ORIGINAL ARTICLE

Incidence, mortality, and survival trends of ovarian cancer in Hong Kong, 1997 to 2006: a population-based study

CME

KH Wong 黃錦洪
Oscar WK Mang 孟偉剛
KH Au 區國雄
Stephen CK Law 羅振基

Objectives To assess the incidence and mortality of ovarian cancer, and the survival patterns of the invasive epithelial ovarian carcinoma in Hong Kong based on population-based cancer registry data.

Design Historical cohort study.

Setting Hong Kong.

Patients All patients with ovarian cancer diagnosed between 1997 and 2006 were included. Patients eligible for survival analysis were followed up until 31 December 2007.

Main outcome measures Age-standardised incidence and mortality rates with their estimated annual percent changes were determined. Cumulative observed and relative survival rates were estimated using a period approach.

Results During the study period, in Hong Kong there was a steadily increasing ovarian cancer incidence rate (1.4% annually) but a steadily decreasing mortality rate (1.9% annually). The improvement in mortality was mainly in the age-group of 50-69 years (4.7% annually). Invasive epithelial ovarian carcinoma accounted for 79.6% of the study cohort. The 2-year and 5-year relative survival rates were 75.8% and 63.1%, respectively. Those diagnosed in the period 2002 to 2006 had significantly better survival than those diagnosed in the period 1997 to 2001 (65.3% vs 60.7%; P=0.008); a significant improvement was evident for patients with stage II disease and in the age-group of 50-69 years. Multivariate analyses confirmed that age, histological subtype, FIGO stage, and the period of diagnosis were independent prognostic indicators of invasive epithelial ovarian carcinoma.

Conclusion In Hong Kong, invasive epithelial ovarian carcinoma showed an increasing incidence and an improving survival trend over the period 1997 to 2006. The survival data derived from this study provides a baseline from which to monitor the effectiveness of ovarian cancer treatment in Hong Kong.

New knowledge added by this study

- A fuller picture of recent incidence, mortality, and survival trends of ovarian cancer in Hong Kong is provided.
- Advent of significantly improved survival for Hong Kong patients with invasive epithelial ovarian cancer in the last few years.

Implications for clinical practice or policy

- The population-based data of this study provide baseline data to monitor the effectiveness of ovarian cancer treatment in Hong Kong, and will have implications for the determination of a territory-wide health care policy towards local patients with ovarian cancer.
- The survival data can help clinicians counsel Hong Kong patients about commencing treatment for ovarian cancer.

Key words
Epidemiologic studies; Incidence; Mortality; Ovarian neoplasms; Survival

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Hong Kong Cancer Registry, Block R, 1/F, Queen Elizabeth Hospital, Jordan, Hong Kong
KH Wong, FHKCR, FRCR
OWK Mang, MPH, CStat
KH Au, FHKCR, FRCR
SCK Law, FHKCR, FRCR

Correspondence to: Dr KH Wong
Email: wongkh@ha.org.hk

Introduction

In 2009, ovarian cancer was the second most common gynaecological cancer and the sixth most common female cancer in Hong Kong, accounting for 3.7% of the cancer incidence in local women and 2.7% of cancer deaths.[1] As in other developed countries, ovarian cancer is the leading cause of death from gynaecological cancers in Hong Kong.

Primary ovarian cancer includes divergent histological types. Invasive epithelial carcinoma is the most common and has a different clinical course and prognosis from other types. Moreover, it is deemed to require different treatment strategies from other types, such as the borderline epithelial ovarian carcinoma, germ cell tumours, and sex-cord stromal tumours.

To our knowledge, few large-scale population-based studies[2,3] have been carried out in Chinese populations to estimate its incidence and mortality rate, or stage-specific survival rates in patients diagnosed to have ovarian cancer. There is a debate as to whether western findings and patterns are applicable to the Chinese patients. Thus, the aims of this study were to use the population-based data of the Hong Kong Cancer Registry (HKCaR) to assess trends for incidence and mortality in local ovarian cancer patients, and to study survival patterns in those with invasive epithelial ovarian carcinoma.

The HKCaR is a population-based cancer registry established in 1963, and covers the entire population in the region. Basic data such as its demographics, anatomical sites, and the pathology of each cancer are recorded. The data collection methods and quality assurance procedures adopted by the HKCaR have been described in detail in our previously published population-based study of cervical cancer.[4] Cancer mortality data, as well as predictions of cancer incidence and prevalence, are fundamental epidemiological parameters necessary for designing adequate cancer control policies.[5] Population-based cancer survival data form a key indicator to monitoring progress in the management of cancer,[6] and is also useful for clinicians when it comes to counselling cancer patients.

1997至2006年卵巢癌在香港的病發率、死亡率及生存趨勢：一個以人口為基礎的研究

目的 按人口為基礎的癌症登記資料，找出卵巢癌在香港的病發率和死亡率，以及侵襲性上皮性卵巢癌的生存模式。

設計 歷史隊列研究。

安排 香港。

患者 所有於1997至2006年期間確診患上卵巢癌的病人，並跟進符合被用作存活分析的病例直至2007年12月31日。

主要結果測量 年齡標準化的病發率和死亡率，以及其估計年度變化的百分比。利用期間方法估計其累積的觀察和相對生存率。

結果 研究期間卵巢癌在香港病發率穩步上升（每年增加1.4%），但死亡率卻穩步下降（每年減少1.9%）。死亡率有改善的現象主要集中在50至69歲的年齡組別中（每年4.7%）。侵襲性上皮性卵巢癌佔卵巢癌的79.6%，其兩年相對生存率為75.8%，五年相對生存率為63.1%。於2002至2006年確診侵襲性上皮性卵巢癌的患者比1997至2001年確診的患者有較佳生存率（65.3%比60.7%；P=0.008）；其中最大改善的為第二期的患者，以及屬50至69歲年齡組別的人士。多元分析確定年齡、組織學亞型、國際婦產科聯盟（FIGO）分期、及確診時間是侵襲性上皮性卵巢癌的獨立預測預後的因子。

結論 1997至2006年期間侵襲性上皮性卵巢癌病發率有上升的趨勢，但同時間，其生存率也有改善。本研究得出的卵巢癌生存率可為監察香港治療卵巢癌的成效提供基本資料。

Methods

The incidence and mortality rates of ovarian cancer in the population over time were described, and a historical cohort study was conducted to examine the overall survival of ovarian cancer patients in Hong Kong. Patients were identified using an electronic database maintained by the HKCaR. A total of 3693 women diagnosed with ovarian cancer (ICD-9 183 or ICD-10 C56) were reported between 1997 and 2006. Their demographic data, date of diagnosis, histological type (according to the International Classification of Diseases for Oncology[7]) and surgical staging (according to the International Federation of the Gynecology and Obstetrics [FIGO][8]) were recorded. If such surgical staging was not available, staging was based on clinical information. Patients were categorised into three age-groups: <50 years, 50-69 years, and ≥70 years and two time-periods: 1997-2001 and 2002-2006.

The annual incidence and mortality rates were standardised by the direct method using the world standard population.[9] Trends in incidence over 10-year periods were analysed for histological types, age-groups and FIGO stage, while trends in mortality over the 10-year periods were analysed for each of the age-groups. The annual percentage change was calculated using the Poisson regression model, by fitting a regression line to the natural logarithm of the annual standardised rates, using calendar year as a regressor variable ($y = mx + b$ in which $y = \ln(\text{rate})$ and x = calendar year). The estimated annual percent change was then calculated as equal to $100^* (e^m - 1)$.

Over the study period, 2941 patients had invasive epithelial ovarian carcinoma. Of these, 560 were excluded from the survival analysis for the following reasons: (a) presence of other pre-existing or co-existing primary malignancies (418 cases, 14.2%), or (b) loss to follow-up (ie zero survival time) since diagnosis (142 cases, 4.8%). To determine the survival status, survival analysis for invasive epithelial

ovarian carcinoma was based on the remaining cohort of 2381 eligible subjects with follow-up until 31 December 2007. The primary endpoint of this study was overall survival. This endpoint was defined as the time (accurate to month) from the date of diagnosis of ovarian cancer to the date of death, last-known alive status, or the date of termination of the study, whichever came first. Patients who were alive at the study end date or died after the study end date were censored. To eliminate the effect of competing causes of death,[10] survival was expressed as relative survival rate, which is the ratio between observed survival and expected survival. Expected survival rates were estimated according to the Hakulinen's method,[11] using Hong Kong population life tables.[12-14] The period approach was introduced to provide more up-to-date estimates of patient survival.[11] With this approach, each conditional probability was estimated based on the survival experience of the most recently diagnosed patients. Thus, in the 2002-2006 period, the conditional survival for the first and second year was based on patients diagnosed in a 5-year period (2002-2006) and who survived up to 1-2 years and conditional survival for the third year was based on patients diagnosed in the 4-year period (2002-2005) and survived up to 3 years, and so on. These conditional survival probabilities within each year were then multiplied to calculate 5-year survival rates. The calculations were carried out using the SURV3 analysis programme.[15] Analysis of data on survival in two time-periods used the Kaplan-Meier estimation of survival functions and log-rank tests for unadjusted comparisons. The prognostic variables analysed in the present study included age at diagnosis, FIGO stage, period of diagnosis, and histological type. The multivariate Cox proportional hazards model[16] was then used to assess the impact of covariates on survival and estimate adjusted relative risks and 95% confidence intervals (CIs) after adjusting for other covariates. These calculations were performed with the Statistical Package for the Social Sciences (Windows version 15.0; IBM Corp, Somers [NY], US). All tests were two-sided and a P value of <0.05 was considered statistically significant.

TABLE 1. Ovarian cancer incidence and mortality in Hong Kong, 1997-2006

Categories	No. (%) of new cases	Mean annual incidence (per 100 000)			EAPC* (%)	P value
		1997-1999	2000-2002	2003-2006		
Ovarian cancer incidence						
All ages†	3693 (100.0)	7.8	8.3	8.5	1.4	<0.01
Age-group (years)						
<50	1826 (49.4)	6.0	7.2	8.0	4.5	<0.01
50-69	1210 (32.8)	20.4	20.5	20.8	0.2	0.78
≥70	657 (17.8)	23.3	23.0	22.0	-0.5	0.63
Histology						
Invasive epithelial carcinoma	2941 (79.6)	7.6	8.4	9.4	3.4	<0.01
Borderline epithelial carcinoma	185 (5.0)	0.5	0.6	0.5	1.5	0.66
Sex-cord stromal tumours	39 (1.1)	0.05	0.14	0.14	14.6	0.04
Germ cell tumours	219 (5.9)	0.7	0.6	0.6	0.9	0.73
Others or no histology	309 (8.4)	0.8	0.9	1.0	2.7	0.25
FIGO stage						
I	1178 (31.9)	2.2	3.6	4.2	11.1	<0.01
II	261 (7.1)	0.6	0.8	0.9	4.8	0.15
III	692 (18.7)	1.6	2.2	2.2	4.4	0.03
IV	320 (8.7)	0.6	0.9	1.2	16.3	0.02
Unstaged	1242 (33.6)	4.6	3.2	3.2	-4.7	0.09
	No. (%) of deaths	**Mean annual mortality (per 100 000)**				
Ovarian cancer mortality						
All ages†	1290 (100.0)	2.9	2.7	2.5	-1.9	0.03
Age-group (years)						
<50	294 (22.8)	1.0	1.1	1.3	1.8	0.56
50-69	512 (39.7)	10.7	8.9	7.5	-4.7	<0.01
≥70	484 (37.5)	14.9	17.3	17.3	1.5	0.80

* EAPC denotes estimated annual percent change of rates over 1997-2006 using a log-linear model

† Rates were age-adjusted to the world standard population

Results

Incidence and mortality trends

From 1997 to 2006, a total of 3693 women were diagnosed with ovarian cancer in Hong Kong. The average crude incidence rate was 10.8 per 100 000 women per year, which accounted for 3.8% of the total cancer incidence in women. Regarding histology, 2941 (79.6%) had invasive epithelial carcinoma, 185 (5.0%) had borderline epithelial carcinoma, 39 (1.1%) had sex-cord tumours, and 219 (5.9%) had germ cell tumours. The remaining 309 (8.4%) had other or unknown histology. For stage distribution, 31.9% had stage I disease, 7.1% stage II disease, 18.7% stage III disease, 8.7% stage IV disease, and 33.6% were unstaged. Nearly half (49.4%) were aged <50 years, 32.8% were 50-69 years old, and 17.8% were in the age-group of ≥70 years (Table 1). During the study period, there was a tendency towards younger age at diagnosis with the median age shifting from 51 years (interquartile range, 42-65 years) to 50 years (interquartile range, 42-62 years) in the periods 1997-2001 and 2002-2006, respectively.

Table 1 shows the average annual incidence rates by age-group, histological type, and period of diagnosis. Over the study period, the age-standardised incidence rate steadily increased annually by 1.4% (95% CI, 0.4-2.4%). Among different age-groups, the incidence rate increased significantly every year in the age-group of <50 years by 4.5% (95% CI, 2.4-6.8%), but not in the age-groups of 50-69 years and ≥70 years. The increasing incidence trend of ovarian cancer was mainly contributed by increases in the incidence of invasive epithelial ovarian carcinoma, which had increased significantly every year by a mean of 3.4% (95% CI, 2.4-4.4%). Sex-cord stromal tumours also showed a significant increase in annual incidence, but the sample sizes were too small to draw any valid conclusions.

During the study period, a total of 1290 women died of ovarian cancer in Hong Kong; the average annual crude mortality rate being 3.8 per 10 000 women. Table 1 shows the average annual mortality rates by age-groups. The age-standardised mortality rate decreased annually by 1.9% (95% CI, -3.5 to -0.1%). This improvement was mainly observed in women in the age-group of 50-69 years, which achieved a mean annual mortality rate decrease of 4.7% (95% CI, -7.1 to -2.4%). The mortality rate remained steady in the age-groups of <50 years and in subjects ≥70 years.

Survival trend of invasive epithelial carcinoma

All invasive epithelial ovarian cancer patients

TABLE 2. One- to five-year relative survival rates of patients with invasive epithelial ovarian carcinoma, 1997 to 2006*

Categories	No.	Survival rate (%)					95% CI of 5-year survival	
		1-year	2-year	3-year	4-year	5-year	Lower	Upper
No. eligible to study	2381	86.5	75.8	69.5	65.2	63.1	60.8	65.5
Histology								
Serous	578	87.4	67.8	57.4	48.8	44.6	39.5	49.6
Mucinous	720	94.4	89.6	87.4	86.7	86.0	82.8	89.1
Endometrioid	316	93.7	87.6	83.1	79.6	77.8	72.1	83.5
Clear cell	358	90.7	79.6	74.5	71.1	69.4	63.8	75.0
Adenocarcinoma, NOS	409	61.8	50.3	40.4	34.4	31.7	26.3	37.1
FIGO stage								
I	853	97.6	93.7	91.8	90.3	90.2	87.6	92.8
II	170	95.3	85.8	74.1	72.0	68.3	59.9	76.8
III	551	81.5	60.5	49.1	37.9	32.9	28.0	37.8
IV	227	53.6	33.6	22.6	18.0	16.1	9.9	22.3
Unstaged	580	84.9	77.4	73.1	70.3	67.9	63.2	72.5
Age-group (years)								
<50	1115	91.8	84.5	80.0	76.9	74.1	71.1	77.1
50-69	868	87.8	73.5	65.8	59.5	57.2	53.3	61.1
≥70	398	68.2	55.7	46.8	42.9	42.1	35.7	48.4
Period of diagnosis								
1997-2001	1049	85.6	74.1	67.1	62.6	60.7	57.4	64.0
2002-2006	1332	87.1	77.2	71.7	68.0	65.3	61.8	68.8

* CI denotes confidence interval, and NOS not otherwise specified

(2381 patients) eligible for survival analysis were categorised based on the calendar years in which they were diagnosed into two time-periods, 1997-2001 and 2002-2006. This was to assess the survival trend over the study period. By the end of this study (31 December 2007), 874 (36.7%) of these patients had died, most (709, 81.1%) from ovarian cancer; 1298 (54.5%) patients were still alive and 209 (8.8%) patients were lost to follow-up. The mean follow-up time of the entire cohort was 44 months (range, 1-132 months). Table 2 shows the relative survival rates of invasive epithelial ovarian carcinoma according to the histological subtype, FIGO stage, age-group, and period of diagnosis. The survival rate dropped mostly within the first 2 years after diagnosis. The respective relative survival rates at 2 and 5 years for the whole group of invasive epithelial ovarian carcinoma patients were 75.8% and 63.1%. Patients in the age-group of <50 years had significantly longer survival than the age-group of 50-69 years, which in turn had significantly longer survival than the age-group of ≥70 years. Patients with early stage disease also had significant better survival than patients with advanced stage disease. Regarding different histological subtypes, those with serous cell adenocarcinoma and adenocarcinoma (not otherwise specified) had poorer survival rates than others. The group of patients diagnosed in the period 2002-2006 survived significantly better than those diagnosed in the period 1997-2001. The respective 5-year relative survival rates were 65.3% (95% CI, 61.8-68.8%) and 60.7% (95% CI, 57.4-64.0%). The Figure shows the overall survival curves of the invasive epithelial ovarian carcinoma diagnosed in the periods 1997-2001 and 2002-2006.

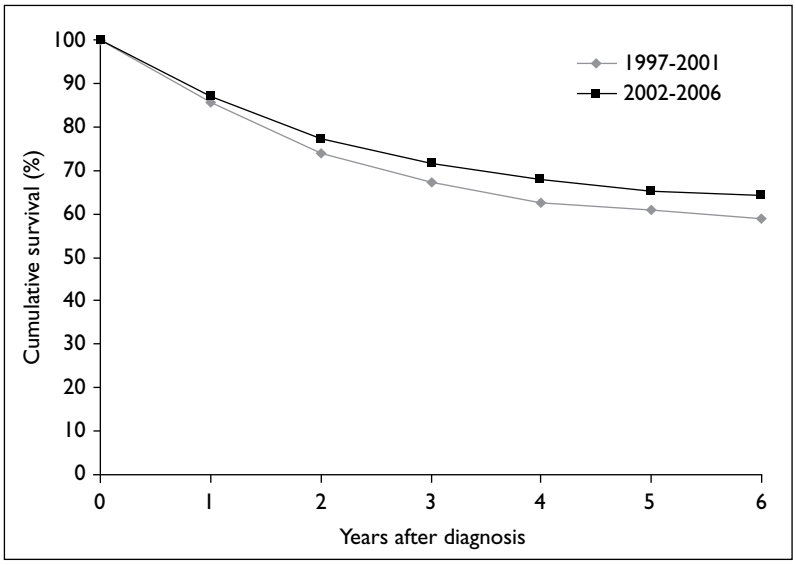

FIG. Relative survival of patients with invasive epithelial ovarian cancer in Hong Kong according to time periods

Table 3 shows the 5-year relative survival rates of invasive epithelial ovarian carcinoma diagnosed in the periods 1997-2001 and 2002-2006 according to histology, FIGO stage, and age-group. On the whole,

TABLE 3. Five-year relative survival rate (RSR) of invasive epithelial ovarian carcinoma patients according to histology, stage, and age-group in the periods of diagnosis 1997-2001 and 2002-2006

Categories	1997-2001		2002-2006		P value
	No. (%)	5-year RSR (%)	No. (%)	5-year RSR (%)	
All	1049 (100)	60.7	1332 (100)	65.3	0.008
Histology					
Serous	267 (25.5)	40.3	311 (23.3)	48.7	0.011
Mucinous	301 (28.7)	84.9	419 (31.4)	87.7	0.348
Endometrioid	148 (14.2)	72.0	168 (12.6)	84.5	0.011
Clear cell	145 (13.8)	70.4	213 (16.0)	67.4	0.888
Adenocarcinoma, NOS*	188 (17.9)	32.9	221 (16.6)	30.3	0.56
FIGO stage					
I	325 (31.0)	91.1	528 (39.6)	89.2	0.924
II	84 (8.0)	60.0	86 (6.4)	76.7	0.016
III	248 (23.6)	30.1	303 (22.7)	36.1	0.097
IV	84 (8.0)	14.8	143 (10.7)	18.8	0.912
Unstaged	308 (29.4)	65.1	272 (20.4)	70.8	0.078
Age-group (years)					
<50	474 (45.1)	73.5	641 (48.1)	74.5	0.605
50-69	377 (35.9)	53.2	491 (36.9)	61.3	0.015
≥70	198 (18.9)	41.9	200 (15.0)	41.4	0.922

* NOS denotes not otherwise specified

the demographic data and tumour characteristics did not vary between two periods. The proportion of women with unstaged invasive epithelial carcinoma decreased noticeably from 29.4% in the period 1997-2001 to 20.4% in the period 2002-2006. This reflected an increasing utilisation of staging procedures for invasive ovarian cancer and improved capture of staging data in the HKCaR over the study period. The significant improvement in 5-year survival rate between these two periods of diagnosis were mainly observed in women with stage II disease and in the age-group of 50-69 years. Multivariate analyses confirmed that age, histological subtype, FIGO stage, and period of diagnosis were all independent factors affecting the relative survival of patients with invasive epithelial ovarian carcinoma (Table 4).

Discussion

Our study showed a gradual increasing age-standardised incidence trend of ovarian cancer from 1997 to 2006 in Hong Kong. The average age-standardised incidence rate in the period 2003-2006 increased to 8.5 per 100 000 women, which was slightly lower than the GLOBOCAN-estimated overall age-standardised incidence of 9.3 per 100 000 women in more developed regions in 2008, but higher than the estimated overall age-standardised incidence rate of 5.0 per 100 000 women in less-developed regions in that year.[17]

Hong Kong has an ageing population. The median age of Hong Kong women rose from 34.2 in 1996 to 39.6 years in 2006[18]; the greatest contribution being from the age-group of 40-59 years. The proportion of this group rose from 22.4% in 1996 to 32.8% in 2006, while over half of invasive epithelial ovarian cancer patients fell within this age range over the same period. Hence, more and more Hong Kong women have become the high-risk cohorts at risk of invasive epithelial ovarian cancer from 1997 to 2006, and this could partly account for the increasing incidence trend of ovarian cancer in Hong Kong over the study period. Even though the age-standardised incidence rate of ovarian cancer steadily increased over the study period, the age-standardised mortality rate of ovarian cancer steadily decreased.

Compared to other reported population-based series (Table 5[2,6,19-21]), the 5-year relative survival rate of ovarian cancer patients in our study was comparable to those reported in urban areas of other developed Asian populations such as Singapore,[2] South Korea,[6] and Turkey,[6] and was better than those in less-developed countries such as Thailand and India.[6] Our 5-year relative survival rate was also better than some reported series from the West.[19-21] As in other

TABLE 4. Univariate and multivariate analyses of overall survival for invasive epithelial ovarian carcinoma patients*

Categories	No. of cases	Univariate†		Multivariate‡	
		Hazard ratio	95% CI	Hazard ratio	95% CI
Age-group (years)					
<50	1115	1	Reference	1	Reference
50-69	868	1.83	1.56-2.15	1.25	1.06-1.47
≥70	398	3.75	3.15-4.45	2.67	2.23-3.19
FIGO stage					
I	853	1	Reference	1	Reference
II	170	3.30	2.41-4.53	2.66	1.93-3.66
III	551	7.54	6.04-9.41	5.91	4.65-7.50
IV	227	15.40	12.04-19.69	9.73	7.46-12.70
Unstaged	580	3.21	2.53-4.08	3.14	2.45-4.03
Histology type					
Serous	578	1	Reference	1	Reference
Mucinous	720	0.25	0.20-0.31	0.52	0.41-0.66
Endometrioid	316	0.37	0.29-0.48	0.80	0.62-1.05
Clear cell	358	0.49	0.39-0.62	1.19	0.94-1.51
Adenocarcinoma, NOS	409	1.67	1.42-1.97	1.71	1.44-2.03
Period of diagnosis					
1997-2001	1049	1	Reference	1.00	Reference
2002-2006	1332	0.83	0.72-0.95	0.86	0.75-0.99

* CI denotes confidence interval, and NOS not otherwise specified
† Use of Cox regression on single covariate
‡ Use of Cox proportional hazards model adjusted for all other covariates in the table

TABLE 5. Five-year relative survival rates of ovarian cancer patients in some population-based series[2,6,19-21]

Population	Period of diagnosis	5-Year survival rate in % (95% confidence interval)
Hong Kong (present study)	1997-2006	63.1 (60.8-65.5)
Singapore[2]	1993-1997	62
South Korea[6]	1993-2001	59 (52-64)
Turkey[6]	1995-1997	60
Thailand[6]	1990-2000	47 (45-58)
India[6]	1990-2000	25 (19-29)
Europe[19]	1995-1999	36.5 (35.9-37.2)
England[20]	1995-1999	38.2
SEER[21]	2001-2007	43.8

developed regions in Asia, high accessibility to medical services and availability of diagnostic facilities in Hong Kong could partially explain the better survival rates than in less-developed regions in Asia. In our cohort, a high proportion of young patients (49.4% below the age of 50 years) with a favourable stage distribution (39% stage I-II disease) may also account for our relatively higher survival rates. The high proportion of favourable stage distribution in our series may be related to the low proportion of elderly patients (17.8%), who are more likely to delay seeking medical advice leading to diagnosis of the cancer at a later stage.[22] Nevertheless, comparison of survival rates among different series should be interpreted with caution, due to the differences in the periods studied and standardisation methods.

As the clinical behaviour of invasive epithelial ovarian carcinoma is different from other histological groups such as sex-cord tumours and borderline epithelial ovarian cancer, we carried out a prognostic analysis of patients with invasive epithelial ovarian carcinoma as a distinct entity, using relative survival as the primary end-point. In contrast to clinical trials or institution-based studies, in which patients are highly selected, population-based studies have little potential for selection bias.[2] As in other population-based studies,[23,24] our study showed that age was an independent prognostic factor for invasive epithelial ovarian carcinoma. Elderly patients are often considered less tolerant to chemotherapy due to co-morbidity and poor performance status. Advanced-age ovarian cancer patients were also less likely to receive standard treatments,[24,25] and were more likely to be treated conservatively than younger patients.[26]

Our study also showed that the FIGO stage was another independent prognostic factor for invasive epithelial ovarian carcinoma. The 5-year relative survival rate was much poorer in advanced-stage disease than early disease. This emphasises the essence of detecting the disease at early stages. However, there is only limited evidence that screening can detect significant numbers of potentially curable early stage ovarian cancer patients before presentation and no survival benefit has been shown by screening.[27] Two large randomised trials designed to determine whether ovarian cancer screening can improve survival have completed patient enrolment (the Prostate, Lung, Colon, and Ovarian Cancer Screening Trial [ClinicalTrials.gov number, NCT00002540[28]] and the United Kingdom Collaborative Trial of Ovarian Cancer Screening [ClincalTrials.gov number, NCT00058032][29]). Routine screening in patients at average risk is not recommended before the final results of these two large ongoing trials are available.[30,31] Screening will only be advocated in women at high risk of ovarian cancer including those who carry a BRCA mutation or who have a family history of breast or ovarian cancer,[27,30,31] but there is little evidence of a survival advantage.[32] Awareness of the disease and access to medical services and diagnostic facilities are essential in achieving earlier diagnosis of the disease.

Many population-based series reported improving survival trends for ovarian cancer patients over time.[20,33-36] Our study also showed a significantly improved survival trend for invasive epithelial ovarian carcinoma in Hong Kong over the period 1997 to 2006. Besides improved knowledge about prognostic factors, increasing availability of diagnostic facilities, improvement in general medical care, more aggressive surgical treatments,[34,37] and advances in chemotherapy no doubt contributed to these improved survival trends over the past two decades. Chemotherapy advances include platinum-based combination regimens[38] and the introduction of paclitaxel.[39,40] In our study, the significantly improved survival trends were limited to women in the age-group of 50-69 years (5-year relative survival rate increased from 53.2% in the period 1997-2001 to 61.3% in 2002-2006). There was no obvious survival improvement trends in the other age-groups. In our study cohort, patients age <50 years had a high proportion with early stage diseases (stage I-II disease: 52.4%; III-IV: 22.6%; unstaged: 25%) whose prognosis was good. In this age-group, any survival improvement over time was not likely to become evident with the patient numbers we were dealing with. On the other hand, the patients in the age-group of ≥70 years in our study cohort had a high proportion with advanced disease (stage I-II disease: 28.1%; III-IV: 41.5%; unstaged: 30.4%). Moreover, elderly invasive epithelial ovarian cancer patients were more likely to receive more conservative treatment than their younger counterparts,[24,41] and thus the survival benefit accruing from advances in chemotherapy would be less obvious in this age-group.

Although there were limitations in collecting important items of prognostic information (socio-

economic status, grading of the epithelial ovarian carcinoma, and details of the mainstay treatment for individual patients), the Registry captures nearly all ovarian cancer patients diagnosed in Hong Kong. Loss to follow-up in survival analysis is always another concern for a historical cohort study but was not a major issue in this study. To ascertain each patient's vital status at the end of the study date, the HKCaR traced all records via the Deaths Registry of the government and the Clinical Management System of the Hospital Authority. The follow-up for vital status was generally complete with a low percentage of loss to follow-up rate (8.8%). With this population-based study and the large sample size, the results could be considered representative of the population. It can therefore provide an accurate record of mortality and survival rates of ovarian cancer in Hong Kong and hence help in monitoring trends over periods of time. With the rapid development of systemic treatments for invasive epithelial ovarian carcinoma in the past decade, a number of therapeutic agents such as topotecan, pegylated liposomal doxorubicin, and gemcitabine have been introduced. As suggested by international guidelines[30] they are being used more widely in Hong Kong. Some agents such as trabectedin,[42] bevacizumab[43] and PARP (poly [ADP ribose] polymerase) inhibitor[44] are currently under active investigation and may also be used more widely in the near future. Population-based survival analysis could become one of the measures to monitor the effectiveness of these advanced treatments in ovarian cancer as a whole in the long run.

Conclusion

Our study showed an increasing incidence but a decreasing mortality trend of ovarian cancer in Hong Kong from 1997 to 2006. The relative 5-year survival of invasive epithelial ovarian cancer had improved significantly for those diagnosed in the period 2002-2006 as compared to those diagnosed in the period 1997-2001. The survival results of our study provide baseline survival data of invasive epithelial ovarian carcinoma that allows monitoring the effectiveness of advances in ovarian cancer treatment in Hong Kong on a population-based level.

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