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## Longer operative time is associated with increased post-operative complications in patients undergoing minimally-invasive surgery for endometrial cancer☆

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#### HIGHLIGHTS

- Longer OR time increases complications after surgery for endometrial cancer.
- · COPD, HTN, DM, ASA class, dependent status, and steroids are also risk factors.
- Lymphadenectomy does not increase OR time or complications.

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#### ABSTRACT

Objective. To examine the impact of operative time on the development of post-operative medical and surgical complications in patients undergoing minimally-invasive surgery for endometrial cancer.

Methods. Patients who underwent laparoscopic surgery for endometrial cancer from 2005 to 2014 were identified from the ACS-NSQIP database. Operative times were initially divided into hour-long intervals and complication rates were determined. Outcomes included development of any complication, medical complication, or surgical complication. Subsequent analysis were based on dividing patients into 2 groups based on operative times <240 min and operative times ≥240 min. Associations between categorical variables were determined using Chi-Squared and Fisher's exact tests. Differences between means of continuous variables were determined using Student's t-tests. Univariate and multivariate analysis using logistic regression were used to identify predictors of post-operative complications.

Results. 9145 patients were included, of which 639 (7%) experienced a complication. As operative time increased, rates of complications also increased. Operative time ≥240 min was associated with increased overall complication rate (11.7% vs. 6%, p < 0.001), medical complication rate (9.3% vs. 4.2%, p < 0.001), and surgical complication rate (3.9% vs. 2.4%, p = 0.001). When performing multi-variate logistic regression of factors associated with increased complication rates, increased operative time, COPD, hypertension, diabetes, ASA class ≥3, dependent functional status, and chronic steroid use were found to be independently associated with increased complications. Lymphadenectomy was not associated with increased operative time or increase in complications.

Conclusion. Increased operative time is independently associated with increased risk of developing complications after laparoscopic surgery for endometrial cancer.

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#### 1. Introduction

Endometrial cancer is the most commonly diagnosed gynecologic malignancy in the United States with an estimated 60,050 new cases diagnosed in 2016 [1]. Comprehensive surgical staging including total

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hysterectomy and bilateral salpingo-oophorectomy, along with pelvic and para-aortic lymphadenectomy in selected patients, remains the standard of care [2,3]. Since the 1990s, minimally invasive surgery (MIS) has slowly replaced traditional laparotomy as the preferred approach. A recent study based on SEER data noted an increase in the performance of minimally invasive hysterectomy for endometrial cancer from 9.3% in 2006 to 61.7% in 2011 [4]. Compared with laparotomy, MIS is associated with fewer post-operative complications, shorter postoperative recovery, and improved quality of life in patients with endometrial cancer [4-8].

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 Table 1

 Incidence of surgical and medical complications in all patients.

Surgical complications:	
Any surgical site infection	170 (1.9)
Superficial surgical site infection	67 (0.7)
Deep surgical site infection	17 (0.2)
Organ space surgical site infection	91 (1.0)
Wound disruption	15 (0.2)
Return to operating room	100 (1.1)
Medical complications:	
Pneumonia	29 (0.3)
Re-intubation	24 (0.3)
Failure to wean from ventilator	16 (0.2)
DVT	42 (0.5)
PE	29 (0.3)
Renal failure	7 (0.1)
UTI	187 (2.0)
Transfusion	163 (1.8)
Cardiac arrest	12 (0.1)
Sepsis or shock	66 (0.7)
Death	19 (0.2)

The literature is ripe with data regarding risk factors for complications in patients undergoing MIS. To date, many of these reports focus on hysterectomy and other procedures done for benign reasons. Obesity, age and medical co-morbidities are all cited as risk factors for both medical and surgical complications in the post-operative period [5,9]. Gunderson et al., in an ancillary review of the LAP2 data, reports that post-operative adverse events increase with incremental increases in BMI. This ancillary study, however, does not report on the surgical mode and length of surgery within the BMI subgroups [10].

With increasing utilization of MIS for endometrial cancer and nationwide focus on quality improvement in healthcare, it is essential to identify potentially modifiable risk factors for perioperative complications. To our knowledge, no study to date has analyzed operative time as an independent risk factor for post-operative complications in MIS for endometrial cancer.

#### 2. Materials and methods

We retrospectively reviewed data from the ACS-NSQIP for all patients undergoing minimally invasive surgery for endometrial cancer from 2005 to 2014. The institutional review board at MetroHealth Medical Center deemed use of this database as exempt from formal review due to its de-identified nature. Specific details of the data collection procedure and its verification methods can be found in the ACS-NSQIP user guide [11].

First, all patients with a diagnosis of endometrial cancer were identified by ICD-9 Code 182.0. Subsequently, we identified patients who underwent laparoscopic hysterectomy with or without removal of adnexal structures and with or without lymphadenectomy using relevant CPT codes. We excluded patients with missing operative time data.

Demographic and clinical characteristics of the patients were collected and included: age, body mass index (BMI), smoking status, and incidence of various medical conditions [chronic obstructive pulmonary disease (COPD), hypertension (HTN), diabetes (DM), dyspnea at baseline, congestive heart failure (CHF), and renal failure]. Use of steroids

for a chronic condition, ASA class, and dependent functional status assessment were also included. Whether a patient underwent lymphadenectomy at the time of hysterectomy was also recorded. As explained by the NSQIP Participant User File, operative time is defined as "total operation time in minutes" [11].

The primary outcome of this study was the development of any complication (medical or surgical) after surgery and how this related to length of surgery. Surgical and medical complications were also assessed separately. Surgical complications included: surgical site infection (SSI) (including superficial SSI, deep SSI, and organ space SSI), wound disruption, and need for re-operation. Medical complications included: pneumonia, re-intubation, failure to wean from ventilator, deep vein thrombosis (DVT), pulmonary embolism (PE), renal failure, urinary tract infection (UTI), need for blood transfusion, cardiac arrest, sepsis or shock, and death. Detailed definitions of these complications can be found in the ACS-NSQIP user guide [11].

To initially compare the relationship between length of operation and incidence of complications, surgery time was divided into hour long intervals as follows:  $\leq$ 119 min, 120 to 179 min, 180 to 239 min, 240 to 299 min, and  $\geq$ 300 min. Subsequent analysis were based on dividing patients into 2 groups: those with operative times <240 min and those with operative times  $\geq$ 240 min. Statistical analysis was performed using SPSS v. 22.0 (IBM, Chicago, IL). Associations between categorical variables were determined using Chi-Squared and Fisher's exact tests. Differences between means of continuous variables were determined using Student's *t*-tests. Univariate and multivariate analysis using logistic regression were used to identify predictors of post-operative complications. An  $\alpha$ -level of 0.05 was considered statistically significant.

#### 3. Results

We identified a total of 9145 patients from the ACS-NSQIP database who underwent laparoscopic surgery for endometrial cancer. Twelve patients were excluded due to missing operative time. The mean length of operation for all patients was  $173.3\pm73.4$  min. A total of 639 (7%) of patients experienced a post-operative complication. Of these, 246 patients (2.7%) had a surgical complication and 469 (5.1%) had a medical complication. A total of 100 (1.1%) patients required a re-operation and 19 (0.2%) patients had a post-operative death. The incidence of all medical and surgical complications for the entire cohort is shown in Table 1.

When broken down by length of operation, 2190 (23.9%) patients had operations lasting  $\leq$ 119 min, 3321 (36.3%) patients had operations lasting between 120 and 179 min, 2089 (22.8%) patients had operations lasting between 180 and 239 min, 1034 (11.3%) had operations lasting between 240 and 299 min, and 511 (5.6%) had operations lasting  $\geq$ 300 min. Table 2 shows the relationship between operative time as divided in the above time intervals and the incidence of overall complications, surgical complications, medical complications, and need for reoperation. When examining the data, we observed a major increase in complications that occurred at the time interval of surgeries lasting 240 min or greater. Therefore, further statistical analyses were performed with the patients divided into 2 groups: those with operative times  $\leq$ 240 min and those with operative times  $\geq$ 240 min.

A total of 7600 patients had surgeries with operative times of <240 min and 1545 patients had surgeries with operative times of

**Table 2**Rates of complications and need for re-operation based on operative time intervals.

	≤119 min (n = 2190)	120–179 min (n = 3321)	180–239 min (n = 2089)	240–299 min (n = 1034)	≥300 min (n = 511)
Any complication	109 (5%)	191 (5.8%)	159 (7.6%)	110 (10.6%)	70 (13.7%)
Surgical complication	47 (2.1%)	73 (2.2%)	65 (3.1%)	39 (3.8%)	22 (4.3%)
Medical complication	76 (3.5%)	136 (4.1%)	113 (5.4%)	84 (8.1%)	60 (11.7%)
Re-operation	24 (1.1%)	27 (0.8%)	24 (1.1%)	18 (1.7%)	7 (1.4%)

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