showed the patients characteristic and outcomes. The patients’ ages ranged from 27 to 40 years old. Preoperatively, as defined by the International Federation of Gynaecology and Obstetrics (FIGO) stages, four patients had stage 1B1 and one had Stage 1A2. Three patients were diagnosed preoperatively with squamous cell carcinoma, while two were diagnosed with adenocarcinoma. Four patients were diagnosed through cervical conization, and one was diagnosed via colposcopically directed biopsy.

**Table 1. Patient characteristics and outcomes**

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| --- | --- | --- | --- | --- | --- |
| **Particular**  | **Patient 1**  | **Patient 2** | **Patient 3** | **Patient 4** | **Patient 5** |
| Age  | 28  | 36  | 40  | 27  | 35 |
| Parity  | 1 | 2 | Nulliparous  | 1 | Nulliparous  |
| Clinical stage  | 1B1  | 1A2 | 1B1 | 1B1  | 1B1  |
| Pathologic stage  | 1B1  | 1A2 | 1A2 | 1B1 | 1B1 |
| Surgical time (min)  | 320  | 480  | 300  | 280 | 350  |
| Blood loss (mL)  | 200  | 1000 | 400  | 600  | 400  |
| Final HPE  | Squamous cell carcinoma | Squamous cell carcinoma | Squamous cell carcinoma | Large Cell Neuroendocrine  | Adenocarcinoma  |
| LVSI | Negative  | Negative  | Negative  | Positive  | Negative  |
| Positive LN  | 0 | 0 | 0 | 0 | 0 |
| Tumor Size (cm)  | 2 | 0.5 | 0.5 | 1.5 | 1.8 |
| Complication  | Cervical Stenosis  | Wound breakdown  | No | Pseudocyst  | No  |
| Follow-up (months)  | 36 | 36 | 36 | 28 | 24 |
| Attempt to conceive | Yes  | No | Yes  | No  | Yes  |
| Pregnancy outcome  | Miscarriage  |  | Miscarriage  |  | Live birth  |

In terms of intraoperative findings, the median estimated blood loss was 400 mL (range, 200 – 1000 mL). The median surgical time was 320 min (range, 280 – 480 min) and median length of hospitalization was 5 days (range 5 to 6 days). The median follow-up time was 36 months (range, 24 to 36). All specimens sent for frozen section analysis had clear margins. No lymph nodes involvement was identified in all patients from the final histology. However, one patient was found to have lymph vascular space invasion. All patients had tumours smaller than 2cm. The final histopathology results showed that four patients had well-differentiated squamous cell carcinoma while one patient was diagnosed with high-grade neuroendocrine carcinoma.

There was no intraoperative complication however, three patients develop postoperative complication. One patient developed a postoperative laparotomy wound breakdown, possibly due to prolong surgery, which lasted approximately 480 minutes. The patient was obese, but the wound was managed conservatively with daily dressing and primary healing (Table 1, patient 2). One patient develops cervical stenosis following radical trachelectomy, and the condition was successfully resolved after undergoing repeated cervical dilatations performed under regional anaesthesia (Table 1, patient 1).

Only one patient who underwent radical trachelectomy with pelvic lymph nodes dissection in year 2020 had recurrence after 18 months follow-up (Table 1, patient 4). She developed a pelvic collection two weeks after surgery, requiring diagnostic laparoscopy for a pseudocyst. Histopathology revealed high-grade neuroendocrine carcinoma, and she was referred for definitive surgery and chemoradiation therapy, but she declined. A follow-up ultrasound and computed tomography (CT) scan revealed a post-surgical collection, and her condition improved with medical treatment. She was regularly monitored as an outpatient after surgery. However, during her cancer surveillance, CT scan was performed showed local recurrence, lung metastasis, and regional lymphadenopathy. Local recurrence and distant metastasis was diagnosed. She agreed to undergo complete debulking surgery and recovered well, followed by concurrent chemoradiation therapy. However, CT imaging 3 months later showed disease progression evidence by worsening lung, liver and nodal metastasis. She received palliative care and passed away 6 months later.

 In our case series, three out of five patients attempted to conceive. Two of them had spontaneous abortion while one had a successful pregnancy. This patient (Table 1, patient 5) underwent In-vitro Fertilization treatment one year after surgery. She underwent an emergency midline classical caesarean section at 36 weeks of gestation in view of preterm prelabour rupture of membrane in the setting of an underlying cervical cerclage post-trachelectomy. During the operation, it was noted that the omentum was adhered to the anterior abdominal wall, the lower segment was not formed, and both tubes and ovaries appeared normal. She delivered successfully a baby girl weighing 1.87 kg with good Apgar Score.

**4. DISCUSSION**

This case series represents one of the first reported experiences of radical trachelectomy in Malaysia, highlighting both the oncological and obstetric outcomes in a highly selected group of early-stage cervical cancer. Out of 104 patients who underwent surgical treatment for early-stage cervical cancer between January 2016 and December 2023, only five were selected for radical trachelectomy, highlighting the careful patient selection criteria applied at our institution. Strict selection criteria such as tumour less than 2 cm and negative pelvic lymph nodes are associated with relapse and mortality rates of 4% and 2% respectively (Pareja et al, 2024).

The limited number of cases reflects the rarity of appropriate candidates, as well as the still-limited uptake of this procedure in our local practice. One of the contributing factors may be because approximately 76% of patients in Malaysia population are diagnosed at Stage 2, where radical surgery and chemoradiation therapy required (Faridah et al., 2019). The second National Health & Morbidity Survey (NHMS II) conducted in 1996 found that only 26% of eligible women underwent cervical cancer screening through Pap smears (Zakiah et al., 2019). By 2006, according to the NHMS III, this figure had increased to 43.7% (Zakiah et al., 2019). However, the NHMS 2011 revealed a significant drop, with only 12.8% of eligible women having had a Pap smear examination five years later (Zakiah et al., 2019). In response to this data, Malaysia implemented Liquid-Based Cytology (LBC) in 2014 to enhance coverage and support HPV testing, aiming to improve early detection and early intervention in cervical cancer (Zakiah et al., 2019).

All of our five patients met key eligibility criteria based on NCCN guideline for radical trachelectomy, including tumour size ≤2 cm, negative nodal status, and early FIGO stage (four Stage IB1 and one Stage IA2) (NCCN, 2024). Histologically, squamous cell carcinoma was the predominant subtype. One patient had high-grade neuroendocrine carcinoma, a histologic subtype typically associated with poor prognosis. The only recurrence in this series occurred in that patient, who developed local and distant metastases despite salvage therapy. This outcome supports existing literature that discourages fertility-sparing surgery in cases of neuroendocrine tumours due to their aggressive behaviour and higher risk of recurrence (Cibula et al., 2023). According to European guidelines, fertility-sparing treatment is not recommended for rare and aggressive histological subtypes of cervical cancers, such as neuroendocrine carcinomas, HPV-independent adenocarcinomas, and carcinosarcomas (Cibula et al., 2023). Neuroendocrine cervical carcinomas have a high tendency for nodal involvement and distant metastases, which aligns with our case, where a follow-up CT scan performed 18 months later revealed abdominal and pelvic lymphadenopathy with lung metastases (Salvo et al., 2019). According to updated management guidelines for neuroendocrine cervical cancer, the overall 5-year survival rate is approximately 36%, with a median overall survival ranging between 22 and 25 months (Salvo et al., 2019). Even though fertility-sparing surgery is not recommended for neuroendocrine cervical cancer based on current guidelines, our literature search identified a case report describing a successful pregnancy following radical trachelectomy, with the patient remaining disease-free after 24 months (Park et al., 2008). In our case series, the patient diagnosed with a neuroendocrine tumour was followed up for 28 months from the initial diagnosis, unfortunately she passed away thereafter.

Her case highlights the critical importance of a thorough histological assessment during the frozen section in the initial surgery (Table 1, Patient 4). The accuracy of frozen section on radical trachelectomy specimen is a significant factor to consider, especially in fertility-sparing surgery for cervical cancer. According to a study by Kay J Park in 2008, there was an 84% concordance between the frozen-section diagnosis and the final histological diagnosis when using histology alone (Li et al., 2015).

The surgical outcomes in our series were acceptable. The median operative time was 320 minutes, with a median estimated blood loss of 400 mL, which is consistent with other reports of laparotomy-based trachelectomy approaches (Chen et al., 2022; Wu et al., 2017). There were no intraoperative complications, although two patients experienced notable postoperative issues, wound breakdown and cervical stenosis, both managed conservatively.

In our initial case of radical trachelectomy, no intrauterine device (IUD) was inserted intraoperatively, and the patient subsequently developed cervical stenosis, necessitating twice cervical dilatation under regional anaesthesia. Based on this experience, we implemented routine IUD placement in subsequent patients, after which no further cases of cervical stenosis were observed. Although no standard guideline exists, some clinicians place devices in the cervical canal or uterine cavity to reduce the risk of cervical stenosis after surgery (Wang et al., 2020). In a systematic review of 1547 patients, such tools were used in 27.4% of cases, and their use was associated with a significantly lower incidence of cervical stenosis (4.6% vs. 12.7%) (Wang et al., 2020). Catheters were the most used tool followed by intrauterine devices (IUDs). The lowest rate of stenosis occurred with IUDs (Li et al., 2015).

Obstetric outcomes remain a key concern in fertility-sparing management. In our series, three out of five patients attempted conception postoperatively, resulting in one successful live birth via in vitro fertilization and two first-trimester miscarriages. The successful pregnancy required a classical caesarean section at 36 weeks due to preterm prelabour rupture of membranes. In our findings, the number of successful pregnancies was relatively low. Other studies report consistently high pregnancy rates following radical trachelectomy, ranging from 53% to 76% (Kohler et al., 2024).

Preserving the uterine artery in radical trachelectomy is a critical aspect that significantly impacts obstetric outcomes (Wang et al., 2020). By carefully preserving the vascular structure during the surgical procedure, the potential for maintaining adequate blood supply to the uterus is ensured. In our case series, surgeon meticulously preserve the uterine artery bilaterally during the radical trachelectomy procedure to ensure the optimal vascular supply to the uterus post-surgery.

4. Conclusion

In conclusion, the case series on radical trachelectomy for early cervical cancer in Malaysia highlights the significance of this surgical approach in preserving fertility while ensuring effective cancer treatment. Through the analysis of these cases, it is evident that radical trachelectomy emerges as a viable option for women desiring fertility preservation without compromising oncological outcomes. Continued research and long-term follow-up studies are essential to further validate the efficacy and safety of this procedure within the Malaysian context. Overall, the findings from this case series contribute valuable insights to the field of gynaecologic oncology and emphasize the importance of individualized treatment strategies in optimizing outcomes for women facing early cervical cancer diagnoses in Malaysia.

Consent

All authors declare that written informed consent was obtained from the patient and next of kin for publication of this case series. A copy of the written consent is available for review by the Editorial Board members of this journal.

Ethical approval

This study was registered under National Medical Research Register (NMRR) of Malaysia and was approved by the committee prior to the commencement of this study (NMRR ID-25-00878-4YG). Research ID (RSCH ID-25-00262-FPZ).

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Abbreviations

NCCN National Comprehensive Cancer Network

HPE Histopathology Examination

LVSI Lymph vascular invasion