New South Wales

Ovarian cancer survival by stage and histological type

Implications for cancer control in Sydney, Australia

September 2007

cancer institute NSW

Tracey, E[1], Roder D[1], Frances J[2], Zorbas H[2], Hacker N[3], Bishop J[1]

[1]Cancer Institute NSW
[2]National Breast Cancer Centre, NSW, Australia
[3] Gynaecological Cancer Centre, Royal Hospital for Women, Randwick, NSW

Poster 152

BACKGROUND

Ovarian cancer is the most common cause of gynaecological cancer death and the sixth leading cause of cancer death in females in New South Wales (NSW) and Australia overall. Although the age-standardised incidence has been stable in NSW since the early 1970s, mortality rates have decreased, such that they were 13% lower in 2000-2004 than in the 1970s. Similar trends have applied for Australia as a whole.

AIM

To investigate:

1. Associations of degree of spread at diagnosis, histological type and socio-demographic factors with the risk of death from invasive ovarian cancers in patients diagnosed in NSW in 1980-2003;

2. Accompanying time trends, socio-demographic and histological differences in degree of spread; and

3. Research and cancer-service implications.

METHODS

Invasive ovarian cancers notified to the NSW Central Cancer Registry with a diagnosis date of 1980-2003 and a recorded degree of spread were investigated in this study, apart from a small number (<1%) identified from autopsy or death records which were excluded. Patients were classified by:

1. Age at diagnosis – categorised in decades, with open-ended categories under 40 years and from age 80 years;

2. Socio-economic status – five ordinal categories using the residential local government area (LGA) based Socio-economic Index of Relative Disadvantage for Areas (SEIFA);

3. Service access – five ordinal categories using the residential LGA-based Accessibility/ Remoteness Index (ARIA); and

4. Country of birth – Australia, other English-speaking country, or non-English speaking country.

5. Patients also were classified by histological type, using the morphology groupings recommended by the International Agency for Research on Cancer, namely: serous, mucinous, endometrioid and clear cell carcinomas; adenocarcinomas not otherwise specified (nos); sex cord-stromal and germ cell tumours; and other specified and unspecified cancers.

6. Years of diagnosis were grouped into five diagnostic periods for statistical analysis from 1980 onwards.

Analyses were undertaken using SAS version 9 software.

The percentages of cases (+ standard errors) surviving ovarian cancer five years from diagnosis were calculated by the Kaplan Meier product-limit method, using the log-rank test to assess inter-group differences. Live cases were censored on December 31st, 2004, whereas those dying before this date were censored at their date of death. Cox proportional hazards regression analysis was undertaken to confirm the predictive importance of degree of spread as a staging measure and to identify other predictors of case fatality.

Diagnostic period, histological type and socio-demographic variables were entered stepwise into the model, retaining those variables that increased model fit ($p<0.05$).

RESULTS

Five-year case survivals approximated 40% for 1999-2003 diagnoses. Compared with localised disease, case fatality was three-to-four and six times higher respectively for cancers with regional spread and distant metastases throughout the study period. After adjusting for degree of spread, socio-demographic differences and histological type, the relative risk (95% confidence limits) of death from ovarian cancer reduced to 0.51 (0.46, 0.57) for 1999-2003 compared with the 1980-1983 baseline.

Relative risks were higher for adenocarcinomas (not otherwise specified) and other specified and unspecified cancers than for the more common serous carcinomas, but lower for endometrioid carcinomas, and sex cord-stromal and germ cell tumours.

A reduction in risk of death in the more recent diagnostic periods was evident, irrespective of whether adjustment was made for degree of spread. The probability of diagnosis with localised as opposed to more advanced disease was lower in older patients, the lowest socio-economic stratum, women born in a non-English speaking country, and those diagnosed in more recent periods.

Compared with serous lesions, localised disease was more common for mucinous, endometrioid and clear cell carcinomas, and sex cord-stromal and germ cell tumours. Approximately 61% of ovarian cancers had distant metastases at diagnosis in 1999-2003 (Table 1).

Table 1 Relative risk of death from ovarian cancer by degree of spread, year of diagnosis, and other descriptive characteristics: New South Wales, 1980-2003*

Explanatory variables	Relative risks (95% confidence limits) All histological groups – (n=6,934)	Relative risks (95% confidence limits) Epithelial histological types only (=5,923)
Age at diagnosis (yrs.):		
Under 40 (reference) (n=559)	1.00	1.00
40-49 (n=857)	1.30 (1.08, 1.57)	1.31 (1.07,1.59)
50-59 (n=1,507)	1.56 (1.31, 1.86)	1.54 (1.28,1.86)
60-69 (n=1,758)	1.79 (1.51, 2.13)	1.79 (1.49, 2.15)
70-79 (n=1,539)	2.51 (2.11, 3.00)	2.46 (2.04, 2.96)
80+ (n=714)	3.65 (3.03, 4.40)	3.64 (2.97,4.46)
Country of birth:		
Australian & unknown (reference) (n=4,938)	1.00	1.00
Other – English speaking (n=817)	0.94 (0.86, 1.03)	0.96 (0.87,1.06)
Other – not English speaking (n=1,179)	0.84 (0.77, 0.91)	0.82 (0.75,0.89)
Histological type:		
Serous (reference) (n=2,734)	1.00	1.00
Mucinous (n=631)	1.03 (0.90, 1.17)	1.06 (0.93,1.21)
Endometrioid (n=602)	0.71 (0.61, 0.81)	0.71 (0.62,0.82)
Clear cell (n=359)	0.97 (0.82, 1.16)	0.99 (0.83, 1.18)
Adenocarcinoma (nos) (n=1,597) not otherwise specified)	1.60 (1.49, 1.73)	1.64 (1.52,1.76)
Sex cord-stromal tumours (n=79)	0.55 (0.38, 0.78)	
Germ cell tumours (n=198)	0.21 (0.13, 0.35)	
Other specified (n=296)	1.56 (1.35, 1.79)	
Other unspecified (n=438)	2.09 (1.85, 2.35)	
Degree of spread at diagnosis:		
Local (reference) (n=1,763)	1.00	1.00
Regional (n=1,522)	3.71 (3.31, 4.17)	4.15 (3.66,4.71)
Distant (n=3,649)	6.08 (5.46, 6.78)	6.86 (6.10,7.72)
Year of diagnosis:		
1980-83 (reference) (n=989)	1.00	1.00
1984-88 (n=1,284)	0.94 (0.85, 1.04)	0.96 (0.87,1.07)
1989-93 (n=1,498)	0.77 (0.70, 0.85)	0.78 (0.71,0.87)
1994-98 (n=1,515)	0.63 (0.57, 0.69)	0.64 (0.57,0.71)
1999-2003 (n=1,648)	0.51 (0.46, 0.57)	0.48 (0.42,0.53)

DISCUSSION

NSW data showed an increase in survival for the more recent diagnostic periods, irrespective of whether adjustment was made for stage. This also applied after re-running the analysis, including cancers with an unknown stage. Furthermore, the increase in survival remained when the analysis was restricted to epithelial types and when each histological type was analysed in turn.

Reasons for survival improvements may include:

- Increased sub-specialization in gynaecological oncology, with two or three-year fellowship training programs now being provided in many countries, and with an emphasis in training on improving surgical expertise. Coincidental with subspecialisation has been the establishment of multidisciplinary teams in Gynaecological Cancer Centres.

- Advances in chemotherapy, initially through the introduction of cisplatin and cyclophosphamide for first-line treatment and then carboplatin and paclitaxel, with the use of back-up agents for non-responsive tumours.

- There is also evidence of more accurate staging, more extensive tumour de-bulking, and better selection of patients for secondary cytoreduction.

- In addition, it is possible that dissemination of evidence-based treatment guidelines have helped.

Victorian data for 1990-2004 showed similar survival differences to NSW by histological type, with higher survivals applying to mucinous, endometrioid and clear cell adenocarcinomas than to serous and other specified and unspecified cancers. Other NSW data cast doubts on the potential to find ovarian cancers at an earlier stage through a greater attention to symptoms.

In a retrospective cohort study of 100 patients with FIGO stage 1 disease and 100 with stage 3 disease, conducted in the Gynaecological Cancer Centre at The Royal Hospital for Women in Sydney, similar proportions of women with early stage (70%) and advanced stage (69%) disease reported symptoms of less than 3 months duration.

Tumour type appeared to be the key determinant of stage. Serous tumours comprised 25% of early cancers, the corresponding figure was much higher at 45% for advanced disease, indicating that cell type was highly predictive of stage.

CONCLUSION

Degree of spread as a summary staging measure is a powerful prognostic factor for survival from ovarian cancer.

Survival has increased over time, irrespective of stage, probably due to treatment advances. Markedly poorer survivals are seen in older than younger patients that are not explained by the more advanced stages of cancers at diagnosis in older women.

Survival differences by histological type indicate that ovarian cancer is a heterogenous disease with different clinical outcomes. Different treatment approaches may be required depending on histological type.

Despite survival gains, only about 40% of women survive five years from diagnosis, largely because around 61 % already have distant metastases at diagnosis.

Localised stage is less common at diagnosis in older patients, those born in non-English speaking countries and residents of low socio-economic areas.

More research is needed to find an effective screening test and to improve treatment outcomes.