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Association between timing of cervical excision procedure to minimally invasive hysterectomy and surgical complications☆

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HIGHLIGHTS

- Surgery within 6 weeks of cervical excision is associated with increased surgical morbidity.
- Radical surgery within 6 weeks of excision is associated with >2-fold risk of morbidity.
- Providers should consider delaying definitive surgery for 6 weeks after cervical excision.

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ABSTRACT

Objective. To determine if the time interval between excision procedure and definitive minimally invasive surgery (MIS) for cervical cancer impacts 30-day postoperative complications.

Methods. A retrospective cohort of patients diagnosed with cervical cancer from January 2000 to July 2015 was evaluated. Patients who underwent a cervical excision procedure followed by definitive MIS within 90 days were included. Early definitive surgery was defined as ≤6 weeks following excision procedure, while delayed was defined as 6 weeks to 3 months. The primary outcome was 30-day complications. Statistical analysis included descriptive statistics and modified Poission regression.

Results. Overall, 138 patients met inclusion criteria. Of these, 33% ($n = 46$) had early definitive surgery and 67% ($n = 92$) had delayed definitive surgery. Median age was 42 years (range 23–72 years) and median BMI was 28 kg/m^2 (range 16–50 kg/m^2). Within demographic and surgical factors collected, only smoking status differed between groups with those in the delayed surgery group more likely to be non-smokers than those in the early surgery group ($p = 0.04$). When adjusting for relevant demographic and surgical factors, patients in the early group were twice as likely to have 30-day complication (aRR 2.6, 95%CI 1.14–5.76, $p = 0.02$). Evaluating only women who underwent a radical procedure, 30-day complications remained higher in the early surgery group (RR 2.56; 95%CI 1.22–5.38, $p = 0.01$).

Conclusions. Performing definitive MIS for cervical cancer within 6 weeks after cervical excision is associated with increased risk for 30-day complications. Providers should consider delaying definitive surgical procedures for at least 6 weeks following excision to reduce surgical complications.

1. Introduction

Due to widespread use of cervical cancer screening, cervical cancer is often diagnosed at an early stage in the United States [1]. Following an abnormal screening pap test, a cervical excision procedure, such as a loop electrosurgical excision procedure (LEEP) or cold knife cone (CKC) is frequently used for diagnosis. After an excision procedure, women diagnosed with cervical cancer often go on to have definitive surgical therapy with either hysterectomy or trachelectomy.

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There is discrepancy in the literature regarding the appropriate timing of definitive surgery after an excision procedure. Initial investigations into the timing between excision procedure and definitive surgery suggested an increased risk of febrile morbidity when hysterectomy was performed within 10 days of a CKC [2]. This increased risk was suspected to be from infection present in the parametrial tissues following CKC and these authors suggested delaying hysterectomy for 4–6 weeks following CKC to reduce febrile morbidity. In the decades following this publication, several additional studies were published with similar findings [3–6]. Given that the parametria was thought to be the source of the infection, it was hypothesized that radical hysterectomy would not confer the same morbidity. Two investigations of radical hysterectomy after CKC found no difference in morbidity, regardless of timing interval [7–8].

The LEEP procedure was first described in the 1980s and has increased in use for diagnosis and treatment of cervical dysplasia [9]. Additionally, increasing use of minimally invasive surgery (MIS) and routine administration of pre-operative antibiotics have changed surgical practice since initial studies on the timing of definitive surgery were published. Data regarding timing of definitive surgery after excision procedure with these key treatment changes is limited [10–12]. Therefore, we sought to determine if the time interval between cervical excision procedure and definitive MIS treatment for cervical cancer impacts surgical complications.

2. Methods

2.1. Study design, setting, and participants

The STROBE guidelines were used in the design and reporting of this study [13]. Following institutional review board approval (#12-1603 on 6/19/2015), a retrospective cohort study of cervical cancer patients diagnosed from January 2000 to July 2015 was performed at The University of North Carolina at Chapel Hill (UNC), a single tertiary care center. There were seven gynecologic oncologists who performed radical hysterectomies at UNC during this time frame and the results of this study reflect a combination of patients and practice patterns from these providers. There was no standardized timing of hysterectomy at UNC during the study period.

Patients were identified for inclusion using the records of a weekly multidisciplinary disposition conference (tumor board). All patients diagnosed with cervical cancer and treated at our institution are presented at this conference, making this the most accurate way to identify all patients with cervical cancer. Patients were eligible for inclusion if they (1) had a diagnosis of cervical cancer, (2) underwent an excision procedure (either a CKC or LEEP), and (3) underwent definitive MIS procedure for treatment of cervical cancer within 90 days of CKC or LEEP. Types of definitive surgery included radical or simple hysterectomy, and radical or simple trachelectomy. Vaginal, laparoscopic, and robotic-assisted approaches were included. Patients were included if their definitive MIS was performed at UNC, however, their excision procedure could be performed at outside institution.

2.2. Variables and data sources

The primary outcome was 30-day surgical complication rate. Complications were chosen from published complications for hysterectomy after excision procedure. These were defined as intraoperative or post-operative gastrointestinal or genitourinary injury, cuff dehiscence, abscess, readmission, or fistula up to 30 days [10–12]. Our secondary outcome was late complications, defined as those occurring >30 days after definitive surgery.

Our exposure of interest was the interval between excision and definitive surgery. An a priori cut-off of 6 weeks was chosen based on previously published literature [3,10–12]. Thus, early definitive surgery was defined as less than or equal to 42 days (within 6 weeks) following excision procedure and delayed definitive surgery was 43 to 90 days (6 weeks to 3 months).

Data was abstracted from electronic medical records by four chart reviewers. After data was abstracted, 50% of charts were re-reviewed by another investigator to ensure accuracy and consistency. Abstracted demographic data included age, BMI, race, insurance status, smoking status, medical comorbidities, previous abdominal surgery, stage, and histology. Abstracted surgical data included type and date of excision procedure, mode, date and extent of definitive surgery, extent of lymphadenectomy, estimated blood loss (EBL), operative time, receipt of post-operative radiation, and 30-day surgical complications.

2.3. Study size and statistical analysis

This cohort represents a convenience sample and no de novo power calculation was performed. For our primary outcome of 30-day complications, there was no loss to follow up among this cohort. Care received at outside institutions and not reported at subsequent follow up visits cannot be accounted for. Descriptive statistics and modified Poisson regression were used for analysis. All statistical analysis were performed using Stata/IC 12.1 College Station, TX. All p-values at a value of <0.05 were considered statistically significant, and all p-values are two-sided.

3. Results

Overall, 138 patients met inclusion criteria. The median age was 41 years (range 23–72 years), median BMI was 28 kg/m^2 (range 16–50 kg/m^2), median operative time was 201 min (range 58–377 min), and median EBL was 50 ml (range 10–300 ml). The median time between excision and definitive surgery was 50 days (range 2–90 days). The distribution of surgical timing is displayed in Fig. 1.

Within our population, 46 (33%) patients had early definitive surgery and 92 (67%) patients had delayed surgery. The early surgery group had a median time to surgery of 35 days (range 2–42 days). The delayed surgery group had a median time to surgery of 56 days (range 43–90 days). There was no difference in age, BMI, race, insurance status, medical comorbidities, stage, previous abdominal surgery, and histology between the two groups. Smoking status did differ between the two groups with the delayed surgery group having relatively more non-smokers and current smokers than the early surgery group (75% and 21% versus 65% and 17%, respectively), while the early surgery group had more former smokers than the delayed surgery group (17% versus 4%, respectively), $p = 0.04$. Preoperative characteristics of the early surgery and delayed surgery group are summarized in Table 1. There was no difference in type of excision procedure, type of definitive surgery, radicality of procedure, extent of lymphadenectomy, EBL or operative time between groups. Of note, there were no para-aortic lymphadenectomies performed in this population. There was no difference in receipt of post-operative radiation for the early surgery group and late surgery group (20% versus 22%, $p = 0.83$). All radiation was initiated at least 30-days following the patients' definitive surgery date and thus would not affect short-term complications. CKC was the most commonly performed excision procedure in both groups, while robotic-assisted radical hysterectomy was the most commonly performed definitive surgery in both groups. Surgical characteristics between the early surgery and delayed surgery group are summarized in Table 2.

Overall, 18.8% (26/138) of patients experienced either a 30-day or late complication with 30% (14/46) in the early surgery group and 13% (12/92) in the delayed group ($p = 0.02$), see Table 3. There were no injuries identified intraoperatively in this cohort of patients. Patients in the early surgery group were twice as likely to have a 30-day complication (RR 2.0; 95%CI 1.02–4.00, $p = 0.02$). After adjusting for medical comorbidities, age, race, BMI, smoking status, type of excision, stage of disease, previous abdominal surgery, extent of lymphadenectomy, type of surgery, and histology, the relationship between timing of

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