

Symptoms of Ovarian Cancer

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OBJECTIVE: To examine the symptoms of ovarian cancer in patients compared with symptoms experienced by healthy women using a case-control design.

METHODS: Cases ($n = 168$) were women with ovarian cancer diagnosed at two hospitals in New York between 1994 and 1997 who were interviewed shortly after diagnosis. They were compared with healthy women ($n = 251$ controls) from the community. Women were asked about the prevalence, duration, and constancy of eight symptoms and about use of three types of medications in the 6 to 12 months before diagnosis (cases) or interview (controls).

RESULTS: Nearly all the cases (93%) reported at least one symptom, compared with 42% of controls. The most common symptoms among cases were: unusual bloating, fullness, and pressure in the abdomen (71%); unusual abdominal pain or lower back pain (52%); and lack of energy (43%). The proportions of controls reporting these symptoms were 9, 15, and 16%, respectively, resulting in odds ratios and 95% confidence intervals of 25.3 (15.6, 40.9), 6.2 (4.0, 9.6), and 3.9 (2.5, 6.1), respectively, for these symptoms. Bloating, fullness, and pressure was of more recent onset among cases than controls (4.9 months compared with 7.6 months, $P = .01$). There were only minor differences in reported symptoms between cases with early and later stage disease.

CONCLUSION: Unusual bloating, fullness, and pressure, abdominal or back pain, and lack of energy are prominent symptoms in women with ovarian cancer and distinguish them from controls. Information on symptoms may make women and physicians more aware of changes associated with ovarian cancer. (Obstet Gynecol 2001;98:212-7. © 2001 by the American College of Obstetricians and Gynecologists.)

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Ovarian cancer strikes about 23,000 women each year in the United States, and about 14,000 women die of this disease.¹ Prognosis is good for women diagnosed at an early stage, whereas the majority, diagnosed at later stages, are likely to survive less than 5 years.² Few studies have systematically examined the symptoms experienced by women before diagnosis of ovarian cancer, and none have done so in light of the background level of common symptoms in unaffected women. Information on symptoms might make women more aware of changes that are indicative of disease and lead to their seeking help more aggressively and might lead physicians to conduct appropriate exploratory tests when symptoms are present.

We investigated the presence, duration, and constancy of various symptoms of ovarian cancer and use of medications in a case-control study conducted in the New York metropolitan area from 1994–1997. We also evaluated the presence of symptoms in women with earlier and later stage disease to determine whether there were specific symptoms associated with earlier stage.

MATERIALS AND METHODS

Cases for this study were identified at two hospitals in New York City, Memorial Sloan-Kettering Cancer Center and New York Presbyterian Hospital, from 1994–1997. Women with ovarian cancer were eligible if they were aged 18 and over, resided in the United States, spoke English or Spanish, and were considered by their physicians to be well enough to take part. Eligible cases were approached while in the hospital for surgery or chemotherapy. The mean time from diagnosis to interview was 4.7 months, and 73% were interviewed within 9 months. Because of the difficulty in recruiting controls in an urban area, we used different sources of controls. Controls from the community were recruited by random digit dialing ($n = 81$) or from commercial mailing lists ($n = 78$). These methods are described in detail elsewhere.³ The controls located by random digit dialing were matched to the cases by 5-year age groups, whereas those from the commercial mailing lists were matched to

the cases on demographic, socioeconomic, and lifestyle characteristics based on their zip+4 codes. We also recruited convenience controls, consisting of friends of cases and other women ($n = 92$) at Memorial Sloan-Kettering Cancer Center and New York Presbyterian Hospital. The convenience controls were not matched to cases. The study was approved by the Institutional Review Boards at both institutions, and informed consent was obtained from all participants.

Women completed an interview designed to provide information on a wide range of possible risk factors for ovarian cancer. To determine symptoms of ovarian cancer, we asked women whether they had experienced eight symptoms or used three types of medications in the 6–12 months before diagnosis (for cases) or before the interview (for controls). Those women who did report a symptom were questioned about its duration and whether it was continuous or intermittent. Parallel questions were asked of those who had used medications. The specific symptoms and medications, in the order in which they appeared in the questionnaire, were: unusual abdominal or lower back pain; unusual bloating, fullness, and pressure in the abdomen or pelvis; nausea; unusual constipation; laxatives to prevent constipation; unusual diarrhea; medicine to prevent diarrhea; unusual lack of appetite; frequent urination, urgency or burning; unusual lack of energy; use of any pain killers; and any other symptoms. The symptoms were selected based on reviews of earlier reports in the literature and in consultation with clinicians, and the medications were those commonly used for these symptoms.

Another section of the questionnaire included questions on ability to digest milk products, development of diarrhea, stomach cramps, or severe gas after consuming dairy products or when under stress, and whether or not respondents thought they had a “sensitive stomach.” For both cases and controls, we also collected a detailed family history of cancer and information on diet using a food frequency questionnaire, as well as blood and saliva samples to be used for analyses of genes and antibodies. Data on stage at diagnosis were obtained from hospital records. Earlier stage encompassed International Federation of Gynecology and Obstetrics stages I and II, and later stage encompassed stages III and IV. Stages III and IV tumors have microscopic peritoneal metastases beyond the pelvis (T3) and/or lymph node involvement (any N) or distant metastases (M1).⁴

We used SAS (SAS Institute, Cary, NC) to analyze the data and present odds ratios (OR) and 95% confidence intervals (CI) based on the χ^2 test to describe differences between cases and controls. Differences between means were compared by t -tests for independent samples.

Table 1. Characteristics of Cases With Ovarian Cancer and Controls

Characteristic	Cases ($n = 168$)		Controls ($n = 251$)	
	n	%	n	%
Age (y)				
<40	28	17	72	29
40–49	44	26	82	33
50–59	52	31	48	19
60–69	27	16	28	11
≥70	17	10	21	8
Parity				
Nulliparous	65	39	84	33
1–2 children	65	39	100	40
3 or more children	38	23	67	27
Family history*				
Ovarian cancer	10	6	3	1
Breast or ovarian cancer	38	23	29	12
Oral contraceptives				
Ever used	75	45	170	68
Digestive problems				
Any digestive problems	86	51	126	50

* In first-degree relatives.

RESULTS

Table 1 shows the distribution of known risk and protective factors for ovarian cancer for the 168 cases with ovarian cancer and 251 controls. Cases were older and were more likely to be nulliparous and to have a family history of breast or ovarian cancer in first-degree relatives. They were less likely to have used oral contraceptives. About half the cases and controls had experienced any of the digestive problems we asked about.

Nearly all the cases (93%) reported at least one symptom, compared with 42% of the controls. The mean number of symptoms in cases was 3.0 ± 1.8 , compared with 0.8 ± 1.3 in the controls ($P < .001$). As shown in Table 2, the most common symptom among the cases was unusual bloating, fullness, and pressure in the abdomen or pelvis, mentioned by 71% of cases and 9% of controls (OR 25.3, 95% CI 15.6, 40.9). Abdominal or lower back pain was also a common symptom, mentioned by 52% of cases and 15% of controls (OR 6.2, 95% CI 4.0, 9.6). Lack of energy was noted by 43% of the cases and 16% of the controls (OR 3.9, 95% CI 2.5, 6.1). Frequent urination, urgency, or burning was experienced by 33% of the cases and 12% of controls (OR 3.5, 95% CI 2.2, 5.7). Other symptoms among cases were less common: constipation, 21%; lack of appetite, 20%; diarrhea, 16%; and nausea, 13%. Although only one-fifth of the cases mentioned lack of appetite, this was much more common among cases than controls (OR 8.8, 95% CI 4.3, 18.2). Thirty-five percent of the cases mentioned other symptoms that were not on our list. The most

Table 2. Symptoms Experienced and Medications Used by Cases With Ovarian Cancer and Controls in the 6–12 Months Before Diagnosis or Interview

Symptoms/medications	Cases (<i>n</i> = 168)		Controls (<i>n</i> = 251)		Odds ratio (95% CI)
	<i>n</i>	%	<i>n</i>	%	
Any symptom	156	93	106	42	
Unusual bloating, fullness, and pressure in the abdomen or pelvis	119	71	22	9	25.3 (15.6, 40.9)
Unusual abdominal or lower back pain	87	52	37	15	6.2 (4.0, 9.6)
Unusual lack of energy	72	43	40	16	3.9 (2.5, 6.1)
Frequent urination, urgency, or burning	55	33	31	12	3.5 (2.2, 5.7)
Unusual constipation	36	21	18	7	3.5 (2.0, 6.3)
Unusual lack of appetite	34	20	7	3	8.8 (4.3, 18.2)
Unusual diarrhea	27	16	15	6	3.0 (1.6, 5.7)
Nausea	21	13	22	9	1.5 (0.8, 2.8)
Other symptoms	59	35	19	8	6.6 (3.9, 11.2)
Analgesics	29	17	44	18	1.0 (0.58, 1.6)
Laxatives	19	11	18	7	1.6 (0.84, 3.2)
Antidiarrheals	8	5	4	2	3.1 (1.0, 9.9)

CI = confidence interval.

common was pain in the side or ribs, mentioned by seven cases.

Use of medications by cases was fairly low: 17% used analgesics; 11% used laxatives; and 5% used medicine for diarrhea, and results were similar for controls. Cases who experienced bloating, fullness, and pressure were significantly less likely than controls with this symptom to use analgesics (19% compared with 41%) or laxatives (12% compared with 32%).

We examined reported symptoms according to characteristics that are related to ovarian cancer or that might have influenced reporting of symptoms: age, parity, oral contraceptive use, history of breast or ovarian cancer in a first-degree relative, and having a history of digestive problems. Overall, there was little association between

these factors and reporting of symptoms in either cases or controls. Controlling for these variables in logistic regression models resulted in ORs (not shown) that were similar to the unadjusted ORs shown in Table 2.

As shown in Table 3, all of the symptoms were of more recent onset in cases. The largest differences were noted for bloating, fullness, and pressure ($P = .01$), nausea ($P = .05$), and other symptoms ($P = .02$). Use of analgesics also began more recently for cases than for controls ($P = .01$).

For each symptom that women experienced, we asked whether they experienced it constantly or intermittently. Cases who experienced bloating, fullness, and pressure were more likely to report that this symptom was constant than were controls who reported this symptom

Table 3. Mean (Standard Deviation) Number of Months Symptoms Were Experienced and Medications Used by Cases With Ovarian Cancer and Controls

Symptoms/medications	Cases (<i>n</i> = 168)		Controls (<i>n</i> = 251)		<i>P</i>
	Mean (SD)	<i>n</i>	Mean (SD)	<i>n</i>	
Unusual bloating, fullness, and pressure in the abdomen or pelvis	4.9 (4.2)	108	7.6 (4.4)	20	.01
Unusual abdominal or lower back pain	6.1 (4.7)	78	6.4 (4.7)	35	.77
Unusual lack of energy	5.7 (4.5)	63	7.5 (6.7)	40	.14
Frequent urination, urgency, or burning	5.5 (4.9)	48	7.5 (5.0)	31	.08
Unusual constipation	5.9 (5.3)	31	7.3 (4.6)	16	.40
Unusual lack of appetite	3.1 (2.5)	31	4.7 (5.0)	7	.44
Unusual diarrhea	5.1 (4.3)	26	6.1 (4.6)	14	.47
Nausea	3.1 (2.8)	20	5.4 (4.4)	22	.05
Other symptoms	5.3 (4.0)	52	8.2 (4.9)	18	.02
Analgesics	6.5 (4.9)	26	10.5 (7.6)	43	.01
Laxatives	9.0 (6.4)	16	7.4 (4.1)	17	.39
Antidiarrheals	7.0 (4.2)	7	3.0 (2.0)	3	.16

SD = standard deviation.

Table 4. Symptoms Experienced and Medications Used by Patients With Early and Late Stage Ovarian Cancer

Symptoms/medications	Early stage (<i>n</i> = 37)		Late stage (<i>n</i> = 118)		Odds ratio* (95% CI)
	<i>n</i>	%	<i>n</i>	%	
Any symptom	33	89	110	93	
Unusual bloating, fullness, and pressure in the abdomen or pelvis	24	65	84	71	1.3 (0.61, 2.9)
Unusual abdominal or lower back pain	18	49	61	52	1.1 (0.54, 2.4)
Unusual lack of energy	10	27	54	46	2.3 (1.0, 5.1)
Frequent urination, urgency, or burning	13	35	37	32	0.87 (0.40, 1.9)
Unusual constipation	11	30	25	21	0.64 (0.28, 1.5)
Unusual lack of appetite	3	8	26	22	3.2 (0.96, 10.7)
Unusual diarrhea	10	27	16	14	0.42 (0.18, 1.0)
Nausea	5	14	13	11	0.79 (0.26, 2.4)
Other symptoms	8	22	46	39	2.2 (0.92, 5.2)
Analgesics	4	11	22	19	1.9 (0.61, 5.8)
Laxatives	5	14	13	11	0.79 (0.26, 2.4)
Antidiarrheals	5	14	3	3	0.17 (0.04, 0.64)

CI = confidence interval.

* Late stage compared with early stage.

(62% compared with 36%, OR 2.8, 95% CI 1.1, 7.1). The other symptoms likely to be experienced constantly were unusual lack of energy and lack of appetite, but cases and controls were similar in reporting these symptoms as constant. Urinary symptoms and nausea were more likely to be intermittent among cases than controls (data not shown).

We examined results comparing cases with community controls, excluding convenience controls. In general, the convenience controls had slightly fewer symptoms than the community controls, resulting in slightly lower ORs for individual symptoms when they were excluded. However, the conclusions about the importance of the major symptoms and their duration and

constancy were similar with the convenience controls excluded (data not shown).

Among the patients with ovarian cancer, there were 37 with earlier stages (I or II) and 118 with later stages (III or IV). (Thirteen patients for whom staging was considered to be incomplete were excluded from this analysis.) There were few differences between those with early and late stage in reported symptoms or use of medications (Table 4). Eighty-nine percent of patients with early stage disease reported one or more symptoms. Unusual lack of energy was reported more frequently by women with later stage disease (OR 2.3, 95% CI 1.0, 5.1), as were symptoms that were volunteered by the patients (OR 2.2, 95% CI 0.92, 5.2). There was an

Table 5. Mean Number of Months Symptoms Were Experienced and Medications Used by Patients With Early and Late Stage Ovarian Cancer

Symptoms/medications	Early stage (<i>n</i> = 37)		Late stage (<i>n</i> = 118)		<i>P</i>
	Mean (SD)	<i>n</i>	Mean (SD)	<i>n</i>	
Unusual bloating, fullness, and pressure in the abdomen or pelvis	6.4 (4.3)	20	4.5 (4.1)	77	.08
Unusual abdominal or lower back pain	7.9 (4.5)	17	5.6 (4.8)	53	.09
Unusual lack of energy	6.9 (4.4)	9	5.3 (4.5)	47	.34
Frequent urination, urgency, or burning	6.7 (5.1)	11	4.6 (3.6)	32	.13
Unusual constipation	5.4 (4.3)	9	6.1 (5.7)	22	.75
Unusual lack of appetite	5.3 (2.3)	3	3.0 (2.6)	24	.15
Unusual diarrhea	8.1 (4.8)	9	3.6 (3.2)	16	.009
Nausea	5.0 (4.3)	5	2.8 (2.0)	12	.33
Other symptoms	6.0 (3.5)	7	5.3 (4.1)	40	.65
Analgesics	9.5 (5.0)	4	5.9 (4.9)	19	.20
Laxatives	7.0 (7.6)	4	9.5 (6.5)	11	.55
Antidiarrheals	7.0 (3.7)	4	7.0 (5.6)	3	1.0

SD = standard deviation.

indication that unusual diarrhea and the use of medicine to prevent diarrhea were somewhat more common in earlier-stage patients: the OR for unusual diarrhea and later stage disease was 0.42 (95% CI 0.18, 1.0) and the OR for use of medicine to prevent diarrhea was 0.17 (95% CI 0.04, 0.64).

Comparing women with early and late stage disease, we found that most of the symptoms were experienced for a longer period of time by women with early stage disease, as shown in Table 5.

Compared with controls, women with early stage disease were much more likely to report bloating, fullness, and pressure (OR 19.2, 95% CI 9.9, 37.5). Other symptoms strongly associated with risk of early stage disease were abdominal or back pain, constipation, and diarrhea, with ORs of 5.5 (95% CI 2.8, 10.8), 5.5 (95% CI 2.5, 12.0), and 5.8 (95% CI 2.6, 13.1), respectively. Risk associated with use of antidiarrheals was also elevated (OR 9.6, 95% CI 3.1, 30.3) (data not shown).

DISCUSSION

Symptoms of ovarian cancer are often described as non-specific, but the prevalence of these symptoms among healthy women, and the extent to which prevalence differs between cases and healthy women, have not been studied previously. Our results indicate that although the eight symptoms we asked about are fairly common, the prevalence of each symptom was much higher among the cases, with the exception of nausea. In addition, all of the symptoms were of more recent onset among the cases.

Our finding that a high proportion of women with ovarian cancer noted some symptoms in the months before diagnosis is consistent with reports of case series,⁵⁻⁸ which found that nearly all patients had symptoms. Another study⁹ found that about 80% did so, whereas another that asked cases whether they had symptoms that prompted them to seek a diagnosis¹⁰ found that only 68% said yes. Our findings among cases are in general agreement with reports based on case series that bloating, fullness, and pressure in the abdomen is the most prominent symptom, with pain and fatigue also important, followed by problems with urination and constipation.^{5,6,8-12} Similar information is available on the Internet through organizations such as the American Cancer Society,¹³ Ovarian Cancer National Alliance,¹⁴ and the National Ovarian Cancer Coalition.¹⁵

The present study indicates that bloating, fullness, and pressure in the abdomen was much more likely to be constant, rather than intermittent, in cases compared with controls; it was also of significantly shorter dura-

tion. Cases with this symptom were less likely than controls to use analgesics or laxatives. These findings suggest that there is a qualitative difference in how this symptom is experienced by cases and controls that affects their use of medications.

In our study, a large majority of women with early stage disease also reported symptoms in the months before diagnosis. In contrast to our findings, some oncology texts state that the disease is asymptomatic in its early stages.^{16,17} Other studies^{7,8,10} have also shown that women diagnosed at early stages are very likely to have symptoms. Diarrhea and use of medication for diarrhea, while experienced by a relatively small proportion of patients, was the only symptom and medication that was more common in early stage than in later stage patients. Women with early stage cancer reported longer duration for nearly all symptoms, indicating that cancer diagnosed at later stages is a more aggressive entity.

The large ORs for symptoms in cases compared with controls reflect, to some extent, recall bias because those who have been diagnosed are likely to have thought about how they felt before diagnosis. Our study was limited by relatively small numbers of cases, especially with early disease. Particularly in analyses of women with early and late stage cancer, we had sufficient numbers to detect only relatively large differences, and our findings need to be confirmed in larger studies. We used a lengthy questionnaire, collected biologic specimens, and conducted our study in the New York area, factors which led to low response.³ Although our controls included a convenience sample as well as randomly chosen community controls, the results did not differ in meaningful ways when the convenience controls were excluded. In future studies, more open-ended questions allowing women to describe their symptoms in their own words and to indicate how the symptoms changed over time and their responses to them would provide additional information that might be useful in identifying symptoms of early stage disease.

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