Epidemiological data of ovarian cancer in Vojvodina and South Great Plain region in Hungary in 2007-2012 period: CrossBiomark IPA PROJECT HUSRB/1203/214/091

Aljoša Mandić[1], László Thurzó[2], Dejan Ninčić[1], Milica Živaljević[1], Tihomir Dugandžija[1], Róbert Berkecz[3]

SUMMARY

Background: *Ovarian cancer is among the sixth leading cancers in Vojvodina and the fifth leading cause of cancer death among female population in Vojvodina according to Cancer Registry of Vojvodina in 2010. The majority of ovarian cancers cases are diagnosed at an advanced stage, FIGO stage III-IV with poor prognosis. The aim of the study was to evaluate newly diagnosed ovarian cancer among female population in Vojvodina (Serbia) and South Great Plain region in Hungary in 2007- 2012 period.*

Methods: *The evaluation was based on the data from hospital registries for malignant diseases at the Oncology Institute of Vojvodina and the Department of Oncotherapy, University of Szeged.*

Results: *The majority of patients were diagnosed in advanced disease (FIGO stage III-IV) in both regions. Serous epithelial ovarian cancer was the most common cancer type among studied women in both regions. The average age of women diagnosed with ovarian cancer was 60 years; there was no significant statistical difference related to patients' age in both studied regions. Advanced stage of ovarian cancer investigated in our study showed a moderate descending liner trend with no significant statistical difference. The results from our study were similar when compared with the epidemiological data from the literature.*

Conclusion: *The lack of efficient screening methods is the major obstacle to improve the prognosis of women affected by this disease. Further investigations and introduction of new technologies applied to medical discoveries offers new hope for finding effective screening policies.*

Key words: *Ovarian Neoplasm; Epidemiology; Neoplasm Staging; Serbia; Hungary*

INTRODUCTION

It is estimated that there are 65,697 new cases of ovarian cancer and 41,448 deaths in Europe each year (1). Ovarian cancer is among the sixth leading cancers in Vojvodina and the fifth leading cause of cancer death among female population in Vojvodina according to Cancer Registry of Vojvodina in 2010 (2). Only one fourth of women present with localized disease at diagnosis. The majority of ovarian cancer cases are diagnosed at an advanced stage of disease (FIGO stage III-IV) (3). The prognosis for survival from ovarian cancer is largely dependent upon the extent of disease at diagnosis.

Approximately 15% of patients are presented with disease confined to the ovaries and after surgery, their 5-year survival is more than 90%. A 5-year survival among patients with advanced disease (FIGO stage III-IV) is less than 30% (4).

The etiology of ovarian cancer is poorly understood. Early diagnostic of ovarian cancer is mandatory. Still, there is not enough sensitive diagnostic tool for early detection that can be recommended. There are numerous methods that have been tested in the preoperative identification of adnexal masses suspicious for malignancy. The results of some trials have reported the efficacy of screening of asymptomatic women with annual measurement of CA 125 and transvaginal ultrasound examination but they have failed to demonstrate a reduction in mortality (5).

Risk factors for developing ovarian cancer are numerous: ages (over 50), gene mutation (BRCA 1, BRCA 2, and Lynch II syndrome), geographic variations (higher incidence in North America, and North Europe), reproductive factors (nullipara, infertility), and hormonal factors (6). The most common histopathological type of ovarian cancer is epithelial cancer and the most common histological subtype is serous carcinoma (7). The clinical symptoms of early ovarian cancer are non-specific such as abdominal pain, bloating, changes in bowel frequency, and urinary and/or pelvic symptoms (8-10).

The aim of this study was to evaluate epidemiological data of newly diagnosed ovarian cancer from Hospital Registry for Malignant Disease in Oncology Institute of Vojvodina and Department of Oncotherapy, University of Szeged in South Great Plain region in Hungary, in the period 2007-2012.

PATIENTS AND METHODS

According to the census of population in Republic of Serbia in 2011, total number of population in region of Vojvodina is 1 916 889 (11). In South Great Plane in Hungary total number of population is 1 355 000 (12).

According to the first goal of the Cross-border biomarker research of ovarian cancer (HURSB/1203/214/091), co-financed by the European Union, we evaluated an epidemiological data from Hospital registry for malignant disease of Oncology Institute of Vojvodina and Department of Oncotherapy, University of Szeged in South Great Plain region in Hungary (SGP), in 2007-2012 period of time. The data was collected from Tumor Board for Gynecological Malignancies at the Oncology Institute of Vojvodina where all patients from Vojvodina with diagnosed ovarian cancer are

evaluated for further therapy and patients that are treated at the Department of Oncotherapy, University of Szeged as center of gynecological oncology for South Great Plane region. For statistical evaluation, we used t-test. Values of p<0.05 were considered to denote significant differences.

RESULTS

From January 1, 2007 to December 31, 2012, 712 newly diagnosed ovarian cancer patients were registered at the Oncology Institute of Vojvodina (average: 118 patients per year) and 175 patients in SGP region, Hungary (average: 29 patients per year) (Figure 1).

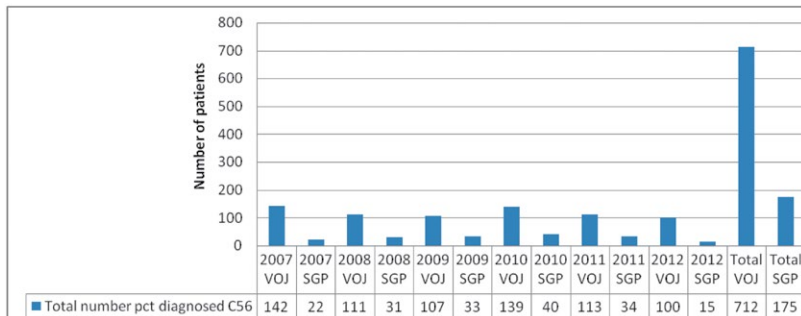|	2007 VOJ	2007 SGP	2008 VOJ	2008 SGP	2009 VOJ	2009 SGP	2010 VOJ	2010 SGP	2011 VOJ	2011 SGP	2012 VOJ	2012 SGP	Total VOJ	Total SGP
Total number pct diagnosed C56	142	22	111	31	107	33	139	40	113	34	100	15	712	175

Figure 1. Distribution of newly diagnosed patients in Vojvodina and South Great Plain, Hungary in 2007-2012 period (VOJ – Vojvodina; SGP - South Great Plain)

The most common histopathological type was epithelial ovarian cancer: 74.44% (530/712) patients in Vojvodina and 89.71% (157/175) in SGP (p>0.05). The non-epithelial ovarian cancer was found in 6.74%, (48/712), patients in Vojvodina and 3.43%, (6/175) in SGP (p≤0.05). Patients with ovarian cancer of unknown histopathology were more common in Vojvodina compared to SGP: 18.82% (134/712) vs. 6.86% (12/175) (p≤0.05).

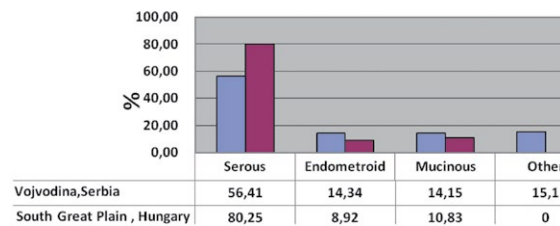|	Serous	Endometroid	Mucinous	Other
Vojvodina,Serbia	56,41	14,34	14,15	15,1
South Great Plain , Hungary	80,25	8,92	10,83	0

Figure 2. Distribution of the most diagnosed subtypes of epithelial cancer in the period 2007-2012

In both regions, the most frequent was serous subtype of epithelial ovarian cancer: 299/530 patients in Vojvodina (average: 49.83 pt /year) and 126/157 (average: 21 pt/year) in SGP (p≤0.05). Endometrioid and
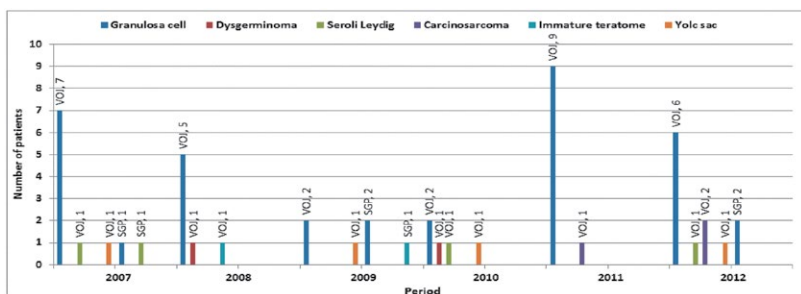

Figure 3. Distribution of the most diagnosed subtypes of non-epithelial in Vojvodina and South Great Plain in the period 2007-2012; (VOJ - Vojvodina, SGP - South Great Plain)

mucinous subtypes were more common among women in Vojvodina than in SGP but difference was not significant (p>0.05) (Figure 2).

The most diagnosed subtype of non-epithelial type of ovarian cancer was granulose cell subtype: 64.58% (31/48) and 71.43% (5/7) in Vojvodina and SGP, respectively (p>0.05). Other subtypes were diagnosed in smaller number (Figure 3).

Ovarian cancer is classified according to FIGO classification.

Due to suboptimal surgical staging in some hospitals in Vojvodina the FIGO stage was not determined in 113/712 (15.87%) patients. Therefore, FIGO classification was done in 599 out of 712 (84.13%) patients in Vojvodina.

In both regions the majority of patients were in FIGO stage III-IV, 59,6% i Vojvodina vs. 65,4 in SGP, Hungary (p>0.05). Similar percent of patients in FIGO stage I and FIGO stage II was diagnosed in both regions (Figure 4).

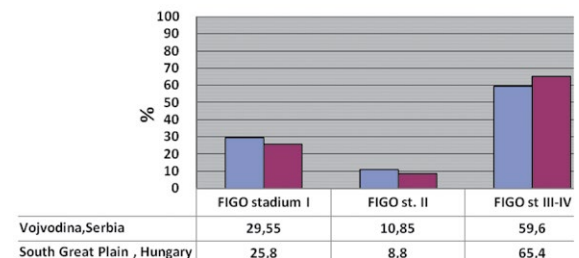|	FIGO stadium I	FIGO st. II	FIGO st III-IV
Vojvodina,Serbia	29,55	10,85	59,6
South Great Plain , Hungary	25,8	8,8	65,4

Figure 4. FIGO stage of newly diagnosed ovarian cancers in the period 2007-2012

As the distribution of ovarian cancer cases by FIGO stage classification was without statistical significance, we created linear trends using epidemiological data from Vojvodina. The linear trends of the reported cases in FIGO stage I and II for the period 2007-2012 showed ascending trends but it was also without statistical significance (p>0.05) (Figures 5 and 6). Epidemiological data for FIGO stages III and IV are summarized (Figure 7) and linear trend showed only moderate descending (p>0.05).

The average age of patient with diagnosed ovarian cancer was 55.94 years. The patients diagnosed with FIGO stage I and II were younger than patients with advanced disease (FIGO stage III-IV) in both regions. The difference in average age of patients based on FIGO classification was statistically significant (p < 0.0001) only for patients from Vojvodina (Figure 8).

Ovarian cancer was diagnosed in most patients that were older than 50 years,(p < 0.0001) (Figure 9).

DISCUSSION

The ovarian cancer is estimated as the most lethal malignant gynecological oncologic disease. The majority of the newly diagnosed cases are in advanced disease (3). In our study, majority of patients (≥60 %) were diagnosed in advanced disease, FIGO stage III-IV, in both Vojvodina, Serbia and South Great Plain, Hungary. The results are comparable with UK epidemiological data where the most women are also diagnosed with advanced stage disease: 60% stage III, IV, and around 30% in the early stages I and II (13). Similar results reported Malenkovic et al. (14) for period 2001-2008 in Vojvodina. In both regions, we found similar percent

of patients in FIGO stage I and FIGO stage II. According to literature data, 56% of ovarian cancers are epithelial cancers by origin (15).

The results of histopathological analyses were also similar in our both regions. The most common epithelial ovarian cancer subtype in both regions was serous ovarian cancer. In 2009 in UK serous subtype accounted for one-third of all cases which is comparable with number of newly diagnosed serous ovarian cancer in Vojvodina (16). The higher prevalence of the serous ovarian cancer was diagnosed in South Great Plain. One of the reasons for such significant differences between two regions may be the higher percentage of unknown histopathological type: 18.82% in Vojvodina population and only 6.86% in South Great Plain. Ovarian cancer is predominantly a disease of older women. Usually, it is diagnosed in women age around 60 years (3). The average age of patients in our study was 55.94 without significant difference between both regions. Our patients were older than 50 years in more than 80% that is in agreement with previous UK report (16).

In our study, advanced disease showed a moderate descending linear trend. Malenković et al. study (14) for the period 2001-2008 in Vojvodina, showed ascending linear trend, but also without statistical significance (14).

Diagnostic approaches in the preoperative identification of ovarian malignancy were also studied (17-22). It is suggested that 3D ultrasonography has higher sensitivity and specificity compared to 2D ultrasound (18, 19). In addition, morphological scoring systems have satisfying sensitivity and specificity (20-22). Explicit scoring systems such as risk of malignancy index (RMI), is based on the score obtained by ultrasound (U), menopausal status (M), and CA-125 data in the following manner: $RMI = U \times M \times CA\text{-}125$. A cutoff of 200 was used to differentiate between malignant and benign masses in the original study (13).Two studies reported on diagnostic accuracy of RMI (23, 24). The overall sensitivity and specificity were 79.2% and 91.7%, respectively. These data were obtained by bivariate random effects model from 13 studies with 15 data sets (23, 24). In evaluation of the three imaging modalities (NMR, CT, PET), NMR appeared the best, but results were not statistically different from CT. PET did not have any better performance than CT or NMR. Tumor biomarker CA 125 was also considered for diagnosis of ovarian cancer. However, its frequent measurement was found to be less reliable than other available assessment methods. In summary, results of bivariate analysis of 51 studies (52 data sets) showed that overall sensitivity was 78.7% and specificity was 77.9% (17).

CONCLUSION

The vast majority of newly diagnosed ovarian cancer in Vojvodina, Serbia and South Great Plain, Hungary were patients with advanced disease stages. Newly diagnosed ovarian cancer was mostly found in women over 50 years old. Trends of FIGO classified stages in evaluated period did not show statistically significance fluctuation. The most diagnosed histological type was epithelial ovarian cancer and serous subtype in both regions. The results were comparable and similar to epidemiological data from the literature.
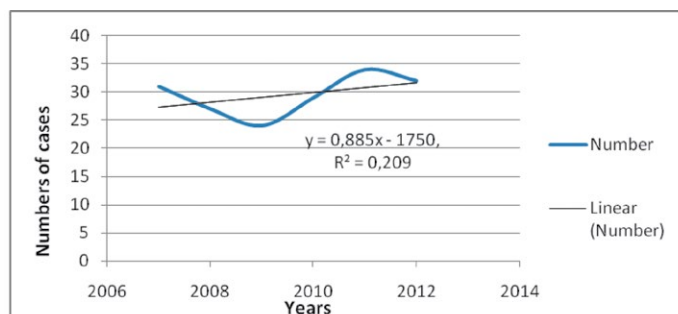

Figure 5. Linear trend of ovarian cancer cases, FIGO stage I in Vojvodina in the period 2007-2012
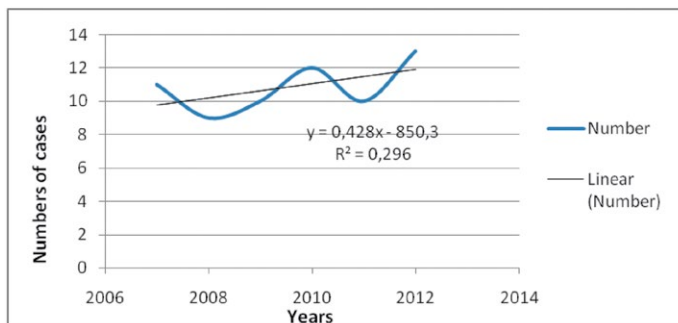

Figure 6. Linear trend of ovarian cancer cases, FIGO stage II in Vojvodina, in the period 2007-2012
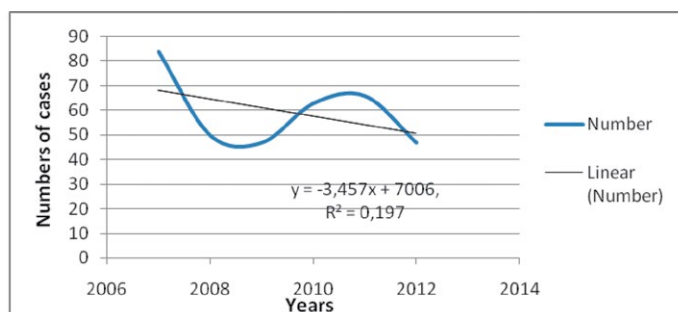

Figure 7. Linear trend of ovarian cancer cases, FIGO stage III-IV in Vojvodina in the period 2007-2012
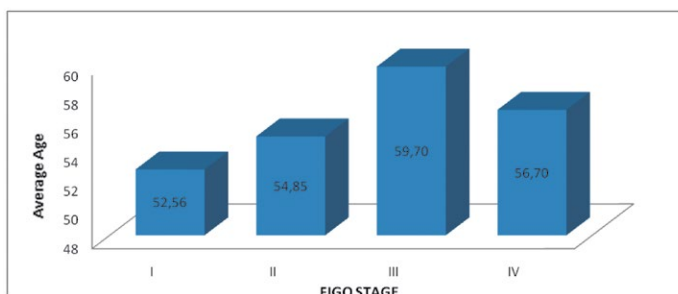

Figure 8. Distribution of average ages in patients with ovarian cancer by FIGO stages I-IV in Vojvodina in the period 2007-2012
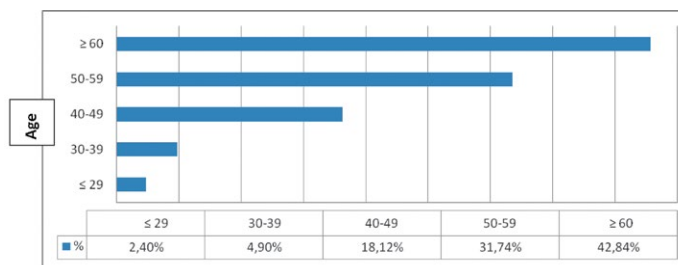

Figure 9. Distribution of ovarian cancer by age in Vojvodina in the period 2007-2012

Conflict of Interest
We declare no conflicts of interest.

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