

# Surgical site infection in patients with endometrial cancer undergoing open surgery

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## Summary

**Purpose:** Women with endometrial cancer have several risk factors for surgical site infection (SSI). The objective of this study was to determine the incidence of, and risk factors for, SSIs in endometrial carcinoma. **Materials and Methods:** Women with endometrial cancer who underwent primary open surgery at this institute between 2012 and 2014 were analyzed. Patients with and without SSI were compared. **Results:** Of all 107 patients, ten (9.3%) were diagnosed with SSI. Univariate analyses assessed age, BMI, diabetes mellitus, hypertension, postoperative body temperature, and serum albumin level as potential risk factors. There was no significant correlation between the mode of lymph node surgery and the occurrence of SSI. Multivariate analysis indicated that BMI was independently associated with a higher risk for SSI. **Conclusions:** Of all the tested, obesity exhibited the most significant risk factor for SSI in patients with endometrial cancer undergoing open surgery.

**Key words:** Endometrial cancer; Surgical site infection; Open surgery; BMI; Risk factor.

## Introduction

Surgical site infection (SSI) places a significant burden on healthcare expenditures by prolonging hospital stay, while also increasing the need for additional medications and procedures to treat the infection and associated morbidities [1-3]. SSIs comprise incisional and organ/space infections. Incisional infections are further divided into superficial and deep incisional infections. Organ/space infections are composed of pelvic cellulitis, pelvic abscess, and vaginal cuff infections [4].

In case of endometrial cancer, besides total hysterectomy and bilateral salpingo-oophorectomy, lymphadenectomy can increase the risk for SSI due to excessive tissue trauma and prolongation of the operative time [5, 6]. Patients with endometrial cancer are often elderly; this reportedly increases postoperative complications and mortality after surgery [7]. Furthermore, women with endometrial cancer tend to be obese, and the prevalence of diabetes mellitus is high in them even in the absence of obesity [8]. A systematic review on various surgery types showed that obesity and diabetes had a significant association with SSI [9].

Thus, women with endometrial cancer have several risk factors for SSI. Considering the morbidity and increased costs associated with SSI, identification of risk factors for SSI is important. So far, risk factors for SSI in patients with endometrial cancer in this institute remain unknown. Therefore, the objective of this study was to determine the inci-

dence of, and risk factors for, SSIs in endometrial cancer patients undergoing open surgery in this institute.

## Materials and Methods

Women with histologically verified endometrial cancer who underwent primary open surgery at the University of the Ryukyus Hospital between January 2012 and December 2014 were retrospectively analyzed. Perioperative laboratory data were collected from medical charts. This retrospective study was conducted according to the principles stated in the 1964 Declaration of Helsinki with subsequent revisions and was approved by the Institutional Review Board of this university on August 12, 2016 (#980).

All patients except one underwent total abdominal hysterectomy; radical hysterectomy was performed for the remaining one patient who had cervical invasion of the cancer. Modes of lymphadenectomy at this institution are as follows: pelvic lymph node sampling for patients with Stage IA, grades 1 and 2 with no or minimum myometrial invasion, pelvic lymphadenectomy for patients with intermediate risk for lymph node metastasis, and para-aortic lymphadenectomy selectively in patients with the highest risk for lymph node metastasis. These are assessed using preoperative magnetic resonance imaging and computed tomography along with endometrial biopsy.

As the antibiotic prophylaxis for the surgery, 1.0 g cefazolin was intravenously administered 30 minutes before the abdominal incision. The prophylaxis was repeated every three hours for a prolonged surgery. Preoperative skin and vaginal preparations were performed using povidone-iodine. SSI was defined as an infection at the site of surgery within 30 days of the surgery. Patients with and without SSI were compared using  $\chi^2$  test or Fisher's exact test for categorical variables and Mann-Whitney

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Table 1. — Patient characteristics (n = 107).

Age (years), median (range)	55 (24-83)
FIGO 2009 staging classification, n (%)	
IA	68 (63.6%)
IB	12 (11.2%)
II	11 (10.3%)
III	9 (8.4%)
IVB	7 (6.5%)
Tumor histology, n (%)	
Endometrioid	94 (87.9%)
Adenosquamous	2 (1.9%)
Serous	5 (4.7%)
Mucinous	1 (0.9%)
Carcinosarcoma	5 (4.7%)
Mode of lymphadenectomy, n (%)	
None	1 (0.9%)
Pelvic lymph node sampling	51 (47.7%)
Pelvic lymphadenectomy	36 (33.6%)
Pelvic and para-aortic lymphadenectomy	19 (17.8%)
Body mass index (kg/m <sup>2</sup> ), median (range)	25.8 (14.9-49.3)
Diabetes, n (%)	16 (15.0%)
Hypertension, n (%)	42 (39.3%)
Current smokers, n (%)	4 (3.7%)
Respiratory disease*, n (%)	12 (11.2%)
Neurological risk**, n (%)	4 (3.7%)
Operative time (min), median (range)	212 (102—600)
Total blood loss (ml), median (range)	425 (20—1871)

FIGO 2009 staging classification; endometrial cancer staging classification in 2009 defined by the International Federation of Gynecology and Obstetrics.

\*Respiratory disease; chronic obstructive pulmonary disease, ventilator dependent, dyspnea, and pneumonia. \*\*Neurologic risk factors; history of stroke with or without residual deficit, transient ischemic attack, hemiplegia, paraplegia, quadriplegia, or impaired sensorium.

U-test for continuous variables. Factors identified as potential risk factors in unadjusted analyses ( $p < 0.30$ ) were used in multiple logistic regression analysis for incisional SSI. Significance was set at  $p < 0.05$ . All statistical analyses were performed using JMP software version 10.0.

## Results

This retrospective study included 107 women with endometrial cancer. The clinicopathological characteristics of the patients are shown in Table 1. The median age was 55 (range, 24–83) years and median body mass index (BMI) was 25.8 (range, 14.9–49.3) kg/m<sup>2</sup>. Of all the patients, 106 underwent total abdominal hysterectomy and radical hysterectomy was performed for the remaining one patient with cervical invasion of the cancer. Regarding mode of lymph node surgery, pelvic and para-aortic lymphadenectomies were performed in 19 patients (median operative time, 233 minutes; range, 127–492 minutes); pelvic lymphadenectomy in 36 patients (median operative time, 238 minutes; range, 129–600 minutes), and pelvic lymph node sampling in 51 patients (median operative time, 201 minutes; range, 102–576 minutes). There was no significant difference in the operative time. Of all the patients, ten

(9.3%) were diagnosed as having SSI, and it was categorized as superficial incisional SSI in all ten of them. Univariate analyses found age  $\geq 50$  years, BMI  $\geq 30$  kg/m<sup>2</sup>, diabetes mellitus, hypertension, postoperative body temperature  $\geq 38.0^\circ\text{C}$ , and serum albumin level  $\leq 4.0$  g/dL to be potential risk factors (Table 2). There was no significant correlation between the mode of lymph node surgery and the occurrence of SSI (OR; 0.68, 95% CI 0.18–2.56,  $p = 0.743$ ). Multivariate logistic regression analysis indicated that BMI was independently associated with a higher risk for SSI (Table 3).

## Discussion

In this study, SSI occurred in ten (9.3%) patients with endometrial cancer who underwent surgery at this institute. Multivariate analysis identified only obesity as an independent risk factor for SSI in this group of women. The incidence of SSI in this study was almost the same as that reported previously (7.1%–8.8%) [7, 8, 10].

Obesity significantly influences the risk for gynecologic and obstetrical SSI, specifically in patients with a BMI of  $\geq 30$  kg/m<sup>2</sup>, which is consistent with the present results, or with depth of subcutaneous tissue  $\geq 2$  cm [11]. Giugale *et al.* assessed the impact of obesity severity on hysterectomy outcomes for uterine hyperplasia/cancer and concluded that surgical complications, including SSI, significantly increased as obesity severity, indicated by its classification, increased (BMI  $\geq 30$  vs.  $\geq 40$  vs.  $\geq 50$  kg/m<sup>2</sup>) [12]. Surgery in obese women is technically difficult and gynecologic oncologists frequently perform surgeries for women categorized as morbidly obese (BMI  $\geq 40$  kg/m<sup>2</sup>) and super obese (BMI  $\geq 50$  kg/m<sup>2</sup>). Studies evaluating the effect of BMI on hysterectomy outcomes have shown that higher perioperative blood loss and increased infection [5], length of hospital stay [13], rates of conversion to open hysterectomy [14], and major complications rates are associated with increasing BMI [15]. Several other well-documented risk factors for SSI, including tobacco use, corticosteroid use, malnutrition, diabetes mellitus, and increased age, have been described in surgical literature [16, 17]. Intraoperative events including increased blood loss  $\geq 500$  mL, prolonged surgical procedure with duration  $\geq 140$  minutes, and need for blood transfusion are associated with development of deep and organ space SSIs [6, 11]. With regards to the mode of surgery for lymph nodes, lymphadenectomy can be expected to increase the rate of SSI by causing excessive tissue trauma and a prolonged operation [9]. However, in the present patients, significant difference was not found within operation time and total blood loss in each mode of lymph node surgery, probably because a less complexed operation procedure was applied to patients with obesity. That is why the present authors could not find any significant risk for SSI in the mode of surgery for lymph nodes. Postoperative anemia has been defined as a significant risk

Table 2. — Univariate analyses for predictors of SSI in endometrial cancer.

		Total (n = 107)	SSI (n = 10)	No SSI (n = 97)	OR (95% CI)	p-value
Age (years)	> 50	36	2	34	Reference	0.280
	≤ 50	71	8	63	2.16 (0.434-10.74)	
BMI (kg/m <sup>2</sup> )	> 30	81	4	77	Reference	0.0126
	≤ 30	26	6	20	5.78 (1.49-22.44)	
Current smoker	No	103	10	93	Reference	0.671
	Yes	4	0	4	0.99 (0.00-12.1)	
Hypertension	No	65	3	62	Reference	0.0414
	Yes	42	7	35	4.13 (1.00-17.01)	
Diabetes mellitus	No	91	7	84	Reference	0.170
	Yes	16	3	13	2.77 (0.63-12.08)	
Respiratory disease*	No	95	8	87	Reference	0.311
	Yes	12	2	10	2.17 (0.40-11.69)	
Neurological risk**	No	103	9	94	Reference	0.329
	Yes	4	1	3	3.48 (0.33-37.03)	
Steroid use	No	104	10	94	Reference	0.748
	Yes	3	0	3	0.78 (0.00-9.90)	
Total blood loss (ml)	> 500	64	6	58	Reference	0.630
	≤ 500	43	4	39	0.99 (0.00-3.02)	
Blood transfusion***	no	95	8	87	Reference	0.311
	yes	12	2	10	2.17 (0.40-11.69)	
Operative time (hours)	> 4	67	6	61	Reference	0.555
	≤ 4	40	4	36	1.13 (0.30-4.27)	
Lymphadenectomy	None	1	0	1	1.57 (0.05-47.19)	0.380
	PEN sampling	51	4	47	0.45 (0.09-2.25)	
	PEN adenectomy	36	3	33	0.48 (0.09-2.68)	
	PEN and PAN adenectomy	19	3	16	Reference	
Postoperative body temperature (°C)	> 38.0	43	2	41	Reference	0.152
	≤ 38.0	64	8	56	2.93 (0.59-14.52)	
WBC (/ml)	> 10,000	100	9	91	Reference	0.507
	≤ 10,000	7	1	6	1.69 (0.18-15.59)	
Hematocrit (%)	≥ 35	84	8	76	Reference	0.633
	< 35	23	2	21	0.90 (0.00-3.53)	
Platelet (x10 <sup>4</sup> /ml)	≥ 15	102	10	92	Reference	0.606
	< 15	5	0	5	0.80 (0.00-9.64)	
Albumin (g/dl)	> 4.0	38	6	32	Reference	0.161
	≤ 4.0	69	4	65	0.33 (0.09-1.25)	
Creatinine (mg/dl)	> 0.9	99	9	90	Reference	0.557
	≤ 0.9	8	1	7	1.43 (0.16-12.95)	

SSI: surgical site infection, BMI: body mass index, OR: odds ratio, CI: confidence interval. \* Respiratory disease; chronic obstructive pulmonary disease, ventilator dependent, dyspnea, and pneumonia. \*\* Neurologic risk factors; history of stroke with or without residual deficit, transient ischemic attack, hemiplegia, paraplegia, quadriplegia, or impaired sensorium. \*\*\* Blood transfusion; receipt of an intraoperative packed red blood cell transfusion. PEN: pelvic lymph node, PAN: para-aortic lymph node, WBC: white blood cell, OR: odds ratio, CI: confidence interval.

factor for all categories of SSI in obstetrical and gynecologic surgery [18]. Of all the tested, age ≥ 50 years, BMI ≥ 30 kg/m<sup>2</sup>, diabetes mellitus, hypertension, postoperative body temperature ≥ 38.0°C, and serum albumin level ≤ 4.0 g/dL were risk factors for SSI by univariate analyses and BMI exhibited the most significant odds ratio for SSI by multivariate analysis.

The present study with a small sample size has several limitations inherent to all retrospective studies. There is reliance on a chart review and complications are undoubtedly underreported; moreover, data relating only the factors present in the records could be collected and analyzed. Furthermore, BMI was used as the means to classify obesity.

## Conclusion

Of all 107 patients in this study, ten (9.3%) were diagnosed as having SSI, and it was categorized as superficial incisional SSI. BMI exhibited the most significant risk factor for SSI in patients with endometrial cancer undergoing surgery.

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Table 3. — *Multivariate analyses for predictors of SSI in endometrial cancer.*

	OR	95% CI	p-value
Age $\geq$ 50 years	3.714	0.664—31.94	0.142
BMI $\geq$ 30 kg/m <sup>2</sup>	5.236	1.002—31.48	0.049
Diabetes mellitus	1.091	0.159—5.653	0.923
Hypertension	2.093	0.398—12.10	0.378
Postoperative body temperature $\geq$ 38.0°C	2.194	0.440—16.45	0.352
Albumin $\leq$ 4.0 g/dl	2.416	0.557—11.31	0.236

SSI: surgical site infection, BMI: body mass index, OR: odds ratio, CI: confidence interval

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