# Ovarian cancer in Alexandria from 1988 to 1997: trends and survival

*N.H. Mahdy,[1] M. Abdel-Fattah[2] and H. Ghanem[3]*

## سرطان المبيض في الإسكندرية (1988–1997): الاتجاهات ومعدل البقاء على قيد الحياة

نهاد حسن مهدي ومعتز عبد الفتاح وحافظ غانم

**خلاصة:** تمت دراسة معدل حدوث سرطان المبيض، وحساب معدل البقاء خمس سنوات على قيد الحياة، وتحديد العوامل الإنذارية للبقاء. فجمعت البيانات اللازمة من سجل السرطان بالإسكندرية والسجلات الطبية بالمستشفيات المختلفة. وتبيَّن أن 358 حالة من سرطان المبيض قد شُخِّصت بين سنة 1988 وسنة 1997. ووُجد ارتفاع ملحوظ في اتجاه معدل حدوث سرطان المبيض من 1.23 لكل مئة ألف في سنة 1988 إلى 3.16 لكل مئة ألف في سنة 1997. وكان معدل البقاء خمس سنوات على قيد الحياة 46%. أما معدلات البقاء خمس سنوات بالنسبة إلى أطوار الورم الأربعة فكانت 85% ثم 71% ثم 41% ثم 22% على التوالي وكانت ذات مغزى إحصائي. كما كانت معدلات البقاء على قيد الحياة في حالات الأورام الضعيفة التمايز أسوأ بدرجة جوهرية عنها في حالات الأورام المتمايزة بدرجة متوسطة أو جيدة.

ABSTRACT The trend of incidence of ovarian cancer was studied, the 5-year survival rate calculated and prognostic factors for survival determined. Data were collected from the Alexandria Cancer Registry and medical records in various hospitals. A total of 358 cases of ovarian cancer were diagnosed from 1988 to 1997. A significant increasing trend in incidence of ovarian cancer from 1.23/100 000 in 1988 to 3.16/100 000 in 1997 was found. The overall 5-year survival rate was 46%. The 5-year survival rates for tumour stages I to IV were 85%, 71%, 41% and 22% respectively, which was statistically significant. Survival rates with poorly differentiated tumours were significantly worse than with moderate or well differentiated tumours.

**Le cancer de l'ovaire à Alexandrie de 1988 à 1997: tendances et survie**

RESUME On a étudié la tendance de l'incidence du cancer de l'ovaire, calculé le taux de survie à 5 ans et déterminé les facteurs pronostiques de survie. Les données ont été recueillies auprès du Registre du Cancer d'Alexandrie et à partir des dossiers médicaux de divers hôpitaux. Au total, 358 cas de cancer de l'ovaire ont été diagnostiqués de 1988 à 1997. On a constaté une tendance à la hausse importante de l'incidence du cancer de l'ovaire qui est passée de 1,23/100 000 en 1988 à 3,16/100 000 en 1997. Le taux global de survie à 5 ans était de 46%. Les taux de survie à 5 ans pour les tumeurs diagnostiquées aux stades I à IV étaient de 85%, 71%, 41% et 22% respectivement, ce qui est significatif sur le plan statistique. Les taux de survie pour les tumeurs peu différenciées étaient considérablement moins bons que pour les tumeurs moyennement ou bien différenciées.

[1]*Biostatistics Department, High Institute of Public Health, Alexandria University, Alexandria, Egypt.*
[2]*Medical Statistics Department, Medical Research Institute, Alexandria University, Alexandria, Egypt.*
[3]*Radiotherapy Department, Faculty of Medicine, Alexandria University, Alexandria, Egypt.*
*Received: 14/01/99; accepted: 02/05/99*

## Introduction

Ovarian cancer presents a tremendous clinical challenge to gynaecologists, medical oncologists and radiotherapists [*1*]. It is a silent menace; it is not associated with significant symptoms and it is not easily detected by physical or laboratory examination [*2,3*]. More than 70% of ovarian carcinomas will have spread beyond the pelvis at initial diagnosis [*2*].

Ovarian cancer is particularly frustrating as the incidence of, as well as the number of deaths from, the cancer has been gradually rising for several decades [*2*]. Incidence has been rising about 1%–2% per year in several countries but survival rates have not changed appreciably [*4*].

Although ovarian cancer ranks third in incidence behind cervical and endometrial malignancies respectively, it is the leading cause of death from gynaecologic malignancies [*2,4,5*]. It accounts for only 25% of gynaecological cancers yet is responsible for approximately 50% of the deaths [*6*].

Ovarian malignancies occur at all ages. The morbidity rate increases until approximately the age of 70 years after which it begins to decline. There appears to be a critical time near the age of 40 years when the rate increases dramatically [*7*].

Patient's age, tumour stage and grade of differentiation, amount of residual tumour remaining after surgery and additional treatment after primary treatment are prognostic factors of ovarian carcinomas [*1*]. Long-term survival for women with ovarian cancer is poor. Women with advanced ovarian cancer can expect a 5-year survival rate of less than 30% [*1*]. Despite the widespread use of chemotherapeutic agents, singly or in combination, more extensive surgery and more sophisticated radiotherapy, the death rate today is approximately the same as it was 25 years ago [*8*].

We investigated the trend of incidence of ovarian cancer in Alexandria, Egypt, from January 1988 to December 1997, determined the 5-year survival rate and identified prognostic factors for survival.

## Methods

### Study design and setting

The study included all cases of ovarian cancer in Alexandria registered by the Alexandria Cancer Registry during the period January 1988 until December 1997. The registry included the Alexandria University Hospital, the Health Insurance Hospital, the Medical Research Institute and the Medical Care Organization, Ministry of Health. The records of this registry were studied in order to collect data from all cases of ovarian cancer registered each year. In addition, clinical data were collected from the medical records of the Radiotherapy Department of Alexandria University Hospital, the Health Insurance Hospital and the Medical Research Institute Hospital.

Histology and pathology were evaluated by means of original pathology reports and clinical descriptions. The cases were assigned to stages according to the modified International Federation of Gynaecology and Obstetrics classification (FIGO). Stage I was defined as growth limited to the ovaries; stage II as growth involving one or both ovaries with pelvic extension; stage III as growth involving one or both ovaries with intraperitonal metastases outside the pelvis; and stage IV as growth in one or both ovaries with distant metastases [*9*].

Follow-up letters were sent to patients requesting them to report to assigned clinics. Those who could not come were asked to explain. A few letters were received from relatives of patients announcing death and date of death. Home visits were made to

patients who missed the follow-up. The total number of cases was 358 of which 39 cases were lost to follow-up (10.8%). At the cut-off date of the study, December 1998, information related to the survival of patients was determined. Categories included: alive, dead (date of death was recorded) or lost to follow-up (date of last visit was determined from the records).

## Statistical analysis

The arithmetic progression method for census estimation was used for the estimation of the mid-year population in Alexandria during the study period [*10*].

The trend of incidence of ovarian cancer during 1988–1997 was plotted and analysed using linear, quadratic and cubic parabolic equations in which $y$ was the predicated value of ovarian cancer incidence and $x$ was time. Results from each of the three equations were compared to select the best fit according to the highest $R^2$ (significant $F$-ratio for trend) and minimum mean absolute error [*11*]. Survival was the main dependent variable. The life table method was used for calculation of the overall 5-year survival rates for patients with ovarian cancer [*12*].

The influence of study variables on survival was subsequently examined by univariate and multivariate analyses. For univariate analysis, survival after diagnosis was estimated using the Kaplan–Meier procedure using the product limit method. The probability of survival over a given length of time with many small intervals was calculated [*12,13*]. The obtained estimates were expressed in graphical form drawn as a step function. The proportion surviving remained unchanged between events even if there were some intermediate censored observations [*12*].

The significance of difference between survival curves was calculated by Breslow test (generalized Wilcoxon analysis) in which:

$$U = \sum_{i=1}^{k} w_i (Oi - Ei)$$

where $Oi$ was the observed value, $Ei$ was the expected value and $w_i$ was the weight for time point, i. Weights were defined as the number at risk during each time period [*13*].

Survival duration was also estimated by fitting data with a multivariate Cox proportional hazard regression model in which explanatory variables were selected using a stepwise forward procedure with a variable entry limit fixed at significant level of 0.05 with confidence intervals (CI) for the hazard ratio calculated [*14*]. The Cox regression model was:

$$h(t) = h_0(t) \times \exp(B_1X_1 + B_2X_2 + B_3X_3 + ... + B_pX_p)$$

where $h_0(t)$ corresponded to the hazard when all the variables were zero, it is called the hazard function. $B_1$ through $B_p$ are regression coefficients; $X_1$ through $X_p$ are independent variables; and exp is the exponential function. Independent variables were defined as: $X_1$: age in years; $X_2$: histological type of the tumour ($X_2$ – 0 for granulosa cell tumours; 1 for serous or mucinous tumours; or 2 for endometroids); $X_3$: grade of differentiation ($X_3$ – 0 for well-differentiated tumours; 1 for moderately differentiated tumours; 2 for poorly differentiated tumours); $X_4$: stage of the disease ($X_4$ = 0 for stage I; 1 for stage II; 2 for stage III; or 3 for stage IV tumours).

All statistical analyses were performed using *SPSS* (version 7.5). $P$-values less than 0.05 were considered statistically significant.

## Results

### Demographic and clinical profiles of the patients

A total of 358 cases of ovarian cancer were diagnosed between 1988 and 1997. The greatest percentage of patients were 50 years of age or more at diagnosis (43.6%); 42.2% and 14.2% were 30 to <50 years of age and <30 years of age respectively with a median age of 46 years. Most of the women were married (88.5%). Approximately 59% were premenopausal. Nulliparity was recorded for 42.5% of the patients (Table 1).

The most common clinical presentations encountered were abdominal distension (38.0%) and pelvic pain (22.6%). More than half had bilateral lesions. The FIGO stage distribution was 27.2%, 24.1%, 27.5% and 21.2% for stage I to stage IV respectively. The most common histological type of tumour was serous adenocarcinoma (46.8%); the second most

Table 1 **Demographic and clinical profiles of patients with ovarian cancer**

| Characteristics | No. | % | Characteristics | No. | % |
|---|---|---|---|---|---|
| *Age (years)* | | | *Site of the tumour (n = 286)* | | |
| 15– | 51 | 14.2 | Unilateral | 140 | 46.1 |
| 30– | 64 | 17.9 | Bilateral | 146 | 53.9 |
| 40– | 87 | 24.8 | *Histological type of the tumour (n = 329)* | | |
| 50– | 118 | 33.0 | Serous cystadenocarcinoma | 154 | 46.8 |
| 60–80 | 38 | 10.6 | Mucinous cystadenocarcinoma | 106 | 32.3 |
| $\bar{X} \pm s$ (median) | 44.99 ± 13.34 (46) | | Endometroid | 35 | 10.6 |
| *Marital status* | | | Granulosa cell tumour | 34 | 10.3 |
| Single | 41 | 11.5 | *Grade of differentiation (n = 355)* | | |
| Married | 317 | 88.5 | Poorly differentiated | 138 | 38.9 |
| *Menopause* | | | Moderately differentiated | 98 | 27.6 |
| Premenopausal | 212 | 59.2 | Well differentiated | 119 | 33.5 |
| Postmenopausal | 146 | 40.8 | *Metastases (n = 355)* | | |
| *Gravidity* | | | No | 136 | 51.3 |
| $\bar{X} \pm s$ (median) | 2.64 ± 2.94 (2) | | Yes | 219 | 48.7 |
| *Parity (n = 306)* | | | *Histological staging (n = 344)* | | |
| Nullipara | 130 | 42.5 | Stage I | 115 | 27.2 |
| Para one or more | 176 | 57.5 | Stage II | 83 | 24.1 |
| *Presenting symptoms (n = 310)* | | | Stage III | 81 | 27.5 |
| Abdominal distention | 116 | 38.0 | Stage IV | 65 | 21.2 |
| Low back pain | 55 | 17.7 | | | |
| Pelvic mass | 24 | 7.7 | | | |
| Pelvic pain | 70 | 22.6 | | | |
| Amenorrhoea | 23 | 7.4 | | | |
| Menorrhagia | 38 | 12.3 | | | |
| Loss of weight | 9 | 2.9 | | | |

*Variation in the total number of cases is a result of missed data.*
s = *standard deviation*

Table 2 Life table survival rates for patients with ovarian cancer

| Year of observation X to X +1 | Number entering the interval | Number withdrawn during interval Lx | Number exposed to risk of dying Wx | Number of deaths Lx | Probability of death dx | Probability of surviving qx | Cumulative probability of surviving at end of interval px | Hazard rate Px | Standard error of cumulative probability | Standard error of hazard rate |
|---|---|---|---|---|---|---|---|---|---|---|
| 0– | 358 | 2 | 357.0 | 14 | 0.0392 | 0.9608 | 0.9608 | 0.0400 | 0.0103 | 0.0107 |
| 1– | 342 | 7 | 338.5 | 43 | 0.1270 | 0.8730 | 0.8387 | 0.1356 | 0.0196 | 0.0206 |
| 2– | 292 | 6 | 289.0 | 55 | 0.1938 | 0.8062 | 0.6762 | 0.2146 | 0.0251 | 0.0285 |
| 3– | 230 | 9 | 225.5 | 45 | 0.1996 | 0.8004 | 0.5413 | 0.2217 | 0.0270 | 0.0328 |
| 4– | 176 | 15 | 168.5 | 25 | 0.1484 | 0.8516 | 0.4610 | 0.1603 | 0.0273 | 0.0319 |
| 5+ | 136 | 136 | 68.0 | | | 1.0 | 0.4610 | | 0.0273 | |

$L'x = Lx - 1/2(Wx)$ $\hat{q}x = dx/L'x$ $\hat{p}x = 1 - \hat{q}x$ $\hat{P}x = p1 \times p2 \times p3 \times p4 \times ...px$ Standard error $= P_x \sqrt{\sum_{x=1}^{x} qx/L'x - dx}$




Figure 1 **Annual incidence rate of ovarian cancer per 100 000 Alexandria population**

common type was mucinous (32.3%). A high percentage had poorly differentiated tumours (38.9%) and 48.7% presented with metastases at diagnosis (Table 1).

## Trend of ovarian cancer

The incidence rate of ovarian cancer during the study period was 2.30/100 000 mid-year Alexandria female population. Annual incidence rates increased from 1.23/100 000 in 1988 to 3.16/100 000 in 1997 (Figure 1). The most appropriate fit to the trend was a linear model ($y = -392.78 + 0.1983x$) indicating that there was an increasing trend in incidence rate of ovarian cancer during the entire study period. This was statistically significant ($R^2 = 0.97$, $F = 305.64$, $P < 0.05$).

## Survival rates for patients with ovarian cancer

The life table 5-year cumulative survival rate was 46.1 per 100 women (Table 2). Survival rates were 96, 84, 68 and 54 per 100 women respectively at first, second, third and fourth year after diagnosis. Survival curves by age of woman are given in

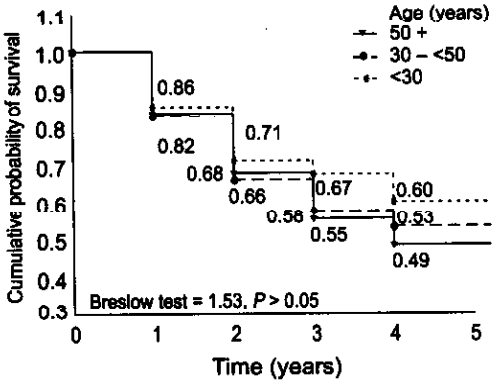


Figure 2 **Kaplain–Meier survival curve for patients with ovarian cancer according to age**

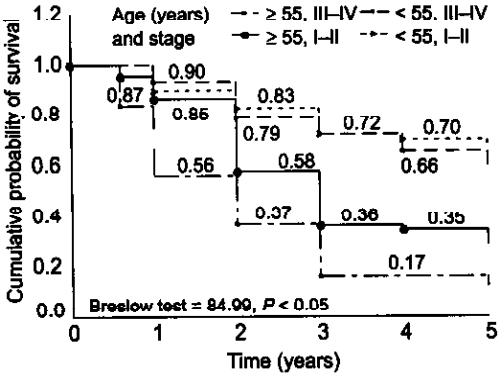


Figure 4 **Kaplain–Meier survival curve for patients with ovarian cancer according to age and tumour stage**

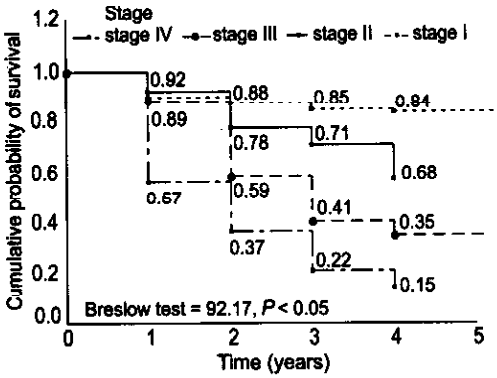


Figure 3 **Kaplain–Meier survival curve for patients with ovarian cancer according to FIGO classification of tumour stage**

Figure 2. Age was not significantly associated with survival of patients with ovarian cancer. Throughout the study period the highest probability of survival was for women aged <30 years, followed by those aged 30 to <50 years and those aged 50 years or more. The 5-year survival rates for these age groups were 60%, 53% and 49.5% respectively (Breslow test = 1.53, $P > 0.05$).

Kaplain–Meier survival curves revealed that women diagnosed with stage I tumours had better survival rates than those with other stages (Figure 3). The 5-year survival rate was 85% among those with stage I tumours as compared with 71%, 41% and 22% with stage II, III and IV tumours respectively. These differences were statistically significant (Breslow test = 92.17, $P < 0.05$).

Kaplain–Meier analysis showed that women aged <55 years who presented with stages I or II had a higher probability of survival than those aged 55 years or more who presented with the same stages (Figure 4); the 5-year survival rates were 70% and 66% respectively. Furthermore, those aged <55 years with stages III or IV also had better survival rates (35%) than those aged 55 years or more with the same stages (17%). These differences were statistically significant (Breslow test = 84.99, $P < 0.05$).

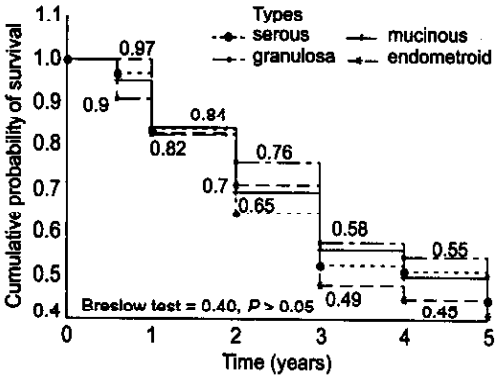


**Figure 5 Kaplain–Meier survival curve for patients with ovarian cancer according to histological type of tumour**

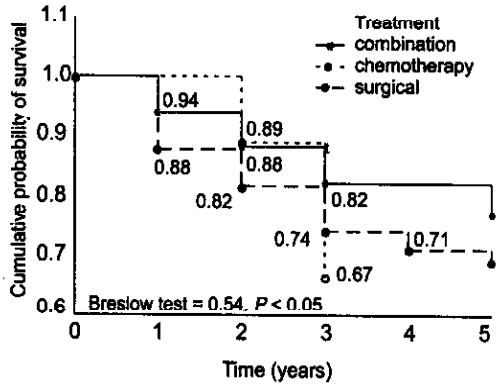


**Figure 7 Kaplain–Meier survival curve for patients with stage I ovarian cancer according to method of treatment**

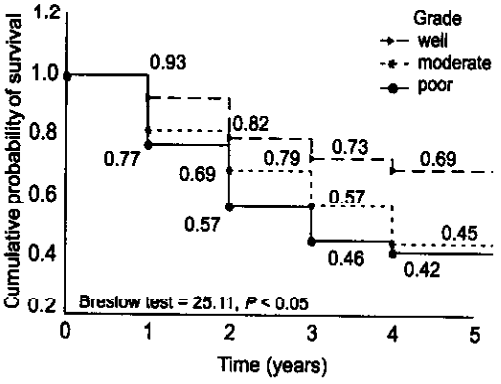


**Figure 6 Kaplain–Meier survival curve for patients with ovarian cancer according to grade of differentiation of tumour**

Survival by cell type is shown in Figure 5. It might appear that substantial differences existed with the best survival rates among patients with granulosa type and the worst among those with endometroid type. The overall 5-year survival rates, however, were 55%, 51%, 50% and 45% for granulosa, serous, mucinous and endometroid type tumours respectively and were not significantly different (Breslow test = 0.40, $P > 0.05$)

Survival varied with grade of differentiation (Figure 6). It was progressively worse with poorly differentiated tumours; this was noticed throughout the study period. The overall 5-year survival rates were 69%, 45% and 42% respectively among well, moderate and poorly differentiated tumours. These differences were statistically significant (Breslow test = 25.11, $P < 0.05$).

Survival per treatment is given in Figure 7. Patients diagnosed as stage I who received surgical treatment plus chemotherapy had a higher 5-year survival rate (82%) than those who received either surgical therapy or chemotherapy alone (71% and 67% respectively), but the difference was not significant. Among those who presented with stage II the addition of chemotherapy did not improve survival. Those who received surgical treatment, however, had the highest 5-year cumulative probability of survival (67/100 women) when compared with those who received chemotherapy or

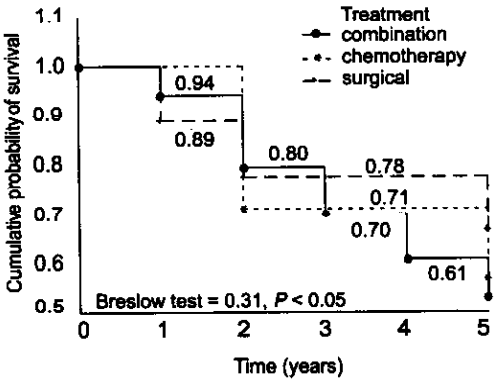


Figure 8 **Kaplain–Meier survival curve for patients with stage II ovarian cancer according to method of treatment**

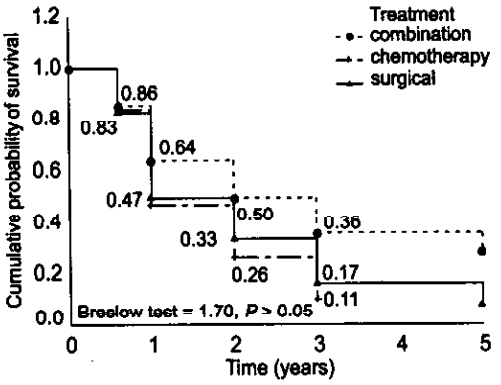


Figure 10 **Kaplain–Meier survival curve for patients with stage IV ovarian cancer according to method of treatment**

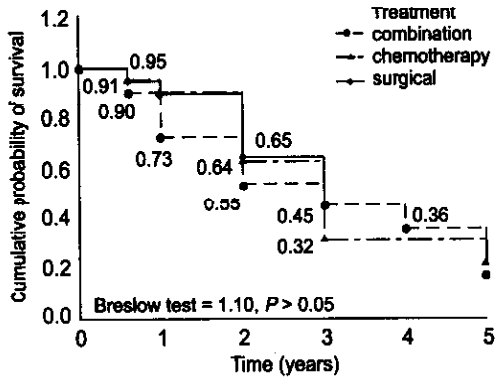


Figure 9 **Kaplain–Meier survival curve for patients with stage III ovarian cancer according to method of treatment**

combined treatment (61/100 and 57/100 women respectively). However, these differences were not statistically significant (Breslow test = 0.31, $P > 0$ 05) (Figure 8).

Although the addition of chemotherapy to surgical treatment was beneficial and had a higher probability of survival among patients presenting with stage III or IV than chemotherapy or surgical management alone, these differences were not statistically significant (Figures 9 and 10). The 5-year survival rates for each treatment of stage IV tumours was 36%, 26% and 17% respectively (Breslow test = 1.70, $P > 0.05$).

## Prognostic factors for survival

Multivariate Cox proportional hazard analysis revealed two significant factors potentially related to the risk of death (Table 3). The first predicting factor was grade of differentiation; those with poorly differentiated tumours had approximately three times the risk of death relative to those with well differentiated tumours. Those with moderately differentiated tumours had a hazard ratio of 1.99 (95% CI = 1.21–3.28). The second predictor was tumour stage; stages III and IV patients had a higher risk of death (hazard ratio = 2.14 and 4.06 respectively) than stage I patients. Patients with stage II tumours had a non-apparent risk of death relative to stage I (Model $\chi^2 = 70.08$, $P < 0.05$).

Table 3 **Stepwise Cox proportional hazards regression of survival to independent factors**

| Factor | *B* | SE | Wald | *P* | Hazard ratio | 95% CI | Model $\chi^2$ |
|---|---|---|---|---|---|---|---|
| *Grade of differentiation* ($X_3$) | | | 15.9007 | 0.0004 | | | |
| Moderate | 0.6900 | 0.2547 | 7.3395 | 0.0067 | 1.99 | 1.21 – 3.28 | |
| Poor | 0.9566 | 0.2401 | 15.6771 | 0.0001 | 2.60 | 1.63 – 4.17 | |
| *Stage of the tumour* ($X_4$) | | | 37.7496 | 0.0000 | | | 70.08[a] |
| Stage II | 0.0785 | 0.2710 | 0.0839 | 0.7721 | 1.08 | 0.64 – 1.84 | |
| Stage III | 0.7626 | 0.2596 | 8.6280 | 0.0033 | 2.14 | 1.29 – 3.57 | |
| Stage IV | 1.4013 | 0.2687 | 27.1953 | 0.0000 | 4.06 | 2.40 – 6.88 | |

[a] $P < 0.05$
*CI = confidence intervals*

## Discussion

Relatively little is known about the epidemiology of ovarian cancer despite the seriousness of the disease [*1*]. It is one of the major problems confronting gynaecologists as it is the most common fatal gynaecologic malignancy. Moreover, it has aroused increasing interest among epidemiologists because of its impact on women's health [*4*].

In our study, trends in the incidence of ovarian cancers registered between 1988 and 1997 were explored. The incidence rate of ovarian cancer increased from 1.23/100 000 in 1988 to 3.16/100 000 in 1997 with a significant linear trend. La Vecchia et al. stated that an epidemic increase of ovarian cancer appears to be in progress [*15*]. Furthermore, ovarian neoplasm appears to me more common this century than previously [*16*].

In Egypt, this sharply increasing trend in incidence might be attributed to two major factors known to influence cancer incidence: parity of Egyptian women and the decrease in contraceptive pill usage. Reduced risk of ovarian cancer is associated with increasing number of pregnancies and deliveries [*17*] and contraceptive pill usage has been considered protective for ovarian cancer [*3,18*]. The increasing trend may also be partly due to improvements in diagnostic techniques [*19*].

Our findings agree with a Norwegian study in which there was an increasing trend in incidence of tumours between 1970 and 1993 [*20*]. In Finland, there was a 50% increase in incidence rate between the periods of 1973–1977 and 1988–1992 [*21*].

There have been decreasing trends of incidence of ovarian neoplasm, however, in Columbia, Jamaica and Hawaii [*15*]. In Sweden a decreasing trend among younger women has been ascribed to the widespread use of oral contraceptives [*22*].

The median age of our patients was 46 years. This was lower than Turkish or Norwegian studies in which median ages were 57 years and 59 years respectively [*23,24*].

A Berlin study found that only 23% of cases were detected in stage I and 65% had advanced tumours of stages III or IV [*25*] and a study in Israel found that the majority of the cases (50%–70%) were in stage III or IV at diagnosis [*26*]. In contrast, the FIGO stage distribution in one Italian study was 39.2%, 6.7%, 41.9% and 12.2% for stages I through IV respectively [*5*]. Massi et al. reported that the higher proportion of stage I

tumours among women <30 years of age might be because ovarian carcinomas among that age group are more likely to be diagnosed at an early stage or because there might have been a large number of referrals of very young patients to their cancer institute [5]. Their findings agreed with those of Plaxe et al. [27]. However, Massi et al. found that in patients aged 31–40 years there was also an increased proportion of stage I disease (35%) in comparison with overall incidence of stage I disease regardless of age [5]. This finding does not agree with the data of Plaxe et al. who reported a stage I incidence of only 17% among this age group [27].

The results of our work show that 27.2% of the women were stage I at diagnosis. This proportion was lower than that of the Italian study but higher than that of the Berlin study. In addition, 48.7% of our patients were in stage III or IV, which is in accordance with the Italian study but lower than the Berlin study. This might be because more than 55% of our patients were <50 years of age.

Among histological types, the most common type found in the present study was serous or papillary adenocarcinomas (46.8%) and 32.2% were mucinous. These findings are similar to an Italian study in which 44.6% were serous carcinomas and 29.7% were mucinous [19] and are consistent with a New Mexico study in which the serous and papillary carcinoma comprised the largest proportion (31%) of ovarian cancers observed from 1969 to 1992 [28]. These were followed by adenocarcinomas (18%) and papillary adenocarcinomas (13%) [28].

Approximately 39% of the patients in our study had poorly differentiated tumours. This was higher than the Florence study (30.6%) but lower than a Californian study (49%) [19,29].

Ovarian cancer is usually recognized and diagnosed too late [30].The 5-year survival rates for ovarian cancer as reported by the National Surveillance Epidemiology and End Results (SEER) programme from 1973 to 1991 increased only minimally from 36% to 42% over that 18-year period [30]. Similarly, a New Mexico study showed only slight gains in 5-year ovarian cancer survival over time. Greater improvement has been observed among women <51 years old versus older women [28]. Malkasian et al. reported that the overall survival of 1938 women receiving primary treatment at the Mayo clinic was 35% at 5-years and 28% at 10 years [31]. The 5-year survival rate in our study was higher (46.1%) but was considerably lower than figures such as 56% in a Turkish study between 1989–1995 and 58.2% in an Italian study between 1969–1994 [5,23]. The 5-year survival rate in our study, however, was the same as the 10-year survival rate of the Italian study. This could be because of the relatively younger age of patients in the Italian study as compared to those in ours.

The percentage of those lost to follow-up in our study was 10.8%; this could affect the survival rate.

In the study by Massi et al., the 5-year survival rates for patients aged 30 years and younger and patients aged 31–40 years were 71.3% and 47.1% respectively. In the former group low malignant potential tumours and well-differentiated carcinomas were significantly more frequent (68.8% and 37.5%, $P < 0.01$) [5]. Our results are consistent with these findings. We found the highest probability of survival was for women aged <30 years, followed by those aged 30 to <50 years and finally by those aged 50 years or more. The 5-year survival rates were 60%, 53% and 49.5% respectively but these were not significantly dif-

ferent. Variances in survival with age might be explained by biological host-related factors. It has been speculated that the hormonal milieu of women of reproductive age might make them less vulnerable to the progression of malignant disease [*5*]. Partridge et al., however, found that relative survival decreased with increasing stage or grade of disease. Survival was poorer with advanced age only for women with stage III or IV disease [*1*]. This concurs with the findings of our work which confirmed the influence of stage adjusted by age; those aged 55 years or more presenting with stage I or II had better survival rates (66%) than those presenting with stage III or IV (17%).

Cmelak et al. reported that 5-year survival rates by initial stage at diagnosis were: stage I and II, 75%; stage III, 40%; and stage IV, 15% [*29*]. These results approach the figures obtained in our study in which survival rates were 84%, 68%, 35% and 15% for stage I to stage IV respectively. Our figures, however, are considerably lower than rates in an Italian study of patients with advanced cancer (stage III and IV) in which overall survival rates were 76% at 3 years, 66% at 5 years and 51% at 8 years [*32*]. It was higher than the study by Averette et al. which reported 5-year survival rates of 74%, 58%, 30% and 19% respectively. Averette et al. found that due to paucity of symptoms early in the disease course, 62%–85% of patients present with stage III or IV tumours [*33*].

Histological type was associated with survival in a study of 85 patients in Texas [*34*]. Those with mucinous and endometroid types had better survival rates. In contrast, we found no significant relationship between tumour type and survival, although those with endometroid type had the poorest survival rates. Better survival rates were observed among those with granulosa cell types. Poorly differentiated tumours are often accompanied by poor prognosis [*5*]. This was confirmed by our study in which the 5-year survival rates were 69%, 45% and 42% respectively for well, moderately and poorly differentiated tumours. Massi et al. reported 5-year survival rates of 72.9%, 37.5% and 23%, respectively [*5*].

The addition of chemotherapy to the treatment of stage I carcinomas did not improve outcome nor was a dramatic improvement in survival brought about by the addition of chemotherapy to treatment of stages II or III. However, we found that surgical treatment plus chemotherapy had a higher but not significant probability of survival for stage I, III or IV disease but had no improvement in survival for stage II disease.

Massi et al., using multivariate analysis, found that only stage and grade were significant independent prognostic factors of survival, while age yielded no independent information [*5*]. These findings are in general agreement with our results and those of other studies [*1,28*].

## Conclusions and recommendations

We found a significant increasing trend of incidence of ovarian cancer. The two most important prognostic factors for survival were grade and stage of the tumour. Those with poorly differentiated tumours had lower survival rates than those with moderately or well differentiated tumours. Better survival rates were observed among those diagnosed with stage I tumours than those with tumours of other stages.

Since the incidence of ovarian cancer is increasing, the development of appropriate methods for early diagnosis, screening and

treatment of this carcinoma is eagerly awaited. Better understanding of the genetic and environmental factors that are involved in the pathogenesis of ovarian carcinoma will lead to new strategies for the early detection and prevention of this tumour. Accurate and reliable staging will be critical to evaluate treatment and screening methods. The improvement of prophylaxis and secondary prevention depends upon adequate work-up and improved therapeutic integration of tumours.

## *References*


1. Partridge EE, Phillips JL, Menck HR. The national cancer database reports on ovarian cancer treatment in United States hospitals. *Cancer*, 1996, 24:2236–46.
2. Weingold AB. Embryology and congenital anomalies. In: Kase NG, Weingold AB, eds. *Principle and practice of clinical gynecology*. New York, John Wiley and Sons, 1983:71–2.
3. Nahhas WA. Ovarian cancer. Current look on this deadly disease. *Postgraduate medicine*, 1997, 102(3):112–20.
4. Franceschi S et al. Risk factors for epithelial ovarian cancer in Italy. *American journal of epidemiology*, 1982, 115(5):714–9.
5. Massi D et al. Epithelial ovarian tumours in the reproductive age group: age is not an independent prognostic factor. *Cancer*, 1995, 77(6):1131–6.
6. Ramzy I. *Essentials of gynecologic and obstetric pathology*. Connecticut, Appleton Century Crofts, 1983:231.
7. Jolles GJ. Ovarian cancer: histological classification, histological grading, staging and epidemiology. *Clinical obstetrics and gynaecology*, 1985, 28(4):785–7.
8. Piver MS. Ovarian carcinoma: a decade of progress. *Cancer*, 1984, 54(11):2706–13.
9. Pettersson F. *Annual reports on the results of treatment in gynaecology cancer*. Stockholm, International Federation of Gynaecology and Obstetrics, 1988.
10. Swaroop S. *Introduction to health statistics*. Edinburgh, E and S Livingstone, 1960:156.
11. Berenson ML, Levine DM, eds. Index numbers, time series and business forecasting. In: *Basic business statistics, concepts and applications*, 5th ed. New York, Prentice Hall International, 1992:739–50.
12. Armitage P, Berry G. Survival analysis. In: *Statistical methods in medical research*, 2nd ed. Oxford, Blackwell Scientific Publications, 1991:421–39.
13. Norusis MJ. Kaplan Meier survival analysis. In: *SPSS for Windows, professional statistics release, version 6.0*. SPSS Incorporated, 1993:259–73.
14. Altman DG. Analysis of survival times. In: Altman D, ed. *Practical statistics for medical research*. London, Chapman and Hall , 1991:387–92.
15. La Vecchia C et al. The clinical relevance of the epidemiology of ovarian cancer. *European journal of cancer clinical oncology*, 1984, 20(2):175–82.
16. Woodruff JD. The pathogenesis of ovarian neoplasia. *Johns Hopkins medical journal*, 1979, 144:117–20.
17. El-Zanaty F et al. *Egypt demographic and health survey*. Calverton, Maryland, Macro International Incorporated, 1995.

18. Devereaux C, Curtain AW, Jenkins DM. Incidence levels for ovarian cancer in Southern Ireland. *International journal of gynaecology and obstetrics*, 1997, 56:327–8.

19. Bettachi S et al. Epidemiological factors and prophylaxis of ovarian tumours. *European journal of gynaecology and oncology*, 1982, 3:192–205.

20. Bjorge T et al. Trends in the incidence of ovarian cancer and borderline tumours in Norway, 1954–1993. *International journal of cancer*, 1997, 71:780–6.

21. Auranen A et al. Borderline ovarian tumors in Finland: epidemiology and familial occurrence. *American journal of epidemiology*, 1996, 144, 548–53.

22. Skjeldestad FE. Choice of contraceptive modality by women in Norway. *Acta obstetricia et gynecologica Scandinavica*, 1994, 73:48–52.

23. Aksu M, Kosebay T, Bese T. Survival of endometrial and ovarian cancers in Cerrahpasa Medical Faculty, Turkey. *Acta obstetricia et gynecologica Scandinavica supplement*, 1997, 76(167):15.

24. Bjorge I et al. Prognosis of 2800 patients with epithelial ovarian cancer diagnosed during 1975–94 and treated at the Norwegian Radium Hospital. *Acta obstetricia et gynecologica Scandinavica*, 1998, 77:777–81.

25. Ebeling K, Nischan P. Bosartige neubildungen des ovars in Berlin, Hauptstadt der DDR, in der periode 1975-1979. [Malignant neoplasms of the ovary in Berlin, capital of East Germany, 1975–1979.] *Archiv für geschwulstforshung*, 1984, 54(2):159–71.

26. Mor-Josef S, Anteby SO. Trends in the incidence of ovarian cancer in a heterogenic population (1960–1976). *Gynecologic oncology*, 1985, 21 (3):287–93.

27. Plaxe SC et al. Profiles of women age 30–39 and age less than 30 with epithelial ovarian cancer. *Obstetrics and gynecology*, 1993, 81:651–4.

28. Schiff M et al. Ovarian cancer incidence and mortality in American Indian, Hispanic, and non-Hispanic white women in New Mexico. *Cancer epidemiology, biomarkers and prevention*, 1996, 5:323–7.

29. Cmelak AJ, Daniel SK. Long-term survival with whole abdominopelvic irradiation in platinum-refractory persistent or recurrent ovarian cancer. *Gynecologic oncology*, 1997, 65:453–60.

30. Ries L et al., eds. *SEER cancer statistics review, 1973–1991: tables and graphs.* Washington DC, National Cancer Institute, National Institute of Health Publication, 1994, 94:2789.

31. Malkasian GD et al. Prognostic significance of histologic classification and grading of epithelial malignancies of the ovary. *American journal of obstetrics and gynecology*, 1984, 149(3):274–84.

32. Bolis G et al. Survival of women with advanced ovarian cancer and complete pathologic response at second-look laparotomy. *Cancer*, 1996, 77(1):128–31.

33. Averette HE, Janicek MF, Menck HR. The National Cancer Database reports on ovarian cancer. *Cancer*, 1995, 76:1096–103.

34. Gershenson DM et al. Prognosis of surgically determined complete responders in advanced ovarian cancer. *Cancer*, 1985, 55:1129–35.