Epidemiological aspects of ovarian malignancies in North Sardinia in the period 1992-2001

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Summary

Malignant ovarian tumors have been continuously increasing in Western countries and represent the leading cause of death for gynecological cancer. In fact, the mortality for malignant ovarian tumors remains very high with a low percentage of 5-year survival in the advanced stage of disease. The aim of this study was to evaluate the incidence trend and epidemiological characteristics of malignant ovarian tumors in the Province of Sassari, Sardinia (Italy) in the period 1992-2001 and to report the variations in comparison to the 1974-1985 period. The analysis of our data regarding the period 1992-2001, if compared with those of the period 1974-85, showed an increase of malignant ovarian tumors which triplicated achieving an incidence of 11.99/100,000 vs 4.27/100,000. The analysis of our epidemiologic data showed an increase of the age of first diagnosis (mean 60.9 years for epithelial ovarian tumors), the occurrence of the cancer in women at low socio-economic levels and a family history of cancer among the patients with malignant ovarian tumors. These data suggest that both local environmental factors combined with genetic characteristics play a role in the pathogenesis of ovarian tumors. The genetic characteristics could be of particular interest because Sardinia has been through the centuries a geographical area with little population migration. The marked increase in the incidence of ovarian tumors in the last several years points out the need to organize systematic screening by ultrasonography in our population.

Key words: Malignant ovarian tumor; Incidence; North Sardinia.

Introduction

Malignant ovarian tumors have been increasing over the decades in Western countries and account for about 20% of all female genital tumors [1]. Ovarian cancer is the fifth leading cause of death due to malignant tumors among women in the European Union. [2] The mortality rate for ovarian cancer remains very high (about 15,000 deaths per year in USA) [3]. Five-year survival is about 30% and 20% for women with Stage III and IV, respectively [4].

The women who have a diagnosis of malignant ovarian tumor in 75% of cases have advanced stage disease [5]. The scanty symptomatology and the lack of a efficacious screening program may explain the low incidence of cases who are diagnosed at Stage I of disease in which a 90% five-year survival may be reached.

In a previous paper [6] we compared the incidence of gynecological tumors in the Province of Sassari in the period 1974-1983 and 1992-2000 and we observed a consistent increase of endometrial carcinomas and a dramatic increase of malignant tumors of the ovary in comparison to the data of previous decades.

The aim of this study was to evaluate the incidence trend and epidemiological characteristics of malignant ovarian tumors in our Province in the period 1992-2001 and to report the variations in comparison to the 1974-1985 period.

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Materials and Methods

In this collaborative study among the Obstetric and Gynecologic Clinic, the Institute of Anatomy and Histopathology of Sassari University, the Multizonal Epidemiologic Observational Center of Local Health Unit no. 1 of Sassari (Italy) and the Institute of Biomolecular Chemistry of C.N.R. of Sassari, all cases of malignant ovarian tumors, which were registered in the Province of Sassari in the period 1992-2001, have been studied in order to evaluate:

– *Absolute and relative incidence per 100,000 women and per year.*

– *Incidence per 100,000 per age-class distribution.*

– *Distribution of cases according to histotype and FIGO stage.*

– *Epidemiological characteristics (age, residence, socio-economic status, family history of cancer) in relationship to the histotype.*

The data obtained have been compared with the results of our previous study [7] which involved the same population in the period 1974-1985.

Results

Absolute and relative incidence per 100,000 women per year:

Table 1 shows the distribution of malignant ovarian tumors with regard to the year of first observation per 100,000 women. In the period 1974-1985 (overall 113 cases) the mean incidence of malignant ovarian tumors was 4.27/100,000 with values ranging from 2.72 (1979)

Table 1. — *Distribution of malignant ovarian tumors in relation to the year of first observation (number of cases and rate/100,000 women).*

Year	No. of cases		Rate/100,000
1974	10		4.54
1975	8		3.63
1976	10		4.54
1977	7		3.18
1978	10		4.54
1979	6		2.72
1980	13		5.90
1981	7		3.18
1982	7		3.18
1983	9		4.09
1984	12		5.44
1985	14		6.36
Total	113		4.27
Year	No. of cases	(Border line)	Rate/100,000
1992	28	(5)	11.7
1993	27	–	11.3
1994	33	(1)	13.8
1995	31	–	13.0
1996	26	–	10.9
1997	38	(3)	15.9
1998	47	(1)	19.7
1999	27	(4)	11.3
2000	28	(2)	11.7
2001	41	(1)	16.4
Total	326	(17)	11.99

to 6.36 (1985). In the period 1992-2001 (overall 326 cases), the mean incidence (including 17 cases of border line tumors without invasive implants) resulted to be 11.99/100,000, with values ranging from 10.9 (1996) to 19.7 (1998).

Incidence per 100,000 women per year:

Table 2 shows the incidence per 100,000 women selected by age group comparing the data of the period 1974-1985 with those of the period 1992-2001. Malignant ovarian tumors in the first period (1974-1985) had their peak of incidence (17.43/100,000) between 65 and 69 years whereas in the second period (1992-2001) the peak (37.1/100,000) was registered in advanced age (80-84 years). If we consider the age groups, the class at highest risk for malignant ovarian tumors was between 50 and 84 years and we reported an incidence of 26.9/100,000 women.

Table 2. — *Incidence of malignant ovarian tumors (rate/100,000 women) for age-class distribution (1974-1985 vs 1992-2001).*

Year	1974-1985 /100,000	1992-2001 /100,000
15-19	–	1.49
20-24	–	4.33
25-29	1.94	3.0
30-34	0.66	6.1
35-39	5.08	3.5
40-44	1.46	9.2
45-49	12.15	10.0
50-54	10.75	20.0
55-59	7.81	21.2
60-64	8.45	23.6
65-69	17.43	24.4
70-74	5.0	28.8
75-79	–	35.3
80-84	–	37.1
85-89	–	27.2
90-94	–	36.3
Mean/100,000	4.27	11.99

Histotype:

In the period 1974-85 (Table 3) we had 113 cases of malignant tumors of the ovary; the histotypes of malignant epithelial tumors were 97/113 (85.8%): 76/113 (67.2%) serous papilliferous cystoadenocarcinomas, 9/113 (8%) mucinous cystoadenocarcinomas, 2/113 (1.8%) endometrioid adenocarcinomas, 8/113 (7.0%) solid carcinomas, and 2/113 (1.8%) clear cell adenocarcinomas. We had 10/113 (8.8%) malignant stromal tumors: two granulous cell tumors, two malignant

Table 3. — *Distribution of histotypes of ovarian tumors (1974-1985 vs 1992-2001).*

Histotype	1974-1985 No. (%)	1992-2001 No. (%)
Epithelial	*97 (85.8)*	*306 (93.9)*
Serous	76 (67.2)	189 (57.9)
Mucinous	9 (8.0)	81 (24.8)
Endometrioid	2 (1.8)	23 (7.0)
Solid	8 (7.0)	6 (1.8)
Clear cell	2 (1.8)	6 (1.8)
Adenosquamous	–	1 (0.3)
Stromal	*10 (8.8)*	*15 (4.6)*
Granulous cell	2 (1.8)	5 (1.5)
MMMT*	–	4 (1.2)
Brenner	2 (1.8)	3 (0.9)
Sarcoma	3 (2.6)	2 (0.6)
Arrenoblastoma	3 (2.6)	–
Cystoadenofibroma	–	1 (0.3)
Germinal	*3 (2.7)*	*4 (1.2)*
Endodermic sinus tumor	–	2 (0.6)
Dysgerminoma	3 (2.7)	2 (0.6)
Peritoneal mesotelioma	–	1 (0.3)
Not classifiable	*3 (2.7)*	–
Total	113	326

MMMT*: Malignant mixed mullerian tumors.

Brenner tumors, three sarcomas, and three arrenoblastomas. There were 3/113 (2.7%) germinal tumors: all were dysgerminomas. There were three cases not classifiable from a histological point of view. In the period 1992-2001 (Table 3) we observed 326 cases of malignant tumors of the ovary; the histotypes were represented by 306/326 (93.9%) malignant epithelial ovarian tumors. Among these forms, we had 189/326 (57.9%) serous cystoadenocarcinomas, 81/326 (24.8%) mucinous cystoadenocarcinomas, 23/326 (7.0%) endometrioid adenocarcinomas, 6/326 (1.8%) solid adenocarcinomas, 6/326 (1.8%) clear cell adenocarcinomas, and 1/326 (0.3%) adenosquamous carcinoma. We observed 15/326 (4.6%) malignant stromal tumors: 5/326 (1.5%) granulous cell

tumors, 4/326 (1.2%) malignant mixed mullerian tumors, 3/326 (0.9%) malignant Brenner tumors, 2/326 (0.6%) sarcomas, and 1/326 (0.3%) malignant cystoadenofibroma. There were 4/326 (1.2%) germinal tumors: two endodermic sinus tumors and two dysgerminomas. We also had 1/326 (0.3%) case of peritoneal mesotelioma.

FIGO Stage:

In the period 1974-1985 the subdivision in stages of the 113 malignant ovarian tumors showed: 29 (25.7%) at IA, two (1.8%) at IB, 13 (11.5%) at IC, ten (8.8%) at IIB, 38 (33.6%) at III and 21 (18.6%) at Stage IV (Table 4). At that time, the 1988 FIGO classification, that divided the III stage in IIIA, IIIB and IIIC, had not yet been introduced.

In the period 1992-2001 the FIGO subdivision in stages of the 326 malignant ovarian tumors showed: 49 (15.0%) at IA, 11 (3.4%) at IB, 14 (4.3%) at IC, 16 (5%) at IIA, 20 (6.1%) at IIB, 14 (4.3%) at IIC, 74 (22.7%) at IIIA, 18 (5.5%) at IIIB, 36 (11.0%) at IIIC and 74 (22.7%) at Stage IV (Table 4).

With regard to the distinction between early forms (I-IIA) and advanced forms (IIB-III-IV), in the period 1974-1985 the early forms were 39% and the advanced forms were 61% whereas in the period 1992-2001 the early forms were 27.7% and the advanced forms were 72.3% (Table 4).

Table 4. — *FIGO stage distribution of cases.*

FIGO Stage	(1974-1985)		(1992-2001)	
	No.	%	No.	%
IA	29	25.7	49	15
IB	2	1.8	11	3.4
IC	13	11.5	14	4.3
IIA	–	–	16	5
IIB	10	8.8	20	6.1
IIC	–	–	14	4.3
IIIA	–	–	74	22.7
IIIB	38	33.6	18	5.5
IIIC	–	–	36	11.0
IV	21	18.6	74	22.7
Total	113	100	326	100

Histotype and FIGO stage:

In the period 1992-2001 (Table 5), the correlation between histotype and FIGO stage for malignant epithelial ovarian tumors showed a quite similar trend for serous and mucinous forms, with the incidence growing at the highest stages. In fact, serous and mucinous tumors were 15.3% and 29.6% at Stage I, 19.6% and 9.8% at Stage II, 39.2% and 37.1% at Stage III, 25.9% and 23.5% at Stage IV, respectively. All four cases of germinal tumors occurred at Stage IA.

Epidemiological characteristics in the period 1992-2001:

Age of diagnosis: the mean age of diagnosis of malignant ovarian tumors was: 60.9 years (range 17-95 yrs) for epithelial tumors; 54.5 (range 28-68 yrs) for stromal tumors and 24.7 (range 19-32 yrs) for germinal tumors, respectively.

Residence: 36% of patients with malignant epithelial tumors lived in the city of Sassari vs 64% in the hinterland; 60% of patients with stromal forms lived in Sassari vs 40% in the hinterland. With regard to four cases of germinal tumors, three cases lived in Sassari whereas one case in the hinterland.

Occupation: With regard to malignant epithelial ovarian tumors 69% of women were housewives, 6.5% teachers, 6.0% state employees, 5.5% tradeswomen, 5.5% unemployed women, 4.5% working women, 2% health workers (medical doctors, psychologists, nurses) and 1.0% nuns.

Family history of cancer: 51.3% of patients with malignant epithelial tumors referred to had at least one first-degree relative with cancer. Fifty percent of patients with malignant stromal and germinal tumors also had at least one first-degree relative with cancer.

Discussion and Conclusions

The analysis of our data regarding the period 1992-2001, if compared with those of the previous period 1974-85 [7], showed an increase of the malignant ovarian tumors which triplicated achieving an incidence of 11.99/100,000 vs 4.27/100,000.

The constant increase of the malignant ovarian tumors in the advanced age-groups (80-84 yrs with a peak of 37.1/100,000 in the period 1992-2001 vs 65-69 yrs with a peak of 17.4/100,000 in the period 1974-1985) may be explained by the increase of the female population higher than 65 years of age that per se constitutes a class of age at enhanced risk of cancer.

Table 5. — *Correlation between histotype and FIGO stage (1992-2001).*

Histotype		FIGO Stage									
	N.	IA	IB	IC	IIA	IIB	IIC	IIIA	IIIB	IIIC	IV
Serous	189	15 (7.9)	8 (4.2)	6 (3.2)	10 (5.3)	16 (8.5)	11 (5.8)	48 (25.4)	9 (4.8)	17 (9)	49 (25.9)
Mucinous	81	21 (25.9)	-	3 (3.7)	4 (4.9)	3 (3.7)	1 (1.2)	18 (22.3)	6 (7.4)	6 (7.4)	19 (23.5)
Endometrioid	23	5 (21.7)	-	4 (17.4)	-	1 (4.4)	-	4 (17.4)	-	5 (21.7)	4 (17.4)
Solid	6	-	-	-	-	-	-	-	3 (50.0)	2 (33.4)	1 (16.6)
Clear Cell	6	-	1 (16.6)	-	2 (33.4)	-	-	-	-	3 (50.0)	-
Adenosquamous	1	-	-	-	-	-	-	-	-	1 (100)	-
Stromal	15	4 (26.6)	2 (13.3)	-	-	-	2 (13.3)	4 (26.6)	-	2 (13.3)	1 (6.9)
Germinal	4	4 (100)	-	-	-	-	-	-	-	-	-
Mesothelioma	1	-	-	1 (100)	-	-	-	-	-	-	-
Total	326	49	11	14	16	20	14	74	18	36	74
Percentage		15.0	3.4	4.3	5	6.1	4.3	22.7	5.5	11.0	22.7

Analysis of the histotypes showed a non significant increase of the epithelial forms in the period 1992-2001 in comparison to the previous period 1974-1985 (93.8% vs 85.8%) whereas the percentage of incidence of the other forms resulted to be unchanged. However we observed a non significant reduction of the stromal forms.

In the period 1992-2001 we reported an increase of the forms at advanced stage of disease (72.3% vs 61% of the previous period) with a reduction of the forms at early stage of disease (27.7% vs 39%); these data indicate that early diagnosis is still difficult today and that screening programs by routine ultrasonography are lacking.

The analysis of epidemiologic data showed an increase of the age of first diagnosis (mean 60.9 yrs for epithelial ovarian tumors) and occurrence of cancer in women at a low socio-economic level. In contrast in the literature malignant ovarian tumors are more frequent among women at a medium-high socioeconomic level [8].

Our data revealed a family history of cancer among the patients with malignant ovarian tumors (about 50% of the patients); these data suggest a strong role of genetic factors combined with environmental factors, as several studies of molecular biology have demonstrated [9-11]. In fact Sardinia has been through the centuries a geographical area with little population migration.

In conclusion, our data show a worrying increase of malignant ovarian tumors that almost triplicated in incidence. Furthermore in a previous paper [6] we reported a change in the percentage of distribution of all gynecologic tumors, with a relative reduction in the incidence of tumors of the corpus uteri (from 52.1% to 45.0%) especially due to the increase in malignant ovarian tumors which achieved second place with 28.0%, which is higher than 17.1% in the period 1974-1983.

Molecular biology studies that are performed to discover the presence of genetic mutations and chromosomal markers in patients with ovarian cancer will have a heavy preventive impact, allowing the screening of a population at high risk of these tumors and follow-up with personalized diagnostic protocols. However screening programs by ultrasonography on large samples of women are needed to achieve earlier diagnoses.

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