Submitted: 25 February, 2023 Accepted: 24 May, 2023 Published: 15 December, 2023 DOI:10.22514/ejgo.2023.095

ORIGINAL RESEARCH

European Journal of Gynaecological Oncology

Surgical site infection after cytoreductive surgery in patients with ovarian, fallopian tube and primary peritoneal cancer, is an independent predictor of poor overall survival *via* significant delays in adjuvant chemotherapy

Yeo-Jin Lee[1], Eun-Ju Lee[1,2,*]

[1]Department of Obstetrics and Gynecology, Chung-Ang University College of Medicine Chung-Ang University Hospital, 06973 Seoul, Republic of Korea
[2]Department of Microbiology and Molecular Genetics, University of California, Irvine, CA 92697, USA

***Correspondence**
ejlee@cau.ac.kr
(Eun-Ju Lee)

Abstract

Surgical site infection (SSI) is associated with substantial morbidity. However, the incidence and clinical significance of SSIs after cytoreductive surgery in Korean females with epithelial ovarian, fallopian tube and peritoneal cancer (EOFPC) are unknown. We aimed to assess the incidence and consequences of SSI within 30 days after cytoreductive surgery in patients with EOFPC. After estimating the effect size, SSIs were retrospectively investigated in 149 patients between 2011 and 2020. Survival and multivariate analyses were performed using Kaplan-Meier estimates and the Cox regression method that included the interaction terms, respectively. Clinical factors for patients with or without SSI were compared using the Mann-Whitney U test and Fisher's exact test. The overall rate of SSI was 9.4% (14 of 149 patients), consisting of five superficial, three deep and six organ/space SSIs. No clinical significance of SSI was observed when analyzing the 149 cases. Among the 91 patients with FIGO stage III–IV serous type carcinomas, eight experienced SSI, and their clinical factors were compared with those of the 83 patients without SSI. A univariate analysis showed that patient age, neoadjuvant chemotherapy, suboptimal debulking status, FIGO stage, chemoresistance, a longer interval from surgery to initiation of chemotherapy (ISIC), and SSI occurrence were significantly associated with overall survival. The multivariate analysis showed that higher FIGO stage (HR 21.138; 95% CI 2.796–159.819; $p = 0.003$) and SSI occurrence (HR 21.999; 95% CI 2.616–184.986; $p = 0.004$) were independent predictors for poor overall survival. The SSI group had a significantly greater body mass index ($p = 0.006$) and a longer ISIC (23 ± 9.1 *vs.* 40.0 ± 25.7 days; $p = 0.006$) compared with the non-SSI group. In conclusion, SSI after cytoreductive surgery in patients with FIGO stage III–IV serous type carcinoma significantly worsened patient prognosis and delayed initiation of adjuvant chemotherapy.

Keywords

Cytoreductive surgery; Ovarian cancer; Overall Survival; Surgical site infection

1. Introduction

The prevalence of epithelial ovarian, fallopian and peritoneal cancer (EOFPC), the most lethal gynecologic neoplasm, is steadily rising in Korea with the Korea Central Cancer Registry identifying an increase in cases from 967 in 1999 to 2505 in 2017 [1]. Over 70% of patients with EOFPC are diagnosed in the advanced stages, in which primary debulking cytoreductive surgery and adjuvant platinum-based combination chemotherapy are the standard treatments [2]. Because having a minor residual tumor status after surgery is significantly associated with a better prognosis, more extensive and complex surgery with a larger incision has become necessary to achieve minimal residual disease [3].

A surgical site infection (SSI) is defined by the Centers for Disease Control and Prevention (CDC) as an infection that occurs within 30 days of a surgical operation or 90 days of a surgical operation with the placement of an implant. SSIs affect either the incision site itself or the tissues within the surgical site [4]. An SSI is a postoperative complication that often leads to increased hospital stays, readmission and reoperation rates and medical costs [4, 5]. There is a significant risk of SSI for EOFPC patients because of the aggressive nature of cytoreductive surgery. Some studies have shown that the SSI rate after cytoreductive surgery varies and is between 6.5 and 20% [6–10]. It is also reported to be significantly

associated with a poor overall survival rate [10], and is linked to delayed or canceled adjuvant chemotherapy [9]. Therefore, preventing SSI can potentially improve prognosis as well as perioperative quality of life. However, the incidence and clinical significance of SSIs after cytoreductive surgery in Korean females with EOFPC are currently unknown.

Therefore, this study aimed to investigate the incidence and clinical consequences of SSI in Korean patients who underwent cytoreductive surgery for EOFPC and to identify the contributing factors of SSIs.

2. Materials and methods

2.1 Sample calculation

Our hypothesis in this study was that the SSI rate in our hospital was similar to that shown in previous reports. In order to effectively test the hypothesis, the expected sample size was estimated prior to the beginning of the investigation. The median value of SSI prevalence in three previous studies was 10.8% [6, 7, 10]. At a 95% confidence interval for p, and with a margin of error equal to 5%, the expected sample size was calculated to be 148, considering a 5–10% follow-up loss (N = 7–15). Follow-up loss was defined as no complete follow-up within 30 days after surgery. A sample size of 155–163 patients was required to conduct this research [11], which we obtained by scrutinizing patient data between 2011 and 2020.

2.2 Patients

A total of 161 patients diagnosed with EOFPC who underwent cytoreductive surgery at Chung-Ang University Hospital between 2011 and 2020 were retrospectively identified (Fig. 1). Of these, 12 were excluded from the study since six patients were not followed-up after transferring to other hospitals within seven days after the surgery and six patients had coexisting cancers, including gastric cancer (N = 4) and pancreatic cancer (N = 2). In total, 149 patients were included in this analysis. The patients underwent primary debulking surgery followed by a minimum of six cycles of adjuvant platinum-based chemotherapy. Neoadjuvant chemotherapy (NAC) was administered for two or three cycles, and interval debulking surgery followed after three or four weeks of rest. A poly adenosine diphosphate-ribose polymerase inhibitor was not administered to all patients yet when the data collection was finished. A total of 134 patients had ovarian cancers (92 serous, 18 clear-cell, 7 endometrioid, 6 mucinous, 3 transitional, 4 malignant mixed mesodermal tumors and 4 undifferentiated tumors), 11 had peritoneal cancers and four had fallopian tube cancers. The 15 combined peritoneal and fallopian tube cancers had serous histology. SSI was defined according to the CDC [4].

2.3 Data collection

Clinicopathological and laboratory data were collected through medical chart reviews. The data included age and body mass index (BMI) at the time of diagnosis, current diabetes or hypertension, menopausal status, previous history of intraabdominal surgery, implementation of NAC, surgical optimality, International Federation of Gynecology and Obstetrics (FIGO) stage, chemo-responsiveness, the presence of an SSI, tumor grade, histological type, serum cancer antigen (CA)-125 level, transfusion during operation and surgery duration. Preoperative laboratory data included white blood cell (WBC) count, hemoglobin and albumin levels. Appendectomies were not considered to be bowel surgery. Surgical complexity was measured with a modified scoring system based on complexity and the number of surgical procedures [12]. Surgical optimality was defined as a residual tumor of <1 cm. Chemoresistance was defined as recurrence within six months of finishing first-line treatment. The interval from surgery to initiation of chemotherapy (ISIC) was defined as the period between the date of surgery and the first day of chemotherapy. Operation time was defined from peritoneal opening to the start of fascia closing.

2.4 Statistical analysis

Disease-free survival (DFS) was defined as the period from the end date of primary therapy to the diagnosis of the first recurrence, and overall survival (OS) was defined as the time in months from the end date of primary therapy to disease-related death. Survival was estimated using Kaplan-Meier estimates and compared with a log-rank test, where indicated. A multivariate analysis was performed using a Cox regression and included the interaction terms. Mean counts were analyzed using the Mann-Whitney U test since the distributions of both populations were not equal. Dichotomous groupings were analyzed using a Fisher's exact test. All p-values reported were two-sided, with a p-value of < 0.05 indicating statistical significance. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS, version 15.0, IBM SPSS Inc., Chicago, IL, USA).

3. Results

3.1 The rate of SSI after cytoreductive surgery is 9.4%

A total of 149 cases were included in the current analysis. The mean age was 56.02 years (range 22–82), and 16 patients had postoperative infections within 30 days after surgery. The remaining 133 patients had no infections that led to fever or caused invasive procedures within three months.

Altogether, 14 of the 16 patients with infections had an SSI (9.4%) on a mean of postoperative day 12.4, ranging from Day 5 to Day 21 (Table 1). Five SSIs were superficial, which caused superficial wound dehiscence, and were managed with primary suturing and antibiotic therapy. Three SSIs were deep, where two patients had full-thickness wound dehiscence that required primary suturing, and one patient had tissue necrosis and dehiscence in the inguinal lymph node dissection area. Another six patients had organ/space SSIs, of which five were peritonitis, and one was an anastomotic leakage.

The other two of the 16 patients were diagnosed with a urinary tract infection (UTI) with associated fever and required antibiotic therapy. One of the patients had diabetes and hypertension, a serous high-grade tumor, and a history of multiple intraabdominal surgeries for stomach, breast and renal cell car-

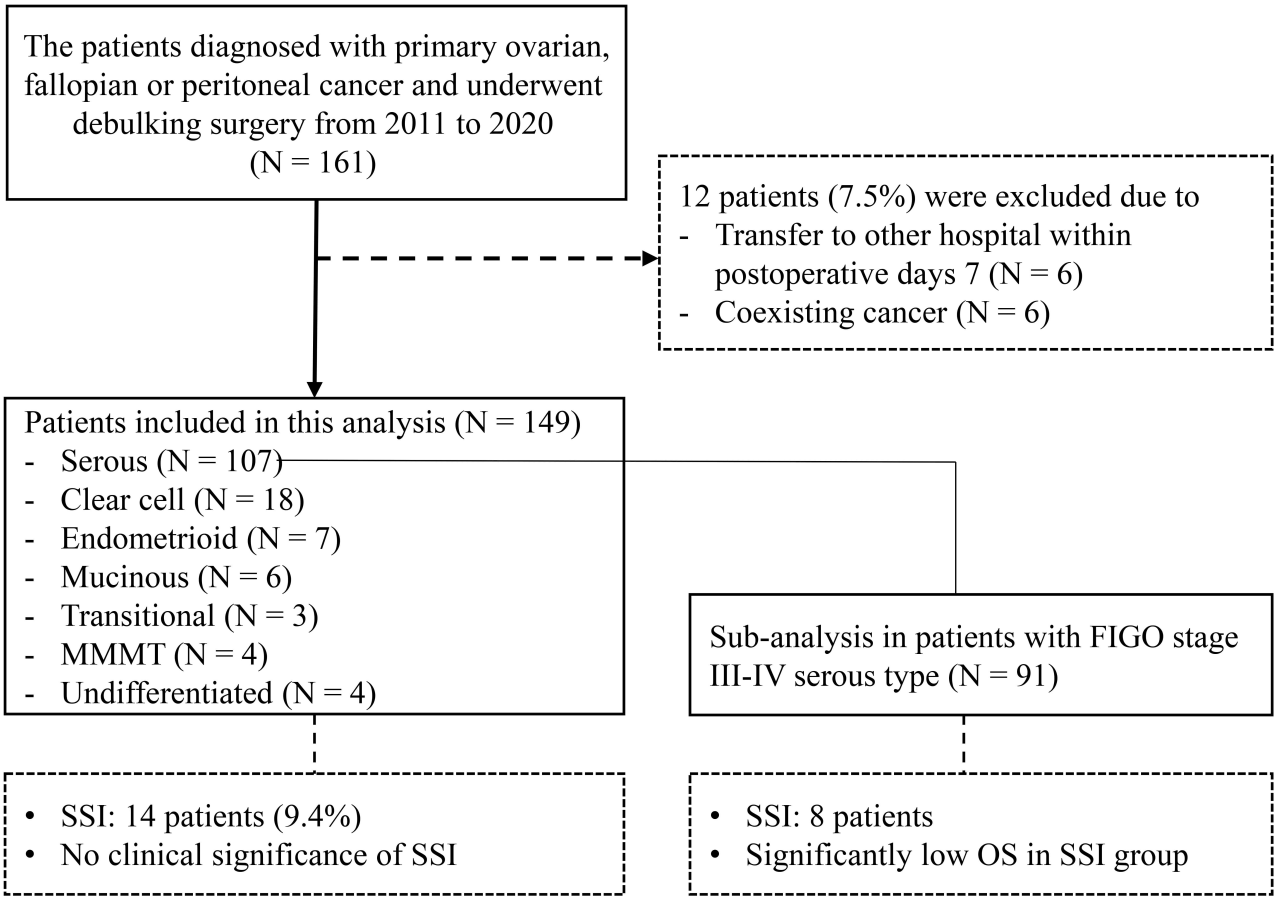

FIGURE 1. Flow diagram depicting the patient selection process. SSI, Surgical site infection; FIGO, International Federation of Gynecology and Obstetrics; MMMT, Malignant Mixed Mullerian Tumor; OS, Overall Survival.

TABLE 1. Summary of 14 cases with a surgical site infection.

Case	Infection site	Time of SSI occurrence	SSI classification	Histology (stage)
1	Peritonitis	POD#12	Organ/space	Serous (IV)
2	Wound full thickness dehiscence	POD#15	Deep	Clear (IIIc)
3	Peritonitis	POD#10	Organ/space	Serous (IIIc)
4	Bowel leakage	POD#9	Organ/space	Serous (IIIc)
5	Wound superficial dehiscence	POD#11	Superficial	Mucinous (IIIc)
6	Wound superficial dehiscence	POD#15	Superficial	Serous (IIIc)
7	Peritonitis	POD#19	Organ/space	Serous (IIIc)
8	Wound superficial dehiscence	POD#21	Superficial	Serous (Ia)
9	Peritonitis	POD#18	Organ/space	Serous (Ic)
10	Peritonitis	POD#8	Organ/space	Serous (IIIc)
11	Wound superficial dehiscence	POD#9	Superficial	Clear (IIIc)
12	Wound superficial dehiscence	POD#5	Superficial	Serous (IIIc)
13	Wound full thickness dehiscence	POD#9	Deep	Unknown
14	Inguinal LN dissection site necrotic tissue/partial dehiscence	POD#13	Deep	Serous (IV)

SSI, surgical site infection; POD, postoperative day; LN, lymph node.

cinomas. The UTI was detected 14 days after surgery, causing sepsis and resulting in the death of the patient. The other patient was diagnosed with a UTI 29 days after surgery and was treated successfully with ceftriaxone antibiotic therapy. The causative microorganisms were *Enterococcus faecium* and *Escherichia coli*, respectively.

3.2 Patients with SSIs have significantly worse overall survival (OS)

We investigated the effect of SSIs on the survival of patients with EOFPC. Although SSIs did not significantly affect the OS of all the 149 patients, they were significantly associated with worse OS in a subgroup of patients (N = 91) with advanced-stage serous carcinoma (Table 2 and Fig. 2). A univariate analysis showed that chemoresistance was a significant prognostic factor for worse DFS (HR 9.595; 95% CI 4.803–19.169). With regard to OS, the univariate analysis showed that old age, implementation of NAC, suboptimality, higher FIGO stage, chemoresistance, ISIC and SSI occurrence had a significant adverse effect on patient prognosis. The multivariate analysis showed that FIGO stage (HR 21.138; 95% CI 2.796–159.819; $p = 0.003$), and SSI occurrence (HR 21.999; 95% CI 2.616–184.986; $p = 0.004$) were independent factors for worse OS.

3.3 SSI occurrence was significantly associated with higher BMI and delay of adjuvant chemotherapy

To assess the factors contributing to SSIs, we compared clinicopathologic parameters between patients with and without an SSI (Table 3). The patients with an SSI had significantly higher BMI ($p = 0.006$) and longer intervals from surgery to initiation of chemotherapy ($p = 0.006$) than those without an SSI. Age, CA-125, previous intraabdominal surgery, current diabetes or hypertension, grade, FIGO stage, implementation of NAC, transfusion, bowel surgery, surgical complexity, optimality, chemoresistance and operative duration were not significantly different between the two groups. In addition, a comparison of preoperative blood test results showed no significant difference between the two groups.

4. Discussion

Our results show that the rate of SSI in Korean females who underwent cytoreductive surgery for EOFPC in one tertiary hospital was 9.4%. As shown in Table 4, two retrospective studies reported the rate of SSI in patients who underwent cytoreductive surgery for EOFPC and epithelial ovarian cancer were 6.5% (25 of 382) and 10.8% (96 of 888), respectively [6, 10]. A prospective study comparing SSI rates before and after the implementation of the prevention bundle showed 20.0% (18 of 91) and 3% (4 of 128) infection rates, respectively [7]. In comparison to the general incidence of SSIs, which is expected to be approximately 1–3% according to the CDC [13], the SSI rates after cytoreductive surgery were significantly raised. As previously stated, this increased rate is likely to be the substantial surgical aspect of cytoreductive surgery for EOFPC. To the best of our knowledge, this study is the first to analyze SSI rates in Korean females who underwent cytoreductive surgery for EOFPC. However, further surveys at the national level will be necessary.

The present study demonstrated that an SSI after cytoreductive surgery for EOFPC was significantly correlated with worse OS, but not with DFS, in the homogeneous high-risk subgroup of patients with advanced-stage serous histology; however, it did not have clinical significance in the analysis of all 149 patients with heterogenous clinicopathologic natures in terms of different prognostic contributions. This result from the cohort of serous histology was comparable to a previous report, which showed that SSIs contracted after primary debulking surgery for epithelial ovarian cancer were independently associated with decreased OS [10]. In addition, another study showed that postoperative infections, including SSIs after cytoreductive surgery for EOFPC, which occurred in 15.9% of patients (44 of 276), were significantly associated with worse OS [14]. Overall, contracting an SSI after cytoreductive surgery may worsen the OS of patients with EOFPC, and steps must be taken to minimize the risk of infection.

This study showed that BMI was significantly higher in patients with SSIs than in those without SSIs. Unsurprisingly, BMI is a well-recognized etiological risk factor for SSI [9, 10, 13, 15]. In addition, two previous reports showed that longer operation time, advanced FIGO stage, gastroesophageal reflux disease, higher surgical complexity, greater residual disease, usage of wound drains, and the usage of staples to close the skin were significantly associated with a higher rate of SSI after cytoreductive surgery [9, 10]. Of these factors, surgical complexity and postoperative drainage are points of contention [8, 14]. Although identifying modifiable risk factors is crucial, the majority are associated with the patient and are, therefore, more difficult to control and there is not enough time to address these issues before surgery. Therefore, a deliberate strategic alternative approach beyond recognizing risk factors is necessary to reduce SSIs.

Notably, the interval from cytoreductive surgery to the initiation of adjuvant chemotherapy, one of the important clinical factors, is significantly prolonged in patients with SSIs compared with those without SSIs (mean 23 *vs.* 40 days). This delay is consistently shown in a previous report, in which 29% of patients with an SSI experienced delays with their adjuvant treatment or had it canceled. However, no information about delayed days or comparison data were provided [9]. An interval of >25 days adversely affected survival for women with FIGO stage IV ovarian cancer (HR 3.44; 95% CI 1.68–7.03) [16], while an interval of >28 days can compromise OS in patients with advanced serous ovarian cancer (HR 1.73; 95% CI 1.08–2.78) [17]. The patients with an SSI in this study had longer delays than the above-indicated thresholds. Because extended hospital stays and readmission are frequently needed to manage SSI, and chemotherapy can adversely affect wound healing by impairing the immune system and leading to poor nutrition [18], treatment should be postponed. Therefore, SSI-related delays in initiating adjuvant chemotherapy could explain the worse OS of patients with SSIs.

As bowel resections have become more common for complete cytoreduction of EOFPC, anastomotic leakage might be a significant side effect. According to the American College of Surgeons National Surgical Quality Improvement Program

TABLE 2. Survival analysis of patients with advanced-stage serous ovarian cancers only (N = 91).

		Univariate			Multivariate		
	N (%)	HR	95% CI	*p*-value	HR	95% CI	*p*-value
Age at diagnosis							
<60	50 (54.9)	1.000			1.000	-	-
≥60	41 (45.1)	2.849	1.254–6.476	0.012	3.770	0.821–17.310	0.088
DM/HTN							
None	56 (61.5)	1.000			-	-	-
DM or HTN	35 (38.5)	1.927	0.877–4.235	0.102	-	-	-
Menopause							
No	19 (20.9)	1.000			-	-	-
Yes	72 (79.1)	3.593	0.840–15.367	0.085	-	-	-
BMI							
<25	55 (60.4)	1.000			-	-	-
≥25	36 (39.6)	1.499	0.655–3.433	0.338	-	-	-
First line therapy							
PDS	71 (78.0)	1.000			1.000	-	-
NAC	20 (22.0)	2.746	1.203–6.271	0.012	0.819	0.147–4.560	0.820
Surgical optimality							
Optimal	71 (78.0)	1.000			1.000	-	-
Suboptimal	11 (12.1)	2.954	1.069–8.167	0.037	0.000	0.000–0.000	0.949
Unknown	9 (9.9)						
FIGO stage							
III	72 (79.1)	1.000			1.000	-	-
IV	19 (20.9)	3.803	1.448–9.984	0.007	21.138	2.796–159.819	0.003
Chemo-response							
Sensitive	56 (61.5)	1.000			1.000	-	-
Resistant	18 (19.8)	4.369	1.534–12.446	0.006	6.934	0.467–103.055	0.160
Unknown	17 (18.7)						
ISIC							
<25 days	49 (53.8)	1.000			-	-	-
≥25 days	31 (34.1)	3.582	1.474–8.704	0.005	-	-	-
Unknown	11 (12.1)						
SSI							
No	83 (91.2)	1.000			1.000	-	-
Yes	8 (8.8)	5.914	1.877–18.630	0.002	21.999	2.616–184.986	0.004

BMI, body mass index; PDS, primary debulking surgery; NAC, neoadjuvant chemotherapy; ISIC, interval from surgery to initiation of chemotherapy; SSI, surgical site infection; FIGO, International Federation of Gynecology and Obstetrics; DM, diabetes mellitus; HTN, hypertension; HR, Hazard Ratio; CI, Confidence Interval.

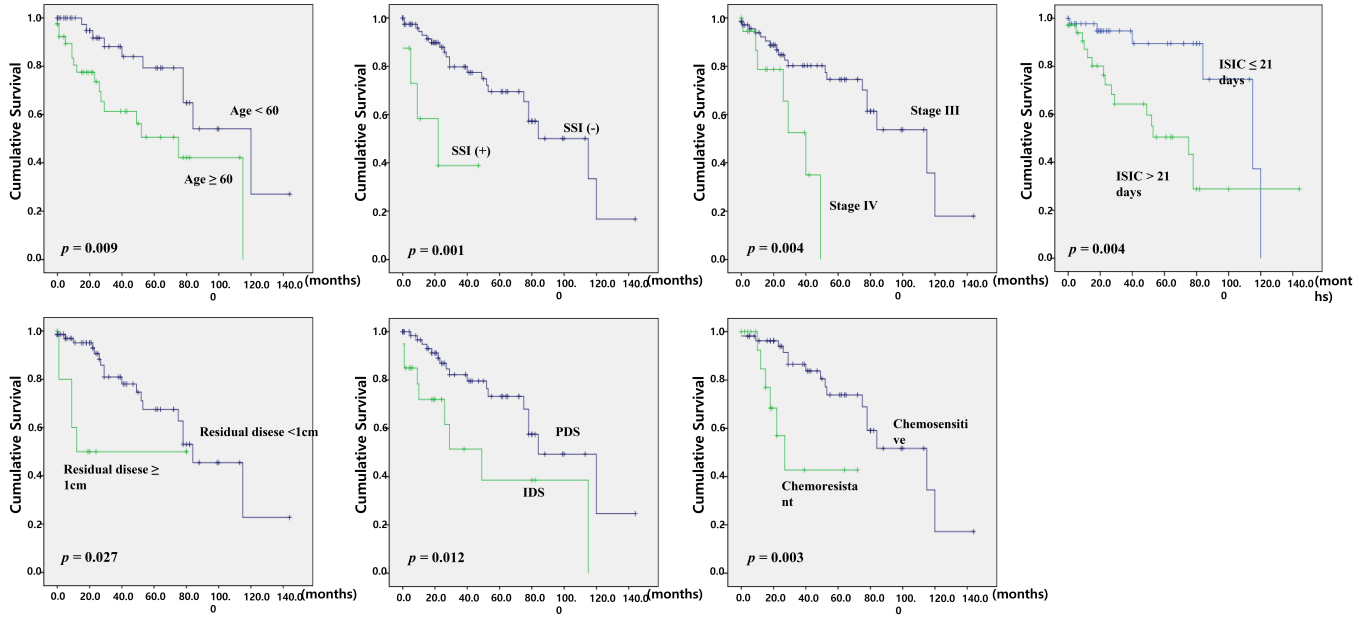

FIGURE 2. Kaplan-Meier survival curves and log-rank tests for overall survival of patients with serous ovarian cancer only. SSI, surgical site infection; ISIC, interval from surgery to initiation of chemotherapy; PDS, primary debulking surgery; IDS, interval debulking surgery.

(ACS NSQIP), anastomotic leakage is not classified as an SSI unless it is accompanied by an abscess or purulence, meaning that its prevalence and contribution to a postoperative course have likely been underestimated [19]. Some studies, including the present study, categorized anastomotic leakage as an organ/space SSI because bowel contents leaking into the peritoneal cavity necessitate reoperation and can act as a nidus for bacteremia and sepsis [10, 19]. Accordingly, bowel resection has a 10–16.9% SSI rate [14, 20], and a patient with anastomotic leakage in this study underwent another operation to fix it. Because anastomotic leakage could potentially lead to infections, a broader definition of SSI that includes anastomotic leakage may be required for the effective prevention of SSIs.

The present study was limited by being a retrospective, single-center investigation. However, we calculated the sample size to ensure sufficient precision in descriptive outcomes prior to the initiation of the investigation. Further well-designed, prospective studies are required. This study is the first to demonstrate the rate and clinical significance of SSIs in Korean women who underwent cytoreductive surgery for EOFPC.

5. Conclusions

In summary, the rate of SSIs after cytoreductive surgery for EOFPC in our institute in Korean females was 9.4%. Infection after cytoreductive surgery in patients with FIGO stage III–IV serous carcinoma delayed the initiation of adjuvant chemotherapy in patients with a higher BMI, which evolved in the postoperative period with infectious conditions and significantly worsened the prognosis.

AVAILABILITY OF DATA AND MATERIALS

The data used to support the findings of this study are included within the article. Raw data are available upon request from the corresponding author.

AUTHOR CONTRIBUTIONS

YJL and EJL—carried out the analysis of the data and drafted the manuscript. YJL—carried out the data collection and analysis. EJL—performed the study design and coordination.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved, and the need for informed consent was waived by the Institutional Review Board of Chung-Ang University Hospital (irb@caumc.or.kr; approval number: 2109-031-19387; date: 25 November 2021).

ACKNOWLEDGMENT

Not applicable.

FUNDING

This study was supported by the Basic Science Research Program of the National Research Foundation of Korea (NRF), grant no: 2020R1A2C1003536.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

TABLE 3. Comparison of parameters between patients with and without an SSI.

	N (%), mean ± SD		
	SSI-no (N = 83)	SSI-yes (N = 8)	*p*-value
Age, year	57.98 ± 11.13	59.38 ± 12.91	NS†
<60	46 (55.4)	4 (50.0)	NS‡
≥60	37 (44.6)	4 (50.0)	
BMI, kg/m^2	24.04 ± 4.79	28.33 ± 4.60	0.006†
<25	54 (65.1)	1 (12.5)	0.006‡
≥25	29 (34.9)	7 (87.5)	
CA-125, U/mL	1503.80 ± 2552.91	1453.07 ± 1689.57	NS†
Menopause			
No	18 (21.7)	1 (12.5)	NS‡
Yes	65 (78.3)	7 (87.5)	
Previous intraabdominal surgery			
No	45 (54.2)	4 (50.0)	NS‡
Yes	38 (45.8)	4 (50.0)	
DM/HTN			
No	52 (62.7)	4 (50.0)	NS‡
Yes	31 (37.3)	4 (50.0)	
Grade			
1	6 (7.2)	1 (12.5)	NS‡
2–3	77 (92.8)	7 (87.5)	
FIGO Stage			
III	65(78.3)	7 (87.5)	NS‡
IV	18 (21.7)	1 (12.5)	
First surgery			
PDS	65 (78.3)	6 (75.0)	NS‡
NAC	18 (21.7)	2 (25.0)	
Transfusion			
No	33 (39.8)	3 (37.5)	NS‡
Yes	50 (60.2)	5 (62.5)	
Bowel surgery, except appendectomy only			
No	53 (63.9)	6 (75.0)	NS‡
Yes	30 (36.1)	2 (25.0)	
Surgical complexity			
1–3	14 (16.9)	0 (0.0)	
4–7	42 (50.6)	6 (75.0)	NS‡
≥8	27 (32.5)	2 (25.0)	
Residual disease			
<1 cm	64 (77.1)	7 (87.5)	
≥1 cm	10 (12.1)	1 (12.5)	NS‡
Unknown	9 (10.8)	0 (0.0)	
Chemo-response			
Sensitive	53 (63.9)	3 (37.5)	
Resistant	15 (18.1)	3 (37.5)	NS‡
Unknown	15 (18.1)	2 (25.0)	
ISIC, days	23.0 ± 9.1	40.0 ± 25.7	0.006†
Preoperative blood test			
WBC, /μL	6718.60 ± 2202.62	6691.40 ± 3447.22	NS†
Hemoglobin, g/dL	11.96 ± 1.39	11.30 ± 1.97	NS†
Albumin, g/dL	3.88 ± 0.56	3.60 ± 0.44	NS†
Operative duration, min	429.62 ± 182.32	462.86 ± 185.63	NS†

†*Mann-Whitney U test;* ‡*Fisher's exact test; BMI, body mass index; DM/HTN, diabetes mellitus/hypertension; PDS, primary debulking surgery; NAC, neoadjuvant chemotherapy; ISIC, interval from surgery to initiation of chemotherapy; WBC, white blood cell; SSI, surgical site infection; FIGO, International Federation of Gynecology and Obstetrics; CA, cancer antigen; SD, standard deviation; NS, no significance.*

TABLE 4. Summary of literature for SSI incidence following cytoreductive surgery.

Rate, SSI case of total case [reference]	Cancer	Case of each SSI	Clinical significance	Research period	Study design	Contributing factors
10.8%, 96 of 888 [10]	EOC	32 superficial; 2 deep; 62 organ/space	Worse OS	2003–2011	Retrospective, single-center	BMI, Operation duration, advanced stage for superficial SSI; GERD, surgical complexity, and residual disease for organ/space SSI
20.0%, 18 of 91† [7]	EOFPC	10 superficial; 7 deep; 1 organ/space	NE	2014–2016	Prospective, single-center	NE
6.5%, 144 of 2231 (ovarian cancer); 5.4%, 369 of 6854 [8]	Gynecologic cancer with 2231 ovarian cancers	212 superficial; 48 deep; 109 organ/space	NE	2005–2011	Retrospective, multi-center (ACS NSQIP)	NE
6.5%, 25 of 382 [6]	EOC	5 superficial; 2 deep; 18 organ/space	NE	2010–2012	Retrospective, single-center	NE
15.9%, 54 of 339 [9]	Gynecologic cancer with 200 ovarian/peritoneal cancer	NE	Prolonged hospital stays, delayed or canceled adjuvant Tx	September to November 2015	Prospective, multi-center	BMI, wound drains, staple close
9.4%, 14 of 149	EOFPC	5 superficial; 3 deep; 4 organ/space	Worse OS and delayed adjuvant chemotherapy in stage III–IV serous type	2011–2020	Retrospective, single-center	BMI

SSI, surgical site infection; EOC, epithelial ovarian cancer; OS, overall survival; BMI, body mass index; GERD, gastroesophageal reflux disease; †, number of patients before introduction of infection prevention bundle; EOFPC, epithelial, ovarian, fallopian tube and peritoneal cancer; NE, not evaluated; ACS NSQIP, American College of Surgeons National Surgical Quality Improvement Program; LN, lymph node metastasis.

REFERENCES

[1] Ha HI, Chang HK, Park SJ, Lim J, Won Y, Lim MC. The incidence and survival of cervical, ovarian, and endometrial cancer in Korea, 1999–2017: Korea central cancer registry. Obstetrics & Gynecology Science. 2021; 64: 444–453.

[2] Kurnit KC, Fleming GF, Lengyel E. Updates and new options in advanced epithelial ovarian cancer treatment. Obstetrics & Gynecology. 2021; 137: 108–121.

[3] Covens AL. A critique of surgical cytoreduction in advanced ovarian cancer. Gynecologic Oncology. 2000; 78: 269–274.

[4] Berrios-Torres, SI, Umscheid, CA, Bratzler, D, Leas B, Stone EC, Kelz RR, *et al*. Centers for disease control and prevention guideline for prevention of surgical site infection, 2017. JAMA Surgery. 2017; 152: 784–791.

[5] Seidelman J, Anderson DJ. Surgical site infections. Infectious Disease Clinics of North America. 2021; 35: 901–929.

[6] Johnson MP, Kim SJ, Langstraat CL, Jain S, Habermann EB, Wentink JE, *et al*. Using bundled interventions to reduce surgical site infection after major gynecologic cancer surgery. Obstetrics & Gynecology. 2016; 127: 1135–1144.

[7] Lippitt MH, Fairbairn MG, Matsuno R, Stone RL, Tanner EJ, Wick EC, *et al*. Outcomes associated with a five-point surgical site infection prevention bundle in women undergoing surgery for ovarian cancer. Obstetrics & Gynecology. 2017; 130: 756–764.

[8] Mahdi H, Gojayev A, Buechel M, Knight J, SanMarco J, Lockhart D, *et al*. Surgical site infection in women undergoing surgery for gynecologic cancer. International Journal of Gynecologic Cancer. 2014; 24: 779–786.

[9] O'Donnell RL, Angelopoulos G, Beirne JP, Biliatis I, Bolton H, Bradbury M, *et al*. Impact of surgical site infection (SSI) following gynaecological cancer surgery in the UK: a trainee-led multicentre audit and service evaluation. BMJ Open. 2019; 9: e024853.

[10] Tran CW, McGree ME, Weaver AL, Martin JR, Lemens MA, Cliby WA, *et al*. Surgical site infection after primary surgery for epithelial ovarian cancer: predictors and impact on survival. Gynecologic Oncology. 2015; 136: 278–284.

[11] Bhalerao S, Kadam P. Sample size calculation. International Journal of Ayurveda Research. 2010; 1: 55–57.

[12] Di Donato V, Di Pinto A, Giannini A, Caruso G, D'Oria O, Tomao F, *et al*. Modified fragility index and surgical complexity score are able to predict postoperative morbidity and mortality after cytoreductive surgery for advanced ovarian cancer. Gynecologic Oncology. 2021; 161: 4–10.

[13] Calderwood MS, Anderson DJ, Bratzler DW, Dellinger EP, Garcia-Houchins S, Maragakis LL, *et al*. Strategies to prevent surgical site infections in acute-care hospitals: 2022 update. Infection Control and Hospital Epidemiology. 2023; 44: 695–720.

[14] Matsuo K, Prather CP, Ahn EH, Eno ML, Tierney KE, Yessaian AA, *et al*. Significance of perioperative infection in survival of patients with ovarian cancer. International Journal of Gynecological Cancer. 2012; 22: 245–253.

[15] Cai B, Li K, Li G. Impact of obesity on major surgical outcomes in ovarian cancer: a meta-analysis. Frontier in Oncology. 2022; 12: 841306.

[16] Tewari KS, Java JJ, Eskander RN, Monk BJ, Burger RA. Early initiation of chemotherapy following complete resection of advanced ovarian cancer associated with improved survival: NRG Oncology/Gynecologic Oncology Group study. Annals of Oncology. 2016; 27: 114–121.

[17] Hofstetter G, Concin N, Braicu I, Chekerov R, Sehouli J, Cadron I, *et al*. The time interval from surgery to start of chemotherapy significantly impacts prognosis in patients with advanced serous ovarian carcinoma—analysis of patient data in the prospective OVCAD study. Gynecologic Oncology. 2013; 131: 15–20.

[18] Beyene RT, Derryberry SL, Barbul A. The effect of comorbidities on wound healing. The Surgical Clinics of North America. 2020; 100: 695–705.

[19] Katsumata K, Enomoto M, Ishizaki T, Fujita S, Kanemitsu Y, Ito M, *et al*. Risk factors for surgical site infection and association of surgical site infection with survival of lower rectal cancer patients without clinical lateral pelvic lymph node metastasis (clinical Stage II/III): analysis of data from JCOG0212. Clinical & Experimental Metastasis. 2021; 38: 459–466.

[20] Bernard L, Boucher J, Helpman L. Bowel resection or repair at the time of cytoreductive surgery for ovarian malignancy is associated with increased complication rate: an ACS-NSQIP study. Gynecologic Oncology. 2020; 158: 597–602.

How to cite this article: Yeo-Jin Lee, Eun-Ju Lee. Surgical site infection after cytoreductive surgery in patients with ovarian, fallopian tube and primary peritoneal cancer, is an independent predictor of poor overall survival *via* significant delays in adjuvant chemotherapy. European Journal of Gynaecological Oncology. 2023; 44(6): 20-28. doi: 10.22514/ejgo.2023.095.