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Risk Factors for Early and Late-Occurring Incisional Hernias After Primary Laparotomy for Ovarian Cancer

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Abstract

Objectives: To evaluate a cohort of gynecologic oncology patients to discover risk factors for early- and late-occurring incisional hernia after midline incision for ovarian cancer.

Methods: We collected retrospective data from patients undergoing primary laparotomy for ovarian cancer at the University of Wisconsin Hospitals and Clinics from 2001–2007. Patient characteristics and potential risk factors for hernia formation were noted. Physical examination, abdominal computerized-assisted tomography (CT) scans, or both were used to detect hernias 1 year after surgery (early hernia) and 2 years after surgery (late hernia).

Results: There were 265 patients available for the one-year analysis and 189 patients for the 2-year analysis. Early and late hernia formation occurred in 9.8% (95% CI, 6.2%−12%) and an additional 7.9% (95% CI, 4.1%−12%) of patients respectively. Utilizing multiple logistic regression, poor nutritional status (albumin < 3 g/dL) and suboptimal cytoreductive surgery (≥ 1 cm residual tumor) were significantly associated with the formation of early incisional hernia after midline incision ($p<0.001$ for both). Late hernia formation was associated only with age ≥ 65 ($p=0.01$).

Conclusions: The formation of early incisional hernias after midline incision is associated with poor nutritional status and suboptimal cytoreductive surgery, while late hernia formation is associated with advanced age.

PRECIS

Development of incisional hernias after midline incision in ovarian cancer patients is associated with poor nutritional status and suboptimal cytoreduction one year after surgery and age greater than 65 at 2 years

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Identifying modifiable risk factors of incisional hernia formation is of critical importance as preventing them is of major interest in the surgical community. Incisional hernia are a common complication with an incidence of 9.8% at 2 years (1). Previously recognized risk factors include obesity, older age, male sex, surgical site infection, bowel surgery, smoking and having multiple comorbid conditions (2–5). A reduction in hernia incidence could bring about a significant improvement in patient outcomes (6). Additionally, hernias can lead to surgical emergencies as 4.3% of hernia repairs are done due to small bowel incarceration (7).

Intraoperative and post-operative factors can also contribute to the development of incisional hernias. The use of non-absorbable or slowly absorbable suture material for abdominal closure is associated with fewer incisional hernias (8). Meta-analyses of randomized trials show that a running closure leads to a lower rate of incisional hernias when compared to an interrupted closure (8,9).

Additionally, post-operative surgical site infections are recognized to increase hernia risk (10–12). In fact, a great deal of clinical data supports wound infection as the most important risk factor for the development of an incisional hernia (5,13).

The primary aim of our study was to investigate the possible risk factors in the development of early and late-occurring incisional hernias in women undergoing laparotomy for ovarian cancer – specifically the contribution surgical site infection, nutritional status and surgical cytoreduction may have. Both early and late hernias were investigated as they relate to surgical factors and patient factors, respectively.

MATERIALS AND METHODS

The Institutional Review Board at the University of Wisconsin School of Medicine and Public Health approved this study. All patients with epithelial ovarian cancer who underwent primary cytoreductive surgery between January 1, 2001 and December 31, 2007 were identified from the cancer registry databases at the University of Wisconsin Hospitals and Clinics.

After initial eligibility screening, the following inclusion criteria were applied to determine the final study sample: 1) utilization of a midline vertical incision; 2) clinical or radiographic determination of an incisional hernia after midline incision with longitudinal follow-up of one to two years in our system. All surgeries were performed by board eligible/board certified gynecologic oncologists. All patients underwent exploratory laparotomy with the intention of achieving optimal cytoreduction (< 1 cm residual disease). Patients were excluded from the study for the following reasons: incomplete surgical-pathologic data and lack of longitudinal follow-up. The following data were extracted from the medical record: age at the time of initial surgery, body mass index (BMI), pre-operative diagnosis of Diabetes Mellitus (DM), nutritional status (normal defined as preoperative albumin ≥ 3 g/dL), cancer stage, histology and grade, whether optimal cytoreduction was accomplished (defined as < 1 cm of residual tumor at the end of surgery), and facial closure technique (running vs. interrupted vs. mass closure vs. combination method).

The length of the surgical incision was not collected. Large scale reviews have not identified this as a risk factor – possibly due to the retrospective nature of most studies and the absence of this data for analysis (14). Surgical site infection was defined using the 1999 CDC criteria up to 30 days after surgery (15). Nutritional status was analyzed as a binary variable using 3 mg/dL as the cutoff because of data from our institution that this was a point at which perioperative complications increased (16).

All the data were reviewed by two of the investigators (KH and AA) for accuracy. Physical examination and abdominal CT scans conducted during routine follow-up were utilized to diagnose postoperative incisional hernias. On physical examination, hernias were diagnosed by a palpable defect in the fascia along the surgical incision. Radiographically, hernias were diagnosed when a fascial defect demonstrated a hernia neck larger than one centimeter in greatest dimension – the smallest reliable defect detectable. The primary outcomes in this study were early-occurring hernias (diagnosed one year after surgery) and late-occurring hernias (diagnosed 2 years after surgery). These time frames were selected because most incisional hernias appear within 2 years after surgery. The incidence does not significantly increase at time periods more distant from surgery (e.g. 3 or 4 years). Therefore, 2 years from surgery has been accepted as a time frame when hernia rate reaches its plateau (17).

Univariate logistic regression analysis was used to test for an association between the above-mentioned variables and the development of an incisional hernia after a midline incision. Multivariate logistic regression models were used to test adjusted associations for any variables that predicted incisional hernia formation with a p-value less than 0.20 in univariate logistic regression. Results were quantified in terms of relative risk. All p-values reported are for two-sided statistical tests that were considered statistically significant at < 0.05. Data analysis was performed in SAS version 9.3 (Cary, NC).

A total of 326 patients who underwent primary cytoreductive surgery during the study period were identified. The final analysis at 1-year included 265 patients after excluding 61 patients for the following reasons: 22 for low malignant potential tumors, 11 for insufficient medical information, and 28 for lack of follow-up at the 1-year interval.

The analysis at 2 years included 189 patients after excluding 76 patients. Twenty-six patients were excluded due to diagnosis of hernia at one year and 50 patients were lost to follow-up. There was no clustering in the timing of the hernia diagnosis and incidence was generally spread evenly throughout the time periods under review. Patient characteristics for both groups can be found in Table 1.

RESULTS

The median age of the study population was 59 years (range 15–85 years) with mean age 58.7 years (SD 12.5). Median BMI was 27.7 kg/m^2 (16.7–56.2) and mean BMI was 29.0 kg/m^2 (SD 6.83). Median estimated blood loss (EBL) was 500 ml (50–5000 ml) and mean EBL was 696 ml (SD 677). Median length of surgery was 287 minutes (114–595 minutes) with mean surgery length 295 minutes (SD 78.7). The majority of the patients were white (251/265, 95%). One hundred and eighty seven patients (187/265, 71%) had papillary serous

histology. Optimal surgical cytoreduction was achieved in 216 patients (216/265, 82%) while 49 patients (49/265, 19%) were suboptimally cytoreduced. One hundred and eighty seven patients (187/265, 71%) had advanced disease and 209 patients (209/265, 79%) had high-grade tumors. One hundred and eighty five patients (185/265, 70%) had their fascia closed with running suture. Surgical site infection occurred in 32 (32/265, 12%) patients.

The majority of patients (238/265, 90%) received IV platinum and taxane combination chemotherapy. The mean number of cycles of adjuvant chemotherapy received was the same in patients with hernia (5.61, SD=1.35, p=0.49) and without hernia (5.83, SD=1.05). No woman in either group received more than 8 cycles of adjuvant chemotherapy. Data regarding time to recurrence was not made available for this study.

The overall incidence of early incisional hernias was 9.8% (95% CI, 6.2%−12%, n=26/265), while the incidence of late-occurring hernias was an additional 7.9% (95% CI, 4.1%−12%, n=15/189). The hernia detection rate was split nearly evenly between physical examination and CT scan (56% and 44% respectively). Obesity was the only limiting factor for detection on examination.

At the 1-year time point for early hernia formation, univariate analysis showed that nutritional status (preoperative albumin ≤ 3 g/dL, RR 60, p<0.001), sub-optimal cytoreduction (RR 5.1, p<0.001), surgical site infection (RR 2.7, p=0.024), and BMI > 30 kg/m^2 (RR 3.2, p=0.003) may be associated with increased risk for incisional hernias (Table 2). However, after incorporating nutritional status, cytoreduction status, surgical site infection, BMI, type of fascial closure and age into a multivariate model, only nutritional status (RR 48, p<0.001) and sub-optimal cytoreduction (RR 4.3, p<0.001) remained significantly correlated with development of incisional hernias. For the 2-year time point corresponding to late hernia formation, age ≥ 65 years (RR 3.7, p=0.014) was the only factor associated with formation of incisional hernias after multivariate modeling (Table 3). This represents a risk factor for patients who did not develop a hernia during their first year.

All patients who had an incisional hernia were evaluated by a general surgeon who specializes in hernia repairs. We recommend this approach be taken to identify the most appropriate candidates and to establish care in the event they need surgical correction close to the time of hernia diagnosis, or emergently in the future. Seven of the patients involved in this study had an elective hernia repair after their consultation. No patient required emergent surgical correction of their hernia.

DISCUSSION

Our study found that approximately 10% of women will have incisional hernias one year after laparotomy for ovarian cancer. Suboptimal cytoreduction and poor nutritional status are significant factors for this occurrence. Remarkably, an additional 7.9% will have an incisional hernia diagnosed one to 2 years after surgery – nearly doubling the overall incidence of incisional hernias in this population. Age appears to be the only significant factor in this one to 2 year postoperative period. These factors are valuable for both pre- and

post-operative counseling. This data can also serve as a helpful reminder for the clinician to remain vigilant during the initial cancer surveillance period – especially in the elderly.

Suboptimal cytoreduction as a risk factor for incisional hernias is an important finding. One reason for this result could be that residual tumor burden strips the body of nutritional resources that would otherwise be dedicated to optimal wound healing. This data provides additional incentive to achieve optimal cytoreduction (18,19).

Nutritionally depleted patients develop significantly more early hernias than well-nourished counterparts. Poor nutrition causes suboptimal fascial healing, leading to early hernias as tissues break down (20). Unfortunately, it can prove difficult to significantly improve the nutritional status of ovarian cancer patients. Even for patients who need parenteral nutrition, the optimal duration to improve wound healing is unknown.

Patients over the age of 65 had an increased incidence of late-appearing incisional hernias. Elderly patients have hematologic issues, vascular deficiencies, and neurologic abnormalities that could account for long-term deficits of fascial tensile strength (21). Existing data suggest that a running closure with delayed absorbable suture is still the most appropriate intervention to decrease risk – even in the elderly (8,9,14).

We were unable to find any correlation with chemotherapy characteristics and the development of incisional hernias. However, because only 5% of patients received intraperitoneal chemotherapy, the data is unlikely powered to detect any association. A previous report in which 36.4% of patients received intraperitoneal chemotherapy did identify it as an independent risk factor (22). Although bevacizumab has also been found to hasten the onset of incisional hernia formation (23), our institution did not routinely use it for primary therapy during the study period. It is thus uncertain how our data may apply to women treated with these two modalities. In general, the risk factors found in this analysis should be applicable to most patients as carboplatin and paclitaxel remain the mainstays of adjuvant therapy.

Traditional risk factors for incisional hernias (e.g. obesity, diabetes and surgical site infection) seen in the general surgery literature were not identified. However, our results are in keeping with previous studies of ovarian cancer patients. Rettenmaier et al reported that BMI did not affect hernia formation with an average BMI of 27.37 kg/m^2 – nearly the same as our data (22). Long et al found BMI to be significant, but their patients had a lower median BMI (25.0 kg/m^2) (23). Neither of those two studies found diabetes alone nor surgical site infection at one year to correlate with hernia formation.

It is impossible to say why these risk factors may not be applicable in ovarian cancer. It may be because chemotherapy, suboptimal cytoreduction and nutritional status are increasingly important for these patients and other factors no longer play as significant a part in hernia development.

The strengths of our study include the large number of patients for which the known risk factors for incisional hernias were collected and a population consisting entirely of ovarian cancer patients. Limitations include the low number of events and patients lost to follow-up

which may affect the power to detect differences, as well as its retrospective nature which introduces both information bias and selection bias.

Important areas for future study include investigating prophylactic nutrition supplementation (24) and the prevention of hernia formation. Secondly, there has been considerable discussion about the use of prophylactic mesh to prevent hernias in high risk patients (25–27).

The Ventral Hernia Working Group (VHWG) has created a grading system for assessing the potential for hernias (28). A prospective study investigating its validity and clinical utility for ovarian cancer patients may be valuable. Additionally, studying how adherence to the VHWG evidence-based guidelines may reduce hernia incidence may be informative. Ultimately, a prospective trial utilizing mesh placement at the time of primary surgery may be warranted for those identified as high risk. The primary outcome should report incidence of incisional hernias 2 years after laparotomy based on our data showing an additional 7.9% of patients will develop a hernia one to 2 years after surgery.

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Table 1:

Patient Characteristics

Variable		1 Year	2 Years
		n=265 (%)	n=189(%)
Age	Under 65 Years	177 (67)	134 (71)
	Over 65 Years	88 (33)	55 (29)
BMI	Obese (≥ 30 kg/m^2)	99 (37)	66 (35)
	Non-Obese (< 30 kg/m^2)	166 (63)	123 (65)
Race	White	251 (95)	180 (95)
	Others	14 (5)	9 (5)
Diabetes Mellitus	Present	26 (10)	16 (9)
	Absent	239 (90)	173 (92)
Nutritional Status	Normal	187 (71)	145 (77)
	Depleted	69 (26)	38 (20)
	Unknown	9 (3)	6 (3)
Disease Stage	Early (Stages I, II)	78 (29)	58 (31)
	Late (Stages III, IV)	187 (71)	131 (69)
Cell Histology	Papillary Serous	187 (71)	130 (69)
	Other	77 (29)	59 (31)
	Unknown	1 (0)	0
Pathology Grade	1 & 2	56 (21)	42 (22)
	3	209 (79)	147 (78)
Cytoreductive Surgery	Optimal	216 (82)	156 (87)
	Suboptimal	49 (19)	24 (13)
Closure Technique	Running	185 (70)	132 (70)
	Other	80 (30)	57 (30)
Estimated Blood Loss	Less than 800 mL	189 (71)	137 (73)
	More than 800 mL	76 (29)	52 (28)
Chemotherapy Mode	Intravenous	238 (90)	169 (89)
	Intraperitoneal	12 (5)	10 (5)
	None	15 (6)	10 (5)
Surgical Site Infection	Present	32 (12)	18 (10)
	Absent	233 (88)	171 (91)
Hernia Incidence	Present	26 (10)	15 (8)
	Absent	239 (90)	174 (92)

Table 2:

Risk Factors for Ventral Hernia in First Year after Surgery

			Univariate			Multivariate[a,b]		
Variable		**% with Hernia**	**Relative Risk**	**95 % CI**	**P-value**	**Relative Risk**	**95 % CI**	**P-value**
Race	Other	14.3	1.5	(0.39 – 5.7)	0.64			
	White	9.6						
Diabetes	Present	7.7	0.77	(0.19 –3.1)	1.000			
	Absent	10.0						
Nutritional Status	Deficient	31.9	***60***[c]	***(8.2 – 434)***	***<.001***	***48***	***(14 –164)***	***<.001***
	Normal	0.5						
Cancer Stage	Late	9.6	0.94	(0.43 – 2.1)	0.83			
	Early	10.3						
Histology	Serous	9.6	1.1	(0.46 – 2.4)	1.000			
	Other	9.1						
Pathology Grade	3	10.1	1.1	(0.44 – 2.9)	1.000			
	1 or 2	8.9						
CRS	Sub-optimal	28.6	***5.1***	***(2.5 – 10)***	***<.001***	***4.3***	***(2.5– 7.3)***	***<.001***
	Optimal	5.6						
Fascia closure	Other	15.0	2.0	(0.96 – 4.1)	0.073			
	Running	7.6						
Chemo Mode	IP	8.3	0.79	(0.12 – 5.4)	1.000			
	IV	10.5						
Surgical Site Infection	Present	21.9	***2.7***	***(1.2 – 5.9)***	***0.024***	1.4	(0.78 – 2.5)	0.25
	Absent	8.2						
Age	≥ 65 yrs	5.7	0.48	(0.19 – 1.2)	0.13			
	< 65 yrs	11.9						
BMI[d]	Obese	17.2	***3.2***	***(1.5 – 6.8)***	***0.003***	1.4	(0.81 – 2.3)	0.25
	Non-obese	5.4						
EBL	≥ 800 mL	11.8	1.3	(0.61 – 2.8)	0.50			
	< 800 mL	9.0						

[a]Model included nutritional status, CRS, surgical site infection, and BMI as well as adjustment for fascial closure and age.

[b]The multivariate analysis column contains empty cells because only variables with p<0.05 on univariate analysis were tested in the model.

[c]Bolded values represent those significant at p<0.05.

[d]Obese = BMI ≥ 30 kg/m^2; Non-obese = BMI < 30 kg/m^2

Abbreviations: CRS = cytoreductive surgery, BMI = body mass index, EBL = estimated blood loss

Table 3:

Risk Factors for Ventral Hernia in Second Year after Surgery

			Univariate			Multivariate[a,b]		
Variable		**% with Hernia**	**Relative Risk**	**95 % CI**	**P-value**	**Relative Risk**	**95 % CI**	**P-value**
Race	Other	0.0	0	(0–3.5)	1.000			
	White	8.3						
Diabetes	Present	6.3	0.77	(0.11 – 5.5)	1.000			
	Absent	8.1						
Nutritional Status	Deficient	10.5	1.4	(0.47 – 4.1)	0.52			
	Normal	7.6						
Cancer Stage	Late	6.1	0.51	(0.19 – 1.3)	0.24			
	Early	12.1						
Histology	PS	8.5	1.3	(0.41 – 3.8)	0.78			
	Other	6.8						
Pathology Grade	3	9.5	4.00	(0.54 –29)	0.20			
	1 or 2	2.4						
CRS	Sub-optimal	12.5	1.7	(0.52 – 5.7)	0.41			
	Optimal	7.3						
Fascia closure	Other	10.5	1.5	(0.58 – 4.1)	0.39			
	Running	6.8						
Chemo Mode	IP	0.0	0	(0–3.0)	1.000			
	IV	8.9						
Surgical Site Infection	Present	11.1	1.5	(0.36 –6.0)	0.64			
	Absent	7.6						
Age	≥ 65 yrs	16.4	***3.7***[c]	***(1.4 – 9.8)***	***0.014***	***3.5***	***(1.3 – 9.4)***	***0.01***
	< 65 yrs	4.5						
BMI[d]	Obese	10.6	1.6	(0.62 – 4.3)	0.40			
	Non-obese	6.5						
EBL	≥ 800 mL	5.8	0.66	(0.19 – 2.2)	0.76			
	< 800 mL	8.8						

[a] Model includes age and adjustment for pathologic grade.

[b] The multivariate analysis column contains empty cells because only variables with p<0.05 on univariate analysis were tested in the model.

[c] Bolded values represent those significant at p<0.05.

[d] Obese = BMI ≥ 30 kg/m^2; Non-obese = BMI < 30 kg/m^2

Abbreviations: CRS = cytoreductive surgery, BMI = body mass index, EBL = estimated blood loss