Effect of delays in primary care referral on survival of women with epithelial ovarian cancer: retrospective audit

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Abstract

Objective To examine referral pathways from primary care for patients with epithelial ovarian cancer and to identify factors related to survival at 18 months.
Design Retrospective review of patient notes.
Setting General practices and receiving hospitals within Mersey region.
Subjects 135 patients with epithelial ovarian cancer identified from an audit in the Mersey area between 1992 and 1994.
Main outcome measures Delays between onset of symptoms and treatment attributable to patient, general practitioner, and hospital.
Results 105 (78%) women first presented to their general practitioner within four weeks of the onset of symptoms. 99 (73%) women were referred to hospital by their general practitioners within four weeks of presentation, and 95 (70%) were seen in hospital within two weeks of referral. Multivariate analysis with survival as the dependent variable identified age (odds ratio 0.96, 95% confidence interval 0.93 to 0.99) cancer stage III or more (0.15, 0.05 to 0.43), and non-specific symptoms (0.36, 0.14 to 0.89) as significant variables.
Conclusion Most patients attended their general practitioner within four weeks and were referred within two weeks. No evidence was found that delays in referral or diagnosis adversely affected survival at 18 months. Stage of disease at surgery was the most important adverse factor. An effective screening programme is the most likely method to improve survival.

Introduction

Reported cancer survival rates in Britain compare unfavourably with those in Europe[1] and North America.[2] The reasons for this are multiple and complex. In breast and colorectal cancer, the differences occur in the first six months after diagnosis.[3] This might be explained by later presentation or delays in diagnosis and treatment. The same may be true of ovarian cancer, a disease with insidious onset and in which three quarters of patients present with advanced stage disease when cure is unlikely.[4] A recent NHS initiative seeks to guarantee that "everyone suspected of having ovarian cancer will be seen by the appropriate specialist within two weeks of their General Practitioner requesting an urgent appointment."[5] It has resulted in various programmes, such as the Cancer Collaborative Project, aimed at increasing awareness of certain cancers, facilitating referral, and streamlining management.

Although the aim of the initiative seems laudable, it assumes that there are currently large delays in referral, diagnosis, and treatment. However, evidence to confirm this belief is lacking because delays in presentation and referral have not been investigated in Britain. The aim of this study was to identify referral pathways from primary care for women with ovarian cancer. In particular, we examined delays between the onset of symptoms and presentation to the general practitioner and delays between presentation and referral to hospital.

Methods

We reviewed the general practice records of patients with epithelial ovarian cancer whom we had previously identified from a network audit of epithelial ovarian cancer in the Mersey area between 1992 and 1994. The audit was authorised by the directors of public health in local health authorities, the local medical committees, and individual family doctors of patients who were still alive at the time of the study. We used the records to identify the patient referral pathway from primary care to hospital treatment. The data set included the number of appointments in the 12 months before the appointment that generated the hospital referral. A patient episode was defined as an appointment with or visit to the general practitioner. Repeat prescriptions, telephone advice, or nurse led clinics were not included.

We calculated the duration of symptoms before attending the general practitioner (patient interval), the time between the first presentation and subsequent referral (general practice interval), and time between attending hospital and definitive treatment (hospital interval) for each patient. The hospital department the patient was referred to, age at first presentation, and death or survival at five years were also recorded. We determined the International Federation of Gynaecology and Obstetrics (FIGO) stage[6] by reviewing the operation notes and histology. For logistic regression, we categorised stage into $\geq$III or $<$III. Women in whom stage was not discernible

were included in stage III as audit results indicated that the mean survival for this group was the same as stage III. We also extracted clinical data from the notes: symptoms at presentation to general practice and hospital, number of general practice appointments in the 12 months before referral, hospital department referred to, preoperative suspicion of ovarian cancer, and stage.

We calculated the total patient pathway duration (in days) from first symptoms to death for all patients by totalling the patient, general practitioner, general practitioner to hospital, hospital, and treatment to death intervals. Patients were then divided into two groups: survival greater than 18 months and less than 18 months. Eighteen months is the mean length of survival after treatment for patients with stage III ovarian cancer.[4]

We analysed the data using SPSS version 10. We used the χ^2 test, t test, and Mann-Whitney U test as appropriate in univariate analyses to identify factors related to survival, with Bonferroni's correction for multiple analyses. For covariates that were significant ($P<0.01$), we did multiple logistic regression with survival at 18 months as the dependent variable.

Table 1 Characteristics of women with ovarian cancer according to length of survival. Values are numbers (percentages) of women unless stated otherwise

Factor	Survival		P value
	>18 months (n=81)	<18 months (n=54)	
Stage:			
I	17 (21)	4 (7)	0.0002†
II	16 (20)	1 (2)	
III	31 (38)	25 (46)	
IV	12 (15)	10 (19)	
Not determined	5 (6)	14 (26)	
≥III	48 (59)	49 (91)	0.0001
Debulking <2 cm	31 (40)	7 (17)	0.01
Mean age (years)	63.7	69.0	0.014
Median (range) No of GP appointments	4 (0-33)	4.5 (0-22)	0.574*
Hospital department referred to:			
Accident and emergency	16 (20)	10 (19)	0.423†
General surgery	14 (17)	13 (24)	
Gynaecology	40 (49)	20 (37)	
Physicians	11 (14)	11 (20)	
Median (range) interval (days):			
Patient	7 (1-395)	14 (1-220)	0.166*
General practice	7 (0-420)	1 (1-210)	0.345*
General practice to hospital	7 (0-190)	4 (1-10)	0.041*
Hospital	25 (1-720)	21 (1-400)	0.255*

*Mann Whitney U test.
†χ^2 test.

Results

We identified 135 patients for whom the general practice notes were available for review. Table 1 shows their characteristics according to length of survival. Eighty one patients (60%) survived more than 18 months after onset of symptoms.

Forty two patients (31%) attended their general practitioner on two or fewer occasions; 14 (10%) did not visit a general practitioner during the previous year. Twenty two patients consulted their general practitioners 2-5 times, and 57 (42%) consulted 10 or more times. Seven patients (5%) attended their general practitioner at least once a month.

One hundred and five patients (78%) presented to the general practitioner within one month of developing symptoms and 64 (47%) within two weeks. Only 11 patients (8%) delayed more than three months before seeking medical advice (table 2). Primary symptoms in the patients' notes were abdominal swelling (25 patients), abdominal pain (65), change in bowel habit (34), weight loss (11), backache (3), vaginal bleeding (15), and other (30). Eleven patients (8%) were asymptomatic and referral was initiated after routine examination or investigation for concurrent illnesses.

General practitioners referred 68 (50%) patients to hospital directly after their first consultation, 82 (60%) within 2 weeks, and 99 (73%) within one month (table 2) experienced delays over three months, half of whom were misdiagnosed as having irritable bowel syndrome. Twenty eight (21%) patients had a pelvic examination.

Sixty (44%) patients were referred directly to a gynaecology department, including 15 (11%) to the designated lead gynaecologist for cancer. Twenty six patients (19%) were referred to the accident and emergency department (table 1). Definitive treatment was delayed in two thirds of patients because of investigation by other hospital departments before referral to the gynaecologist.

The mean duration of symptoms at the time of attendance at hospital was 95.3 (SD 15.1) days. The median time from the general practice referring appointment to the woman being seen in the hospital was six days (range 0-190). Two women were immediately referred by telephone and seen the same day; one woman refused referral until terminally ill. Seventy two patients (53%) were seen in hospital within one week of the appointment, 95 (70%) within two weeks, and 115 (85%) within a month (table 2).

The mean age of the survivors was less than that of patients who died (63.7 years *v* 69.0 years, $P=0.014$). The general practitioner to hospital interval was longer in patients who survived (median 7 days *v* 4 days, $P=0.041$). Vaginal bleeding was significantly more common in the survivors (13 (16%) v 2 (4%), $P=0.025$) but non-specific (other) symptoms were significantly less common (12 (15%) *v* 18 (33%), $P=0.011$). Forty eight (59%) survivors had disease of stage III or worse compared with 49 (91%) of those who died ($P=0.0001$), and optimal debulking (less than 2 cm disease remaining) was achieved in 31 (40%) survivors compared with seven (17%) of those who died ($P=0.01$). Multivariate analysis using these six variables with survival as the dependent variable identified age (odds ratio 0.96, 95% confidence interval 0.93 to 0.99; $P=0.02$), stage III or more (0.15, 0.05 to 0.43; $P<0.01$), and presence of non-specific

Table 2 Delays between onsest of symptoms and diagnosis for 135 women with ovarian cancer. Values are numbers (percentages) of women

Interval	Onset to first presentation at general practice	First presentation to referral	From referrral to hospital appointment	First hospital appointment to diagnosis
<2 weeks	64 (48)	82 (60)	95 (70)	45 (33)
2-4 weeks	41 (30)	17 (13)	20 (15)	29 (21)
3-6 months	19 (14)	20 (15)	16 (12)	48 (36)
≥6 months	11 (8)	16 (12)	4 (3)	13 (10)

symptoms (0.36, 0.14 to 0.89; P = 0.03) as the significant variables.

Discussion

The idea that delays in diagnosis and treatment of cancer patients adversely affect survival is deeply ingrained in our psyche. Our study suggests that delays attributable to the patient and general practitioner are roughly equal but that these intervals do not affect survival beyond 18 months in women with ovarian cancer. Survival was related to age of the patient, stage of disease, and the presence of diverse symptoms. The mean age was significantly younger in the good outcome group. This could be a result of later presentation, different disease biology, or a different attitude toward treatment of older people. The association of advanced age with poor survival is well known and to be expected.[7]

Few studies have examined referral patterns in ovarian cancer.[8] Kjellgren reported that 53% of women consulted a doctor within three months and 73% within six months of symptoms,[9] and other studies confirm these figures.[10] However, our data show that most patients present to their general practitioner within one month. This may represent an improvement in patient awareness of potentially serious symptoms or reflect the fact that the previous studies were mostly hospital based. Indeed, duration of symptoms on attendance at hospital was similar in our study to that in the other studies, indicating that the populations were comparable.

Importance of symptoms

Our audit shows that general practitioners are already referring two thirds of patients within one month of presentation. Although general practice delay did not influence overall survival, it may be a factor in the small number of patients in whom delay did occur. Sixteen patients were not referred for more than three months, half of whom initially had irritable bowel syndrome diagnosed. Differentiating ovarian cancer from irritable bowel syndrome can be difficult, and the predictive ability of the classic symptoms diminishes with age.[11] Other studies have highlighted the relevance of abdominal symptoms and disturbances in bowel habit in diagnosing ovarian cancer.[8 12 13] These studies were either hospital based or symptoms and information on time to diagnosis were obtained directly from the patients without verification from general practice or hospital records.[12]

The only symptoms associated with poor outcome were non-specific symptoms. This group includes symptoms such as shortness of breath, which are probably associated with more advanced disease. One of the main difficulties in primary care is to differentiate between patients whose symptoms may be due to cancer and the much larger but similar group of patients who do not have cancer.[14] For example, the association between cough and lung cancer is low.[15] Ovarian cancer is relatively rare, and the average family doctor will see only one case every five years.[4]

With vague non-specific symptoms such as abdominal distension, irregular bowel habit, backache, and weight loss, the delay in diagnosis of ovarian cancer could be up to a year.[8] It is therefore vital that women and general practitioners are informed that ovarian cancer is an insidious disease and that they should not ignore new symptoms. We could not validate the accuracy of the information recorded in the practice notes in this study. Patients often give the information they think the general practitioner wants, and the records are an interpretation of what the patient describes. We can see no other way to obtain the relevant data.

Early detection

Our analysis showed that the most significant independent variable was stage of disease at surgery. Consequently, the most effective way to improve survival for ovarian cancer is likely to be through screening. Attempts at screening for ovarian cancer have not been successful so far.[16] A recent pilot study suggested that screening might improve survival,[17] although a definitive answer will not be available until the results of the United Kingdom collaborative trial of ovarian cancer screening are available. The trial aims to include 120 000 women but has only recently begun recruiting. In the meantime, since most women attend their general practitioner within four weeks of new symptoms and are already referred within two weeks, there is a danger that rigid monitoring of a two week wait may divert scarce resources from more important components of the management of this disease.

What is already known on this topic

Epithelial ovarian cancer is the most common gynaecological cancer in the United Kingdom

75% of patients present with advanced incurable disease, and five year survival is 30%

The Department of Health recommends that everyone suspected of having ovarian cancer should be seen within two weeks of referral by their general practitioner

What this study adds

78% of patients have had symptoms for less than 4 weeks when they present to general practice and are referred to hospital within four weeks of presentation

70% of patients are seen in hospital within two weeks of the referral

Delay by patients and general practitioners does not affect survival beyond 18 months

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Depression and unintended pregnancy in the National Longitudinal Survey of Youth: a cohort study

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Psychological maladjustments after abortion are significantly associated with a history of depression.[1] It has been suggested that prior psychological state is equally predictive of subsequent depression among women with unintended pregnancies regardless of whether they abort or carry to term.[1] To examine this hypothesis we examined the National Longitudinal Study of Youth begun in 1979 with a nationwide cohort of 12 686 American youths aged 14-21.

Methods and results

The outcome variable of interest, depression, was assessed in 1992 for a subset of 4463 women using the Center for Epidemiological Studies depression (CES-D) scale scored by professional interviewers. This 20 item scale has good test-retest reliability among diverse population subgroups. In 1992 women were also asked whether their first delivered pregnancy had been the result of an intended pregnancy. Women who responded "yes" or "didn't matter" were excluded from our sample.

To control for prior psychiatric state we used the four item version of the Rotter internal-external locus of control scale, which was administered in 1979 (n = 6215; mean 8.95, SD 2.1). The Rotter scale is intended to measure the extent to which people feel in control of their own destiny as opposed to having their fate decided by environment or chance. This abbreviated scale correlates well with self esteem, social class, and education. Higher external scores on the Rotter scale have been found to correlate with higher depression scores.[2]

Among all women surveyed depression scores were found to correlate with total family income in 1992 ($r(3762) = -0.104$, $P < 0.0001$), highest educational grade completed in 1992 ($r(4459) = -0.202$, $P < 0.0001$), age at first pregnancy event ($r(3363) = -0.164$, $P < 0.0001$), and 1979 Rotter scores ($r(4423) = 0.135$, $P < 0.0001$). Depression scores were also significantly different between white (mean 9.48, SD 9.5) and non-white people (mean 11.69, SD 10.0; $t = 7.47$, $P < 0.0001$). These variables were used as controls.

The final sample used in these analyses includes only women for whom all control variables were available and who had their first abortion or first unintended delivery between 1980 and 1992 (n = 421). On average, aborting women had had their first pregnancy in 1984 at age 22, and delivering women gave birth in 1986 at age 24. The mean Rotter score for aborting women and delivering women was 8.88 (SD 2.1) and 9.09 (2.2) respectively.

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Women scoring in "high risk" range for clinical depression (CES-D score >15) who had their first abortion or first unintended childbirth between 1980 and 1992

	Women with unintended births (who did not abort)			Aborting women			Adjusted odds ratio*	95% CI
	Total	High risk	% High risk	Total	High risk	% High risk		
Married	75	13	17.3	164	43	26.2	2.38	1.09 to 5.21
Unmarried	53	16	30.2	129	37	28.7	0.94	0.43 to 2.03
All women	128	29	22.7	293	80	27.3	1.54	0.91 to 2.61

*Adjusting for family income, education, race, age at first pregnancy, and 1979 Rotter score.