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Ovarian Cancer Incidence: Current and Comprehensive Statistics

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1. Introduction

Ovarian cancer is a commonly diagnosed and particularly deadly gynecologic malignancy worldwide. It ranks among the top ten diagnosed cancers and top five deadliest cancers in most countries (Ferlay et al., 2010). Several cancer incidence data sources have been used to measure ovarian cancer burden across the world; however, the statistics presented are often not population-based, which can lead to misrepresentation of the burden due to incomplete or inaccurate data. An accurate assessment of ovarian cancer burden is essential as incidence data are used for many purposes including to generate hypotheses regarding etiology, allocate resources and funding toward new treatment discovery and clinical trials, and determine which populations of women may benefit from more education or greater surveillance for the disease. The purpose of this chapter is to present global comprehensive ovarian cancer incidence data. Data collected are from several resources, and every effort is made to present only high-quality data from population-based data sources. Because of changing age structures of populations and differences in data quality and coverage of various data sources over time, only the most recent data are presented. This will aid in preventing misinterpretation of temporal trends.

2. Data sources and interpretation

Data on the incidence of ovarian cancer (the number of new cases per year) is collected by population-based cancer registries; however, only certain countries have national registries that collect this information. In the United States, a law passed in 1992 established nationwide cancer surveillance. This law resulted in the establishment of the National Program of Cancer Registries (NPCR), which is administered by the Centers for Disease Control and Prevention (CDC), and provides cancer incidence data for 96% of the U.S. population (U.S. Cancer Statistics Working Group, 2010). When combined with data from the existing Surveillance, Epidemiology, and End Results (SEER) program, administered by the National Cancer Institute (NCI), 100% of the U.S. population is accounted for. Several other countries including Canada, Singapore, Denmark, Finland, Iceland, Norway, and Sweden have nationwide registry systems (Thun et al., 2011). Many other countries base their incidence on cancers collected in certain regions or groups of regions, and therefore these results vary in quality (Thun et al., 2011). Cancer registries typically require a period of one to two years to collect all required information on cancer diagnoses in the geographic areas covered. For that reason, most incidence data reported is two to three years behind the current calendar year.

Incidence rates take into account the number of new cases of cancer (numerator), and also the population at risk for the cancer (denominator). Most incidence rates are age-adjusted or standardized in order to allow comparisons across populations with differing age structures. Several age distributions are available for standardization. In international data, which is compiled from population-based registries by the International Agency for Research on Cancer (IARC), the 1960 world standard population is used (Ferlay et al., 2010). Within specific countries, such as the United States, the 2000 U.S. standard population is used (Thun et al., 2011; U.S.Cancer Statistics Working Group, 2010). Differences in age standardization methodology can result in a variance of rates reported from the same country. Age-specific rates for certain age populations (e.g., children) are often reported; these rates are often not age-adjusted or standardized. Most rates are expressed per 100,000 persons, and in the case of ovarian cancer per 100,000 women.

In this chapter, data are presented from a variety of sources, including monographs and peer-reviewed literature. Data are presented from the IARC public-use monograph (GLOBOCAN 2008) on case counts and rates for countries around the world (Ferlay et al., 2010). Since the United States also produces a comprehensive monograph annually, data are also presented for this country from the public-use *United States Cancer Statistics* (USCS) website (U.S.Cancer Statistics Working Group, 2010). Overall case and rate data from peer-reviewed articles are also included for countries (including the United States) that have published ovarian cancer incidence information from population-based registries. These articles may be a better source of data for some countries than monographs, as they may contain more complete or up-to-date information. Demographic- and clinical factor-specific data, and temporal trends are presented from monographs when available, and are supplemented with data from the most recent peer-reviewed publications for all countries available. Clinical factor data and temporal trends especially (histology, stage, laterality) are most often contained in peer-reviewed publications as opposed to monographs. To prevent misinterpretation, only data from the most recent publications (monograph or peer-reviewed publication) are presented. Table 1 lists data sources, years and population covered for each.

3. Global ovarian cancer incidence

A total of 224,747 new cases of ovarian cancer were reported worldwide in 2008, with 99,521 cases being diagnosed in more developed regions, and 125,226 being diagnosed in less developed regions (Ferlay et al., 2010). Ovarian cancer was the seventh most common cancer diagnosis among women in the world overall, and fifth most common cancer diagnosis among women in more developed regions (Ferlay et al., 2010). The world rate is estimated to be 6.3 per 100,000, and is higher in developed countries and regions (9.3) compared to others (Ferlay et al., 2010). Incidence rates for selected regions, continents and countries are shown in Table 2. Rates range from 3.8 in the Southern and Western African regions to 11.8 in the region of Northern Europe. Continental rates are highest in Europe (10.1), followed by North America (8.7), Australia (including New Zealand, 7.8), South America (6.2), Asia (5.1), and Africa (4.2).

Figure 1 displays a categorization of ovarian cancer incidence rates around the world. Rates for individual countries range from 1.8 in Samoa to 14.6 in Latvia (Ferlay et al., 2010).

Author and publication year	Data year(s)	Population*
Ferlay et al., 2010	2008	World
U.S. Cancer Statistics Working Group, 2010	2007	United States (99.1%)
Koper et al., 1996	1989-1991	Netherlands
Ioka et al., 2003	1975-1998	Osaka, Japan
Mahdy et al., 1999	1988-1997	Alexandria, Egypt
Zambon et al., 2004	1986-1997	Several regions in Italy
Kohler et al., 2011	Rates: 2003-2007; Trends: 1998-2007	United States (93%)
Tamakoshi et al., 2001	1975-1993	Several regions in Japan
Jin et al.,1993	1979-1989	Shanghai, China
Dey et al., 2010	1999-2002	Tanta, Egypt
Minelli et al., 2007	1998-2002	Umbria, Italy
Goodman & Howe, 2003	1992-1997	United States (52%)
Goodman et al., 2003	1992-1997	United States (52%)
Boger-Megiddo & Weiss, 2005	1992-2000	United States (26%)
Stiller, 2007	NR	World
Brookfield et al., 2009	1973-2005	United States (9%)
Poynter et al., 2010	1975-2006	United States (9%)
Smith et al., 2006	1973-2002	United States (9%)
Goodman and Shvetsov, 2009	1995-2004	United States (64%)
Jaaback et al., 2006	1993-2003	Royal United Hospital, UK
Stewart et al, 2007	1998-2003	United States (83.1%)
Riska et al., 2003	1953-1997	Finland
Pfeiffer et al., 1989	1978-1983	Denmark

Table 1. Data years and populations covered for monographs and articles cited throughout this chapter. *The population coverage for a particular country or region is provided when available from reports. NR=not reported.

In the United States, 20,749 ovarian cases were diagnosed in 2007 (the most recent year for which data are available), for an incidence rate of 12.2 per 100,000 women (U.S.Cancer Statistics Working Group, 2010). Koper et al. reported a rate of 14.9 in the Netherlands, similar to that found in the United States (Koper et al., 1996). In Osaka, Japan the overall rate reported was 5.4 (Ioka et al., 2003), and in Alexandria, Egypt, the rate was 3.16 (Mahdy et al., 1999). An Italian network of cancer registries reported 7,690 cases of ovarian cancer from 1986 through 1997 (Zambon et al., 2004). Few countries publish trends in ovarian cancer incidence over time. This may be due to differing methods of data collection and data quality issues, especially for countries that do not have a national registry. In the United States, a recent report estimates that ovarian cancer incidence has been decreasing since 1998, with a significant decline of 2.3% per year from 2003-2007 (Kohler et al., 2011). The

reasons for this decrease are unclear, but are likely not artefactual due to the long-standing high-quality data available for the United States. A Japanese analysis based on data from several regional cancer registries reported a 1.5 fold increase in ovarian cancer rates from 1975 to 1993 (Tamakoshi et al., 2001). The Chinese Shanghai Cancer Registry also reported an increase in ovarian cancer incidence from 1979-1989 (Jin et al., 1993). Some of these increases may be due to increases in population coverage or completeness of data within the registry; however, the Chinese increase is thought to be a birth cohort effect in women born between 1925-1935 (Jin et al., 1993).

Region	Case count	Rate
World	224747	6.3
More developed regions	99521	9.3
Less developed regions	125226	5.0
Africa	13976	4.2
Sub-Saharan Africa	9961	4.0
Eastern Africa	3840	4.0
Middle Africa	1728	4.3
Northern Africa	4015	4.8
Southern Africa	893	3.8
Western Africa	3500	3.8
Latin America and Caribbean	16981	5.9
Caribbean	1005	4.3
Central America	3571	5.2
South America	12405	6.2
Northern America	23895	8.7
Asia	102408	5.1
Eastern Asia	40831	4.3
South-Eastern Asia	18580	6.6
South-Central Asia	38797	5.5
Western Asia	4200	4.8
Europe	65697	10.1
Central and Eastern Europe	27071	11.0
Northern Europe	10256	11.8
Southern Europe	11751	8.4
Western Europe	16619	8.9
Oceania	1790	7.6
Australia/New Zealand	1601	7.8
Melanesia	161	5.1
Micronesia/Polynesia	28	5.5
Micronesia	15	6.1
Polynesia	13	5.0

Table 2. Ovarian cancer incidence counts and rates for selected regions and continents worldwide. Rates are per 100,000 women and age-standardized to the 1960 world standard population. Source: Ferlay et al., 2011.

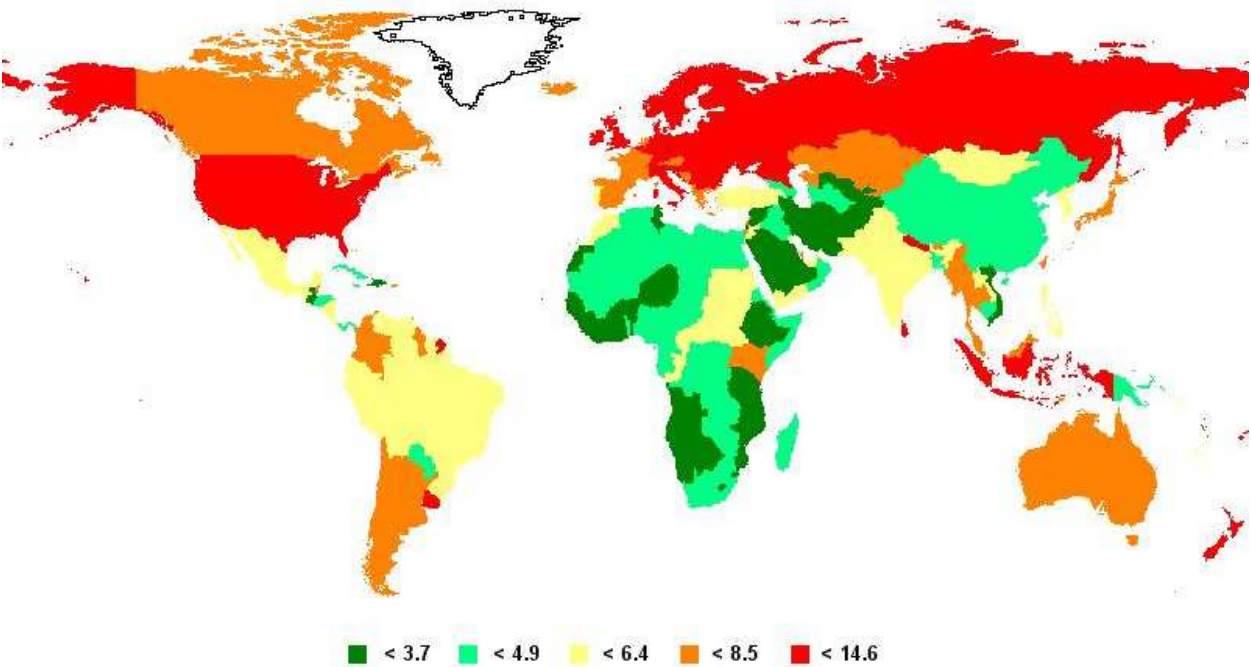


Fig. 1. Map of ovarian cancer rates worldwide. Rates are per 100,000 women and are age-standardized to the 1960 world standard population. Data were not included for white areas on the map. Source: Ferlay et al., 2011.

Incidence patterns stratified by region can assist with assessment of environmental or cultural factors that may increase risk. Regional variation in ovarian cancer rates exists, and this variation can sometimes be substantial. Percentages of ovarian cancer cases in World Health Organization regions are shown in Figure 2, these percentages range from 4.4% in the Eastern Mediterranean region (EMRO) to 31.0% in the European region (EURO) (Ferlay et al., 2010).

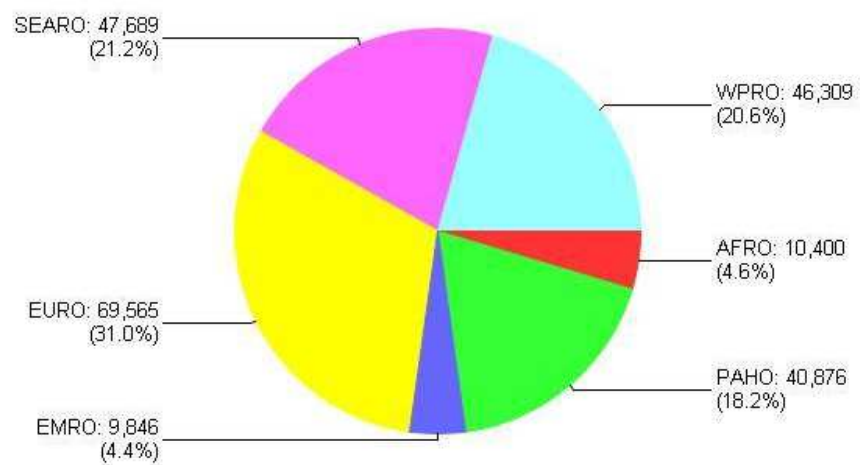


Fig. 2. Percentage of ovarian cancer cases by World Health Organization (WHO) health organization region. SEARO=Southeast Asia Regional Office, EURO=European Regional Office; EMRO=Eastern Mediterranean Regional Office; WPRO=Western Pacific Regional Office; AFRO=Africa Regional Office; PAHO=Pan American Health Organization. Source: Ferlay et al., 2011.

These numbers do not take into account the population, and may likely be reflective of the population coverage of cancer registration in these areas. In the United States, ovarian cancer incidence rates are similar among the Northeast, Midwest, and South U.S. Census regions (11.7-12.9), and individual state rates range from 7.3 to 15.4 (U.S.Cancer Statistics Working Group, 2010). Studies in Egypt (Dey et al., 2010) and Italy (Minelli et al., 2007) have found ovarian cancer rates to be higher in urban compared to rural areas. Table 3 displays the ovarian cancer case counts and incidence rates by U.S. census region and division, and by state in the United States.

Geographic Area	Case count	Rate
United States	20,749	12.2
Northeast	4,375	12.9
New England	1,057	11.9
Connecticut	268	12.1
Maine	98	11.8
Massachusetts	473	11.8
New Hampshire	99	12.5
Rhode Island	77	11.8
Vermont	42	10.8
Middle Atlantic	3,318	13.3
New Jersey	696	13.3
New York	1,516	13
Pennsylvania	1,106	13.7
Midwest	4,724	12.3
East North Central	3,318	12.4
Illinois	896	12.6
Indiana	428	11.7
Michigan	755	13.1
Detroit	320	13.7
Ohio	827	12
Wisconsin	412	12.7
West North Central	1,406	12.1
Iowa	248	13.7
Kansas	196	12.6
Minnesota	352	12.1
Missouri	403	11.5
Nebraska	108	10.4
North Dakota	46	12.9
South Dakota	53	11.4
South	7,298	11.7
South Atlantic	4,045	11.9
Delaware	78	15.4
District of Columbia	31	9.4
Florida	1,391	11.8

Geographic Area	Case count	Rate
Georgia	638	13.2
Atlanta	191	12.1
Maryland	367	11.2
North Carolina	612	12
South Carolina	295	11.4
Virginia	491	11.3
West Virginia	142	11.9
East South Central	1,187	11.2
Alabama	312	11.1
Kentucky	278	11.3
Mississippi	173	10.3
Tennessee	424	11.8
West South Central	2,066	11.6
Arkansas	188	11
Louisiana*	237	9.6
Oklahoma	272	13
Texas	1,369	11.8
West	NR	NR
Mountain	NR	NR
Arizona	397	11.6
Colorado	334	13.3
Idaho	119	15
Montana	65	11
Nevada	NR	NR
New Mexico	129	11.9
Utah	103	9.1
Wyoming	22	7.3
Pacific	3,183	12.4
Alaska	37	13.1
California	2,319	12.3
San Francisco-Oakland	317	12.8
San Jose-Monterey	158	12.8
Los Angeles	626	12.6
Hawaii	92	12.2
Oregon	280	12.7
Washington	455	12.5
Seattle-Puget Sound	332	13.2

Table 3. Ovarian cancer incidence counts and rates for the United States, U.S. Census regions and divisions and individual states. Rates are per 100,000 women and age-adjusted to the 2000 U.S. standard. Data presented cover 99.1% of the U.S. population. *Indicates that data differ from that presented by the Louisiana Tumor Registry and the SEER Program. NR=not reported. Source: (U.S.Cancer Statistics Working Group, 2010).

3.1 Clinical factors (histology, stage, laterality) and ovarian cancer incidence

Ovarian cancers are classified into three main histologic groups: epithelial tumors, sex cord-stromal tumors, and germ cell tumors (Cannistra et al., 2011). Epithelial tumors are believed to originate from the surface epithelium of the ovary (Chen et al., 2003). There are four main subtypes of epithelial tumors: serous, mucinous, endometrioid, and clear cell adenocarcinomas (Chen et al., 2003). Sex cord-stromal tumors originate in granulosa or thecal cells, or other stromal cells. Germ cell tumors are formed by cells that are believed to be derived from primordial germ cells, and they include the subtypes dysgerminomas, teratomas, and yolk sac tumors, among other subtypes (Chen et al., 2003). Several histologic-specific ovarian cancer incidence studies are published in the peer-reviewed literature, and most are based on populations in the United States. In a 2003 publication, Goodman et al. reported that 91.9% of ovarian tumors were epithelial, 1.2% were sex cord-stromal, and 1.9% were germ cell (Goodman & Howe, 2003). Serous adenocarcinoma was the most incident epithelial subtype, accounting for 37.7% of all ovarian tumors (Goodman & Howe, 2003). These U.S. data are consistent with those from the Netherlands, where 89% of all ovarian cancer diagnoses were reported to be epithelial tumors (Koper et al., 1996).

Effective early detection methods for ovarian cancer do not currently exist, and symptoms for ovarian cancer can be vague and gastrointestinal (as opposed to gynecologic) in nature. Because of this, many ovarian tumors are diagnosed at advanced stages. In the United States, studies show that about 20% of all ovarian cancer cases are localized stage at diagnosis, about 13% are regional stage, and the majority are distant stage (58%) (Goodman et al., 2003). This distribution differs by histologic type. Sex cord-stromal and germ cell tumors are more often diagnosed at localized stages (>50%) compared to epithelial tumors (19%) (Goodman et al., 2003). In the Netherlands, two thirds of all ovarian cancers were found to be extended to the pelvis or beyond at diagnosis (Koper et al., 1996).

There is a paucity of analyses on laterality. In a U.S. population, serous adenocarcinomas were found to be bilateral at diagnoses in 57.5% of cases, and other epithelial tumors ranged in bilaterality from 13.3% to 35.6% (Boger-Megiddo & Weiss, 2005).

3.2 Demographic factors (age and race/ethnicity) and ovarian cancer incidence

Age is commonly reported in most ovarian cancer incidence publications. Globally, ovarian cancer incidence rates increase with advancing age and range from 0.2 among those aged 0-14 to 29.2 among those aged 75 years and older (Ferlay et al., 2010). A similar pattern is seen in more developed countries; however, the incidence rates are higher and range from 0.3 to 42.6 (Ferlay et al., 2010). In the United States, ovarian cancer incidence rates range from 0.3 in those aged 5-9 years to 44.2 in women aged 85 and older (U.S.Cancer Statistics Working Group, 2010). The peak ovarian cancer incidence rate of 50.6 is found among women aged 80-84 in the United States (U.S.Cancer Statistics Working Group, 2010). In developing countries, ovarian cancer occurs in younger women. In Ghana, the mean age of ovarian cases seen in a teaching hospital was 46.4 years (Nkyekyer, 2000), and in Kyrgyzstan, the average age of ovarian cancer patients was 37.9, with the highest incidence rate (11.2 per 60,000 women) observed among those aged 40-49 (Igisinov & Umaralieva, 2008).

Several published studies limit their age-specific ovarian cancer analyses to children and adolescents, and many of these specifically report on ovarian germ cell tumors, which are

diagnosed in high numbers among children and adolescents (Young et al., 2003). In an international study of cancer among adolescents, ovarian germ cell tumors were found in the highest rates among those aged 15-19 (Stiller, 2007). A study from the United States reported an overall ovarian cancer incidence rate of 0.102 for girls aged 9 years and younger, and 1.072 for girls aged 10-19 years (Brookfield et al., 2009). Other studies in the United States comparing germ cell tumor rates concluded that the incidence of ovarian germ cell tumors was significantly higher in Hispanic compared to non-Hispanic girls aged 10-19 (Poynter et al., 2010; Smith et al., 2006), and Asian/Pacific Islanders (0.059) compared to other ethnicities (Smith et al., 2006). Consistent with international studies, girls aged 15-19 years had the highest germ cell rates in the United States and it was reported that these rates are increasing (Smith et al., 2006).

Most reports examining ovarian cancer by race and/or ethnicity are in the United States population. This is likely due to the diversity in the racial and ethnic make-up of the United States. In 2007, it was reported that ovarian cancer incidence rates were highest among U.S. white women (12.6), followed by black (9.1), Asian/Pacific Islander (A/PI) (9.0), and American Indian/Alaska Native (AI/AN) women (8.0) (U.S. Cancer Statistics Working Group, 2010). Rates were lower in Hispanic women (10.2) compared to non-Hispanic women (11.3) (U.S. Cancer Statistics Working Group, 2010). Some U.S. studies have used enhanced population denominator data to probe race-specific rates further in an attempt to provide more accurate or meaningful rates. Studies using denominator data adjusted for Indian Health Service delivery regions in the United States (Espey et al., 2007; Kohler et al., 2011) report ovarian cancer incidence rates of 11.3 (Kohler et al., 2011) among AI/AN women. The most recent report examining trends concluded that ovarian cancer incidence rates have been decreasing at about 1.0% per year since 1998 among most racial and ethnic groups in the United States, with the exception of A/PI women (Kohler et al., 2011).

4. Primary peritoneal and primary fallopian tube cancers

Primary peritoneal cancer (PPC) and primary fallopian tube cancer (PFTC) are rare malignancies, but share many similarities to ovarian cancer. These three cancers are clinically managed in a similar manner (Cannistra et al., 2011). Due to their rarity, these cancers are generally not reported as a distinct or separate category in statistical monographs; reports of their incidence are limited to relatively few peer-reviewed publications. In the United States, the incidence rate of PPC is estimated to be 0.678 (Goodman & Shvetsov, 2009a). PPCs were diagnosed at later ages (mean age 67 years) and more advanced stages (85% regional/distant diagnoses) than ovarian cancer (mean age 63, 75% regional/distant diagnoses) in this same population (Goodman & Shvetsov, 2009a). In contrast, a study from a UK cancer center examining PPC found that age and tumor characteristics (stage and grade) were similar among ovarian and primary peritoneal tumors (Jaaback et al., 2006). The U.S. incidence rate of PFTC is 0.41 (Stewart et al., 2007). The vast majority of PFTCs (89%) are unilateral at diagnosis, and about 30% are diagnosed at each localized, regional and distant stages (Stewart et al., 2007). U.S. PFTC rates are similar to those reported from Finland (0.3) (Riska et al., 2003) and Denmark (0.5) (Pfeiffer et al., 1989). U.S. studies have suggested that the rates of both PPC (Goodman & Shvetsov, 2009a; Howe et al., 2001) and PFTC (Goodman & Shvetsov, 2009a; Stewart et al., 2007) are increasing. It is thought that some of this increase may be due to

reduction in the misclassification of PPC and PFTC as ovarian cancer (Stewart et al., 2007, Goodman & Shvetsov, 2009b).

5. Discussion

Ovarian cancer incidence rates reported from countries with nationwide cancer registration and those from more developed countries are generally similar to each other. In less developed countries and regions, ovarian cancer rates are relatively lower, and this is likely due in part to the lack of quality data from large portions of the population in these countries. Additionally, cancers that are related to infectious agents (i.e. not ovarian cancer), are some of the most incident cancers in developing countries (Thun et al., 2011). It should be noted; however, that while cancer overall has typically been more incident in industrialized and comparatively wealthy nations, it is suggested that cancer incidence is increasing in low and medium resource countries (Thun et al., 2009). This increase may be a result of an increased lifespan due to advances in medical treatment in these countries, as well as the adoption of Western patterns of diet, physical activity, and tobacco use (Thun et al., 2011).

Several factors, including genetic, reproductive, hormonal and behavioral factors have been suggested to increase risk for ovarian cancer. Genetic factors perhaps have the strongest and most consistent association with increased risk for ovarian cancer. At least 10% of all epithelial ovarian cancers are reported to be hereditary, with the majority (about 90%) of these related to mutations in BRCA genes and 10% related to mutations associated with Lynch syndrome (Prat et al., 2005). Hereditary ovarian cancers have distinct patterns from sporadic ovarian cancers. Many are diagnosed at younger ages and less advanced stages than sporadic ovarian cancers (Prat et al., 2005). Regarding reproductive factors, studies over several years have consistently associated nulliparity with increased risk of ovarian cancer (Modan et al., 2001; Risch et al., 1994; Vachon et al., 2002). It is estimated that nulliparity may increase risk only slightly in the average-risk population (relative risk [RR]=1.4, 95% confidence interval [CI] 1.9-2.4), but may have a more substantial effect in women with a family history of ovarian cancer (Vachon et al., 2002). Hysterectomy and tubal ligation have been consistently associated with conferring a decreased risk for ovarian cancer. Tubal ligation has been estimated to decrease risk substantially (RR= 0.33, 95% CI 0.16 to 0.64), while hysterectomy may have a weaker, but still protective association (RR= 0.67, 95% CI 0.45 to 1.00) (Hankinson et al., 1993). Oral contraceptive use has been suggested to decrease risk for ovarian cancer, while post-menopausal hormone replacement therapy use is suggested to increase risk for ovarian cancer. However, conclusions from hormonal studies have generally been less consistent and more difficult to interpret than genetic and reproductive factor studies. Although some studies have shown a protective effect of oral contraceptives on ovarian cancer (Beral et al., 2008), IARC classifies estrogen, combined estrogen-progesterone oral contraceptives, and combined estrogen-progesterone hormone replacement therapy as class one carcinogens, concluding there is sufficient evidence for their carcinogenicity in humans (IARC 2007). The relationship between behavioral factors, such as tobacco use, physical activity, and obesity and ovarian cancer has been less reported compared to the other factors mentioned. Available results are generally inconclusive. Some studies have suggested a modest increased risk of ovarian cancer in obese women (Leitzmann, et al., 2009); however, others have found no relationship between body mass index and ovarian cancer (Fairfield et al., 2002). Similarly with physical activity, one study

concluded there was a modest inverse association of physical activity and ovarian cancer risk (Biesma et al., 2006), while another concluded there was no association (Hannan et al., 2004). Smoking has been shown to increase risk for the epithelial subtype mucinous adenocarcinoma, but does not increase risk for other more incident subtypes (Jordan et al., 2006).

6. Conclusion

Although ovarian cancer patterns vary widely around the world, incidence rates are high in several regions. The etiology and natural history of ovarian cancer are poorly understood, and much more research is needed to elucidate factors that may increase or decrease risk for ovarian cancer. The analysis of incidence patterns both within and between populations is essential to revealing potential causes of and risk factors for ovarian cancer. Incidence rates from countries with high-quality data should continue to be analyzed with respect to histology and stage variation, as these types of analyses may provide clues to the pathogenesis of the disease. Currently, a major goal of ovarian cancer research is to develop an effective test that can detect the disease at its earliest stages, which would ultimately result in decreased mortality. Increased knowledge of ovarian cancer etiology and pathogenesis would greatly enhance the development of this tool. Expansions in ovarian cancer incidence registration and analyses will be very valuable in this endeavor.

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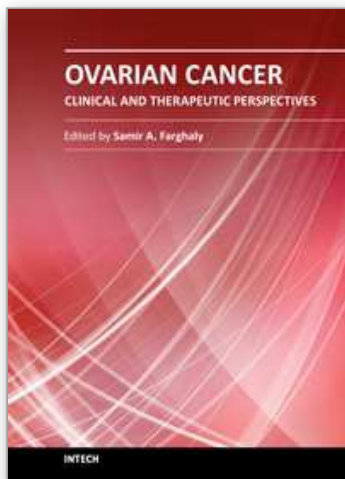
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Worldwide, Ovarian carcinoma continues to be responsible for more deaths than all other gynecologic malignancies combined. International leaders in the field address the critical biologic and basic science issues relevant to the disease. The book details the molecular biological aspects of ovarian cancer. It provides molecular biology techniques of understanding this cancer. The techniques are designed to determine tumor genetics, expression, and protein function, and to elucidate the genetic mechanisms by which gene and immunotherapies may be perfected. It provides an analysis of current research into aspects of malignant transformation, growth control, and metastasis. A comprehensive spectrum of topics is covered providing up to date information on scientific discoveries and management considerations.

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