Incidence and mortality trends of ovarian cancer in central Serbia

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Summary

Purpose: *Ovarian cancer (OC) is the most fatal cancer in females. The objective of this paper was to determine the incidence and mortality trends of OC in central Serbia from 1999 to 2003.*

Methods: *Data about all new cases and deaths of OC were obtained from the Serbian Cancer Registry. Data were analyzed for the central of Serbia which encompasses the territory of Serbia without its northern and southern regions. Data of the female population were obtained from the population censuses in the years 1991, 2002 and 2011. World population was used as a standard. Trend and annual percentage change (APC) of the incidence and mortality rate with corresponding 95% confidence intervals (CI) were calculated by performing jointpoint regression.*

Results: *Jointpoint analysis showed increased incidence trend of annual standardized rate (ASR) for OC from 1999*

to 2013 with APC 0.3% (95%CI: 0.3, 0.8). Significantly increased trend in OC mortality was recorded continuously from 1999 to 2007 with APC 2.25% (95%CI: 0.9, 3.6). Decreased mortality trend was observed in the period 2010-2013 with APC -7.34% (95%CI:-15.8, 2.0). The majority of the new cases of OC were aged 40-74 (78.7%). OC was the sixth most common cancer of all cancers in females and the sixth most common cause of cancer death in females.

Conclusions: *During 1999-2013 there was an increasing trend of incidence of OC. In 1999-2007 there was a significant increasing mortality trend and non-significant decrease of the trend from 2010 to 2013 in central Serbia. The incidence and mortality rates of OC in central Serbia were higher than the corresponding rates in neighboring countries.*

Key words: *incidence, mortality, ovarian cancer, trend*

Introduction

OC is the most lethal malignancy in females [1]. OC causes more deaths in females per year than any other cancer of the female reproductive system [2,3].

There are large variations in the incidence of OC in different areas of the world. In developed areas OC is a common malignancy in females ranking seventh or sixth most frequent cancer for incidence and mortality [4]. Worldwide, age-adjusted incidence rates range from more than 11 per 100,000 females in central and eastern Europe to less than 5 per 100,000 in parts of Africa [4].

Incidence rates were 11.7 per 100,000 in the United Kingdom (UK), 8.0 per 100,000 in USA, 5.2 per 100,000 in Brazil and 4.1 per 100,000 in China [5]. In 2013, age-adjusted incidence rate of OC was 11.9 per 100,000 females per year in USA [6].

In 2012, Fiji had the highest rate of OC, followed by Latvia and Bulgaria. About 58% of OC cases occurred in less developed countries. The

highest incidence of OC was in Europe and North America and the lowest was in Africa and Asia. In 2012, Serbia ranked fifth country in the world by value of age-adjusted incidence rate (on world population) for OC, which was 12.8 [7].

The etiology of OC is not clear but certain factors are established, such as family history of breast or OC, and considered as prominent risk factors for OC, with 5-10% of OC due to heritable risk [8,9]. Reproductive factors such as age at menopause and infertility contribute to greater risk of OC, whereas pregnancy, tubal ligation, and hysterectomy reduce the risk. Large epidemiologic studies found hormone replacement therapy (HRT) to be the greater risk factor for OC.

Lifestyle factors such as cigarette smoking, obesity and diet may affect OC risk.

Exposure to certain environmental agents such as talc, pesticides and herbicides may increase risk of OC; however, these studies are limited [9].

The objective of this article was to determine trends in age-adjusted incidence and mortality rates of OC in central Serbia from 1999 to 2013.

Methods

A descriptive epidemiological study was carried out. Data about new cases and deaths of OC were obtained from the Serbian Cancer Registry for the period 1999-2013. Data about all new cases and deaths of OC in female population of the Republic of Serbia were analyzed for the central Serbia that encompasses the territory of Serbia without its northern and southern regions. OC was coded according to the 10th Revision of International Classification of Diseases (code C56) [10]. Data of the population of the Republic of Serbia were obtained from the population censuses in the years 1991, 2002 and 2011; for inter-census years, estimates published by the Statistical Office of the Republic of Serbia were used.

In Serbia, cancer reporting is obligatory by law. The Serbian Cancer Registry was established in 1970 and after 1998, a new methodology was applied which substantially improved data quality and the Registry became a member of International Agency for Research on Cancer (IACR) and European Network of Cancer Registries (ENCR). Sources of data collection for The Registry are hospitals and out-patients health institutions, oncology clinics, dispensaries and institutes, pathology laboratories, death reports and health insurance funds [11].

Statistics

Crude rates, age-specific and age-adjusted incidence and mortality rates were calculated per 100,000 inhabitants. The method of direct standardization was performed and world population was used as a standard. Trend and annual percentage change (APC) of the incidence and mortality rate with corresponding 95% confidence intervals (CI) were calculated by performing jointpoint regression analyses to identify the years in which a significant change in trends occurred.

For regression analyses, the Joinpoint Regression Program version 4.1.0 was used (available at http: //surveillance.cancer.gov/joinpoint). The trend was considered to be significantly increasing (positive change) or decreasing (negative change) when the p value was below 0.05 (p<0.05).

Results

During the observed period the total number of new cases of OC was 7003. In the period 1999-2009 OC comprised 4.8% of all cancers registered in female population, and in the period 2010-2013 OC accounted for 4.4% of the registered cancers in females. In the observed period the total number of deaths of OC was 4,403. OC was the sixth most common registered cancer in females and the sixth most common cause of cancer death in females.

Crude and age-adjusted incidence and mortality rates (to the world standard population)-ASR, by the year of registration are presented on Table 1.

Crude incidence rates ranged from 14.6-20.5 and age-adjusted incidence rates ranged from 9.3-11.3 per 100,000 inhabitants.

Crude mortality rates ranged from 7.9 to 10.9 and age-adjusted mortality rates ranged from 4.3-5.5 per 100,000 inhabitants.

A new case of OC was registered in all ages but it was not common before the age of 40. Rapid increase of new cases was registered in females after 40 years of age. The vast majority of new
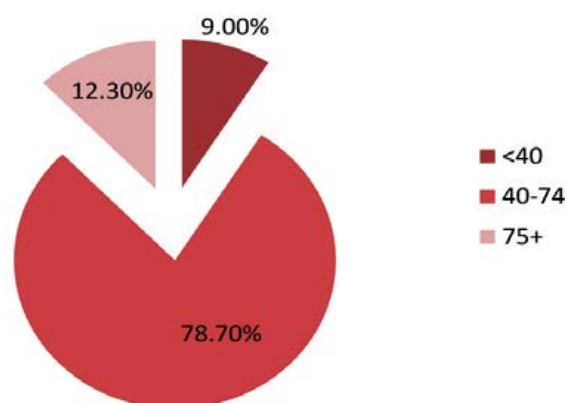

Figure 1. Distribution of new cases of ovarian cancer by age in the period 1999-2013, central Serbia.

cases of OC included patients aged 40-74 years (78.7%). The number of new OC cases decreased in females aged above 75 years (Figure 1).

Considering OC (ICD-10, C56), the jointpoint analysis showed that the increased incidence trend of ASR for OC was in the period 1999-2013 with APC 0.3% (95% CI: 0.3, 0.8) (Figure 2).
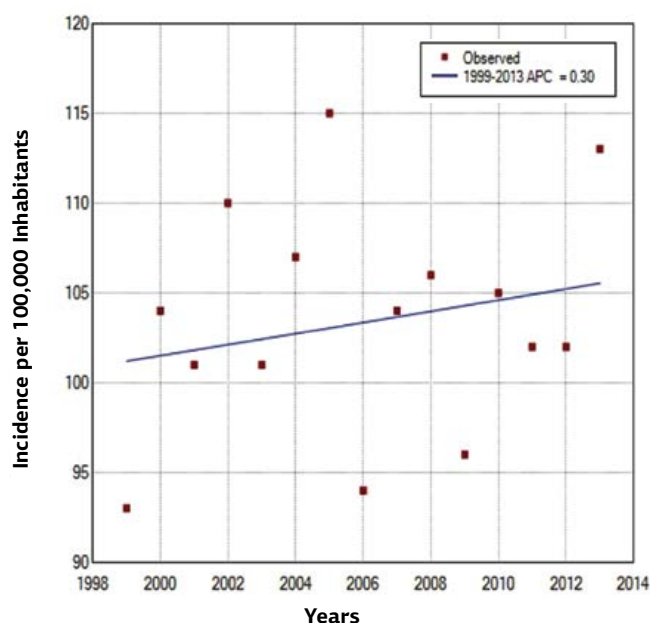
Figure 2. Joinpoint analyses of age standardized incidence rates in females (world standard population) of ovarian cancer in central Serbia, 1999-2013, with annual percentage change (APC).
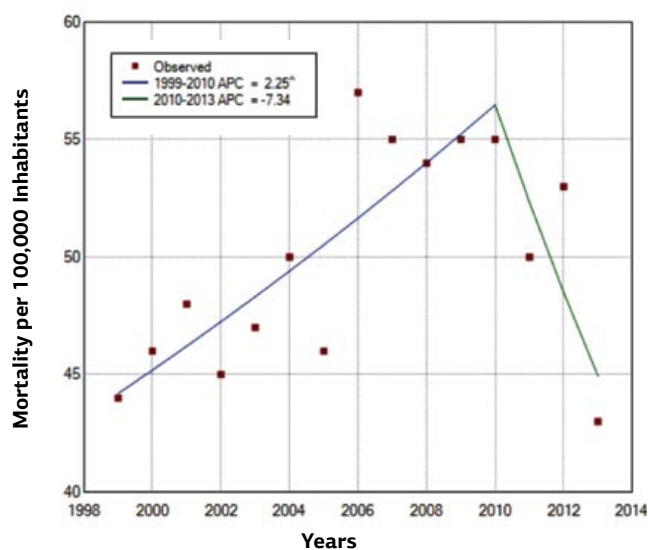
Figure 3. Joinpoint analyses of age adjusted mortality rates in females (world standard population) of ovarian cancer in central Serbia, 1999-2013, with annual percentage change (APC).

Jointpoint regression analysis showed statistically significant increasing mortality trend of ASR for OC during 1999-2007 with APC 2.25% (95% CI:0.9, 3.6) and a decreasing mortality trend during 2010-2013 with APC -7.34% (95% CI:-15.8, 2.0) (Figure 3).

Discussion

During 1999-2013 both crude and age-adjusted incidence rates of OC increased in central Serbia. Crude and age-adjusted mortality rates increased in the period 1999-2007, but after 2010 mortality rates decreased.

The presented results have shown a continuous increase of incidence trend of OC during the 15-year study period and statistically significant increase of mortality trend in the period 1999-2007. In 2010-2013 there was a decreasing mortality trend of OC.

According to the findings of this study, OC was the sixth most common cancer of all registered cancers in females and the sixth most common cause of cancer death in females in central Serbia in the period 1999-2013.

Among women in USA, OC is the ninth most common cancer and the fifth leading cause of cancer death, after lung and bronchus, breast, colorectal, and pancreatic cancers. OC causes more deaths than any other cancer of the female reproductive system, but it accounts for only about 3% of all cancers in females in USA [12].

OC is the eighth most common cancer among females, and includes about 4% of all women's cancers [13]. In central Serbia, OC comprised 4.8% of all cancers registered in female population in the period 1999-2009, and in the period 2010-2013 it accounted for 4.4% of registered cancers in females. These findings show that OC is more common among females in central Serbia as a cause of malignant disease than in other countries.

In 2012, the age-adjusted incidence rate of OC was higher only in Bulgaria compared with central Serbia.

The age-adjusted incidence rate for OC was higher in central Serbia than in Montenegro (12.0), FYROMacedonia (11.3), Hungary (10.6) and Slovenia (10.3) [14].

Decline in mortality of OC but not in incidence were observed in the Czech Republic and Hungary [4]. In most central and eastern European countries, OC incidence and mortality rates were originally relatively low, but tended to rise over time.

In the UK both OC incidence and mortality trends have decreased in recent years whilst survival has improved. Mortality rates were stable between 1989 and 2002 but fell by over 20% between 2002 and 2010 [15].

According to the presented results of this study, the incidence and mortality of OC increased with age. In the observed period, OC was registered in females of all ages but it was not common before the age of 40. Most cases were aged between 40 and 74 years.

There are various links between the development of OC and age. Not only does the rate of OC increase with age, but several known risk factors involve a female's age with certain reproductive events. OC is relatively rare in women under the age of 40 according to the American Cancer Society. Fifty percent of all cases of OC involve females aged 63 or older, and the highest recorded rates were in females aged 55 to 64 [16].

During the last 10 years, incidence and mortality rates have decreased most notably in females aged 50-69. The recent downward trend in the incidence of OC among females aged 50 and over may reflect the protective benefit of the oral contraceptive pill [17].

An increasing trend in the incidence rate of OC with a mean annual percentage increase in ASR ranging from 0.7 to 2.4% was recorded in India [18].

The recorded significant increasing mortality trend of OC in central Serbia in the period 1999-2007 seems to be connected with the problem of early diagnosis and the absence of screening for OC. The declining mortality trend of OC could be partially explained by better diagnosis and improvements in the treatment of OC in the period 2010-2013.

Mortality due to OC is high because of the difficulty in early diagnosis of the disease and limited effective treatment options [2]. Most of the patients are diagnosed in stage 3 (71%) or 4 (31%). Identifying this disease is hard, and the survival rate is low [16].

Early detection of OC has been a goal of clinical research [19]. A recent consensus statement [20] jointly issued by the Gynecologic Cancer Foundation, Society of Gynecologic Oncologists and the American Cancer Society identified four symptoms that are more likely to occur in women with OC: 1) bloating; 2) pelvic or abdominal pain; 3) difficult eating or feeling full quickly; and 4) urinary symptoms (i.e., urgency or frequency). Taken together, these symptoms are called the Ovarian Cancer Symptom Index [19].

Two studies have provided evidence to support the clinical use of the Ovarian Cancer Symptom Index [21,22].

There is inadequate evidence to support screening for OC in the general population. There are two large, ongoing prospective randomized controlled trials (RCT) [23,24] that could provide important information about the efficacy of using transvaginal ultrasound (TVU), CA125, and screening examinations for the early detection of OC.

The first RCT, being conducted in USA, is the Prostate, Lung, Colorectal, and Ovarian (PLCO) screening trial, sponsored by the National Cancer Institute (NCI). This study includes 37,000 healthy postmenopausal women between 55 and 74 years of age who were randomized to either an annual CA125, TVU, and pelvic examination or standard care [23]. The endpoints are cost and the establishment of important time-points for screening. The outcome variable is mortality. Patients will be followed for 13 years. Based on preliminary analyses, 1,338 participants (4.7%) had abnormal TVU and 402 (1.4%) had abnormal CA125 (only 34 had abnormal results of both tests) [24].

Screening for OC with CA 125 and TVU increased the number of OC diagnosed but did not reduce the number of deaths from this cancer [25].

The second study, being conducted in the United Kingdom, has enrolled 200,000 postmenopausal women and is called the North Thames Ovarian Cancer Study (UKTOCS). This study is attempting to determine the sensitivity of CA125 plus TVU versus TVU alone as screening measures for OC. The study endpoints include quality of life, morbidity, and cost [19].

Althought the basic plan of screening program was made in 2000 [26], the National program "Serbia against cancer" [27] defined the baseline of mass screening of breast, cervical and colorectal cancer, few years ago [18]. OC screening doesn't exist. Only opportunistic screening has been implemented in the Republic Serbia [28].

Conclusion

The presented results of this study showed an increasing incidence trend of OC in the period 1999-2013. There was a statistically significant increasing mortality trend in the period 1999-2007 but after 2010 the mortality trend was decreasing. The incidence and mortality rates of OC in central Serbia were higher than the corresponding rates in neighboring countries.

Conflict of interests

The authors declare no conflict of interests.

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