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The frequency of primary ovarian neoplasms at King Chulalongkorn Memorial Hospital during 1990-1997

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Objective : *To determine the frequency, age distribution and bilaterality of primary ovarian neoplasms at King Chulalongkorn Memorial Hospital during the period January 1990 - December 1997*

Study design : *Retrospective descriptive study*

Methodology : *All ovarian neoplasms diagnosed at the Cytopathological Unit, Department of Obstetrics and Gynecology of King Chulalongkorn Memorial Hospital between January 1990 and December 1997 were assessed for age, bilaterality and histologic types.*

Result : *Among 1,193 cases of all ovarian tumors, 1,173 cases of primary ovarian tumors were diagnosed with 47.4% common epithelial tumors 46.8%, germ cell tumors and 4.1% sex cord stromal tumors. The most common histologic type was mature cystic teratoma, 45.3% followed by mucinous cystadenoma 14.5% and serous cystadenoma 11.2%. Among 302 cases with primary malignant neoplasms, common epithelial type tumors accounted*

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for 84.6%, germ cell tumors 9.8% and sex cord stromal tumors for 5.6%. Mucinous tumor was more common than serous type with a ratio of 1.3:1 for the benign group and 5:1 for the borderline group. Serous and endometrioid tumors were the most common malignant tumors (29.8% versus 28.0% of the malignant tumors) and bilaterality (34.3% versus 28.6%), respectively. The proportion of malignant ovarian neoplasms increased with age, peaking in the 55 - 64 year decade (46%) and risk increased 9.91 - fold from 15 - 24 year to ages 55 - 64.

Conclusions : *Mature cystic teratoma was the most common primary ovarian neoplasm. Serous and endometrioid carcinomas were the most common malignant tumors and bilaterality but mucinous tumor was more common in benign and borderline epithelial tumors. The risk of malignant ovarian neoplasm increased with age.*

Key words : *Primary ovarian neoplasms, Histology, Bilaterality, Age.*

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วัตถุประสงค์ : *เพื่อหาความชุกของชนิด, การกระจายตามอายุ และโอกาสพบที่รังไข่ทั้ง 2 ข้างของเนื้องอกรังไข่ชนิดปฐมภูมิในโรงพยาบาลจุฬาลงกรณ์ ระหว่าง พ.ศ. 2534 - 2540*

ชนิดการศึกษา : *เป็นการศึกษาย้อนหลังเชิงพรรณนา*

วิธีการ : *ตรวจข้อมูลย้อนหลังในหน่วยเซลล์พยาธิวิทยา ภาควิชาสูติศาสตร์ - นรีเวช-วิทยา โรงพยาบาลจุฬาลงกรณ์ ที่วินิจฉัยว่าเป็นเนื้องอกรังไข่ ตั้งแต่เดือน เดือน ม.ค. 2534 ถึง ธ.ค. 2540 โดยดูอายุ, การวินิจฉัยทางพยาธิวิทยาและการพบเนื้องอกที่รังไข่กี่ข้าง*

ผลการศึกษา : *พบเนื้องอกรังไข่ 1193 ราย เป็นชนิดปฐมภูมิ 1173 ราย โดยเป็นชนิด Common epithelial tumor 47.4%, Germ cell tumor 46.8% และ Sex cord stromal tumor 4.1% เนื้องอกรังไข่ที่พบบ่อยที่สุดเรียงตามลำดับ คือ Mature cystic teratoma (45.3%), mucinous (14.5%) และ serous cystadenoma (11.2%) มะเร็งรังไข่ที่พบมากที่สุด คือ กลุ่ม common epithelial type โดย serous (22.2%) และ endometrioid carcinoma (20.8%) พบบ่อยที่สุด แต่ mucinous tumor จะพบบ่อยในเนื้องอกธรรมดา และ borderline tumor. ความเสี่ยงในการพบมะเร็งรังไข่จะเพิ่มสูงขึ้น 9.91 เท่า จากกลุ่มอายุ 15 - 24 ปี เป็น 55 - 64 ปี*

สรุป : *Mature cystic teratoma เป็นเนื้องอกปฐมภูมิรังไข่ที่พบบ่อยที่สุด ส่วนมะเร็งปฐมภูมิรังไข่ที่พบบ่อยที่สุดคือ Serous และ Endometrioid carcinoma ซึ่งจะพบพยาธิสภาพของรังไข่ทั้ง 2 ข้าง บ่อยที่สุดด้วย แต่เนื้องอกรังไข่ชนิด Mucinous จะพบบ่อยใน benign และ borderline epithelial tumor ผู้ป่วยที่อายุมากจะมีความเสี่ยงสูงต่อการเกิดมะเร็งรังไข่*

In Asian countries, including Thailand, there is a paucity of information concerning the relative frequency of various types of ovarian neoplasm and which have histologic types and age distributions different western countries.[1-4] Before 1961, ovarian tumors had been diagnosed in each medical institution on the basis of different diagnostic criteria, so the data were difficult to compare. After the World Health Organization (WHO) and the International Federation of Gynecology and Obstetrics (FIGO) proposed the histological classification and diagnostic criteria of ovarian neoplasm,[5,6] comparisons became relatively easy. The objective of our study was to analyze the relative frequency, age distribution and bilaterality of the various specific types of ovarian neoplasms at King Chulalongkorn Memorial Hospital. Then our findings were compared with those reported elsewhere in Thailand, Asian and Western countries

Material and Methods

King Chulalongkorn Memorial Hospital (1350 beds) is one of the largest general hospitals in Bangkok. The hospital serves a population of approximately five millions, and as a referral center for other private, regional and community hospitals in all parts of Thailand.

This study looked at all cases of ovarian neoplasms diagnosed at the Cytopathological Unit, Department of Obstetrics and Gynecology from January 1990 to December 1997. Cases of ovarian endometriosis, functional cysts and tumorlike lesions were excluded. Hematoxylin and eosin stained (H&E) sections were performed routinely in each case. Some cases were examined with special stains, including periodic acid-Schiff (PAS), Mayer 's mucicarmine and immunohistochemicl studies (antibodies for cytokeratin, carcinoembryonic antigen, alphafetoprotein, chromogranin and myoglobin).

All ovarian tumors were classified according to the WHO histological classification.[5,6] Age and laterality of tumor were recorded the pathological reports. We calculated the frequency of the various types of primary ovarian neoplasms by 10 year age groups except the first one covering patients up to 15 years old. We also determined rates of malignancy and calculated relative risks with 95% confidence intervals using Bailey's method.[7]

Results

Table 1 provides the relative frequency of all 1,193 ovarian tumors of which 871 (73.01%) had benign, 286 (23.97%) malignant and 36 (3.02%) borderline neoplasms. Common epithelial tumors and germ cell tumors were found with nearly equal frequency (47.4% versus 46.8%). The first category was the most common among malignant tumors and the other in benign group. Twenty cases of matastatic ovarian tumor were excluded from the study.

The relative frequency of the histologic subtype of primary ovarian neoplasm (1,173 cases) is shown in Table 2. The most common tumor was mature cystic teratoma (532 cases or 45.3% of all primary ovarian tumors); then the second and third most common tumors were mucinous cystadenoma (170 cases or 14.5%) and serous cystadenoma (131 cases or 11.2%). The next three most common tumors were malignant neoplasms of which serous cystadenocarcinoma was the most common (67 cases or 5.7%), endometrioid carcinoma with 63 cases or 5.4% and mucinous cystodenocarcinoma

with 45 cases or 3.8%. Granulosa cell and endodermal sinus tumors were the most common malignant sexcord-stromal and germ cell neoplasms of the ovaries, respectively.

Table1. Relative frequency of each histological category of all ovarian tumors.

Histologic type	Benign	Borderline	Malignancy	Total
Common epithelial tumor	305	36	225	566 (47.4%)
Germ cell tumor	532	-	26	558 (46.8%)
Sex cord stromal tumor	34	-	15	49 (4.1%)
Metastatic tumor	-	-	20	20 (1.7%)
Overall	871	36	286	1193
	(73.01%)	(3.02%)	(23.97%)	(100%)

Table 2. Relative frequency of primary ovarian neoplasms.

Primary ovarian neoplasms	No. of cases	%
Mature cystic teratoma	532	45.3
Mucinous cystadenoma	170	14.5
Serous cystadenoma	131	11.2
Serous cystadenocarcinoma	67	5.7
Endometrioid carcinoma	63	5.4
Mucinous cystadenocarcinoma	45	3.8
Fibroma / thecoma	34	2.9
Mucinous borderline tumor	30	2.6
Clear cell carcinoma	30	2.6
Mixed epithelial carcinoma	16	1.4
Granulosa cell tumor	14	1.2
Endodermal sinus tumor	8	0.7
Dysgerminoma	6	0.5
Serous borderline tumor	6	0.5
Immature teratoma	6	0.5
Brenner tumor	4	0.3
Mixed germ cell tumor	4	0.3
Carcinosarcoma	2	0.2
Others	5	0.4
	1,173	100

A comparison between mucinous and serous tumors is presented in Table 3. Obviously, borderline lesions were much more frequent among the mucinous tumors than among serous tumors, The ratio of mucinous to serous tumors was approximately 1.3:1 for benign lesions, 5:1 for borderline lesions and 0.67:1 for malignant lesions. On the other hand, the serous carcinoma was seen more frequently than mucinous carcinoma with a ratio 1.5:1 . Among both mucinous and serous tumors, there were about twice as many benign lesions as malignant and borderline lesions (301 cases, 148 cases).

Table 4 demonstrates the percentage of primary ovarian malignant tumors in each histologic type. Malignant common epithelial and sex cord stromal tumors were found in 39.8% and 30.6% of the total number of cases of each group whereas malignant germ cell tumors was about 4.7%. Common epithelial tumors were the most common malignant tumor of primary ovarian neoplasm (84.6%). The rest were 9.8% germ cell tumors and 5.6% sex cord stromal tomors.

Age distribution of primary ovarian neoplasms is presented in Table 5. It is notable that 77% of all benign tumors and 50% of all borderline tumors occurred in patients under the age of 45 years while 87% and 56.4% of the malignant epithelial tumors were from patients over the age of 35 years and 45 years, respectively.

Table 3. Frequency of subtypes of mucinous and serous tumors.

Type	Mucionous	%	Serous	%	Ratio of Mucinous /serous
Benign	170	69.4	131	64.2	1.3
Borderline	30	12.2	6	2.9	5
Malignant	45	18.4	67	32.9	0.67
Total	245	100	204	100	

Table 4. Frequency of primary ovarian malignant tumors.

Histologic type	Number of malignancies	Percentage of group	Percentage of primary malignant tumors
Common epithelial tumors (566) [a]	225	39.8	84.6
Germ cell tumors (558)[a]	26	4.7	9.8
Sex cord-stromal tumors (49) [a]	15	30.6	5.6
Total (1157) [a]	302	-	100.0

[a]Number of all cases in each group

Table 5. Types of primary ovarian tumors related to patient age.

Age	Benign	Borderline	Epith.	Malignant Non-Epith	Total Malignant
< 15	21	-	1	4	5
15 – 24	180	8	10	7	17
25 – 34	266	2	21	8	29
35 – 44	210	8	66	3	69
45 – 54	102	4	76	8	84
55 – 64	41	6	36	4	40
65 – 74	25	6	9	6	15
> 74	9	1	4	1	5
Unknown	17	1	2	-	2
Total cases	871	36	225	41	266

Table 6 demonstrates the risk of having a malignant ovarian neoplasm as related to the age distribution. The proportion of benign ovarian tumors was highest at ages 15-24 years, accounting for 91.7% of all ovarian neoplasms found in this age group, and were less common with increasing age, with the lowest proportion in women aged 55-64 years (54%). Conversely, the proportion of malignant ovarian neoplasms increased with age, peaking in the 55-64 year decade (46%). The risk of malignant potential of ovarian neoplasms increased 9.91- fold ages 15-24 to 60-69. This increase in risk was significant ($p<0.005$, X^2 test for trend).

Table 6. Rate of malignant ovarian neoplasms by age.

Age	Patient with Malignant ovarian neoplasms	Total patient with ovarian neoplasms	Rate*	Odds Ratio	95 % confidence interval
≤ 15	5	26	19.2	2.31	1.02-12.41**
15 – 24	17	205	8.3	1	Referent+
25 – 34	29	297	9.8	1.2	0.65-2.47
35 – 44	69	287	24.0	3.69	2.03-6.76**
45 – 54	84	190	44.2	9.23	5.04-17.07**
55 – 64	40	87	46.0	9.91	4.94-20.06**
65 – 74	15	46	32.6	5.64	2.38-13.36**
≥ 75	5	15	33.3	5.82	1.52-21.60**
Unknown	2	20	-	-	-
Total	263	1173			

* Per 100 patients, **$p<0.005$, + Based on an index rate of 8.3 for 15-24 years.

Bilaterality by each histological type and grade of malignancy is shown in Table 7. Serous, endometrioid and clear cell carcinomas showed bilateral involvement of 34.3%, 28.6% and 16.7% of each tumor, respectively. Borderline serous tumors had 16.7% bilaterality while 8.3% of mature cystic teratoma and 7.3% of granulosa cell tumors were found involving both ovaries. Benign and borderline mucinous type had 2.4% and 3.3% bilaterality in each group, respectively.

Discussion

Cancer registry data of the Cancer Incidence in Five Continents (CIFC) has demonstrated that ovarian cancer is four to five times more prevalent in Scandinavian nations than it is in Asian countries[8] but there has been no analysis of specific histological types of ovarian cancer. Stalsberg et al reported an international comparison of histologic types of benign and malignant ovarian tumors in general hospital material,[9] In this study, we attempted to compare

Table 7. Frequency of bilaterality by histologic subtype and grade of primary ovarian malignant tumors.

Histologic type	Benign (%)	Borderline (%)	Malignant (%)
Common epithelial tumor			
Serous tumor	4.6	16.7	34.3
Mucinous tumor	2.4	3.3	11.1
Endometrioid tumor	-	-	28.6
Clear cell tumor	-	-	16.7
Brenner tumor	0 [a]	-	-
Mixed epithelial tumor	-	-	0 [a]
Germ cell tumor			
Mature cystic teratoma	8.3	-	0 [a]
Malignant transformation	-	-	0 [a]
Immature teratoma	-	-	0 [a]
Dysgerminoma	-	-	0 [a]
Endodermal sinus tumor	-	-	0 [a]
Mixed germ cell	-	-	25 [a]
Sex cord – stromal tumor	0	-	7.1

[a]Number of cases is small

the relative frequency, age distribution and bilaterality in those general hospitals between Chulalongkorn Hospital and other reports from different hospitals in Thailand, Japan and other Western countries.[1-4,10-13]

Common epithelial tumors accounted for 47.4% of all ovarian tumors at King Chulalongkorn Memorial Hospital, 50.9% at University Hospital in the northern part of Thailand,[4] 47-55% in Japan, [2] and 54-59% in western countries.[10-13] Because of the different frequency of germ cell tumors, and which occurred more common in Asian countries than in the west, the relative frequency of common epithelial tumors is lower in Asian countries than in western ones.[14] Among benign and borderline epithelial tumors, the mucinous type was more common than the serous type with a ratio of 1.3:1 and 5:1 for the benign and borderline groups respectively and which agrees with other reports in Thailand and Japan.[2-4] On the other hand, western countries reported ratios of 0.45–0.76:1 and 0.5 – 0.7:1 for the benign and borderline groups respectively.[10-13,15] This difference may be influenced by geographically different distributions[16] and variations in the diagnostic criteria for borderline and malignant mucinous tumors in the different institutions. [17]

Malignant epithelial tumors accounted for 84.6% of all primary malignant ovarian tumors and this was comparable to the reports from Western countries (85.5 to 92.3%)[10-13] but different from other reports in Thailand and Japan (57.4% and 63.9% respectively)[2,4] because of the lower incidence of malignant germ cell tumors in our hospital but it had nearly the same frequency as in a previous report by one of our authors.[3] However, the most common malignant epithelial tumor was serous carcinoma (29.8% of all malignant epithelial neoplasms), followed by endometrioid and mucinous carcinoma (28.0% and 20%) which was comparable with reports from both Asian and Western countries.[1-4,10-13,18]

Germ cell tumors accounted for 46.8% of all ovarian tumors in this study, 39.5-43.1% in University Hospital in the northern part of Thailand[4] and in Japan[2] which was much more than in western countries (21.7-32.9%).[10-13] It is notable that mature cystic teratoma accounted for 45.3% of all ovarian tumors and 95.3% of all germ cell tumors in our hospital. This was different from other reports in Thailand and Japan (35.3% and 32.3-39.1% of all ovarian tumors versus 85.2% and 81.7-91.4% of all germ cell tumors, respectively).[2,4] These results generally indicated that mature cystic teratoma was relatively more frequent but malignant germ cell tumors were less frequent in our hospital as compared to other Asian reports.[2,4] Malignant germ cell tumors accounted for 2.2% of all ovarian tumors and 9.8% of all ovarian malignant tumors and which was comparable to western countries (1.5-2.2% of all ovarian tumors and 5.8-7.3% of all ovarian malignant tumors),[10-13] but much different from other reports in Thailand and Japan (6.1% and 3.3-6.5% of all ovarian tumors versus 14.8% and 17.2-25% of all ovarian malignant tumors respcetively).[2,4] Endodermal sinus tumor and dysgerminoma were the first and second most common malignant germ cell tumors and accounted for 3% and 2.25% of all ovarian malignant tumors. Conversely, other reports revealed dysgerminoma was a little more common than endodermal sinus tumor, 4.7-11.7% and 3.7-4.3%

of all ovarian malignant tumors in Japan[2] versus 2.9-4.7% and 2% of all ovarian malignant tumors in Western countries respectively.[10-13]

Sex cord stromal tumors were relatively infrequent in all series with no different frequencies between Asian and western countries.[1-4,10-13] However, the relative frequency of malignancy, almost all of which were due to granulosa cell tumors, accounted for 30.6% of all sex cord tumors and this was comparable with other reports in Thailand (37.6%)[4] but higher than in reports from Japan and western countries (23.4% and 5.4-20.4% respectively).[2,10-13]

The age distribution for primary ovarian neoplasms revealed that most benign tumors (77%) occurred in patients less than 45 years old, but most malignant epithelial tumors (87%) occurred in patients over 35. For borderline lesions, these were a little more common below 45 years old but for diagnosis there must be adequate tissue sampling, especially in mucinous type. These figures were fairly close to other reports.[1-4,10-13,19] In addition, the relative frequency of primary malignant ovarian neoplasms increased with each decade of life through the 60s, varying from 8.3% in the 15-24 year age group to 46% in the 55-64 year age group. The odds ratio was 9.91 in the latter one which was comparable with western countries (odds ratio12.1).[15]

Bilateral involvement were most frequent in serous, endometrioid and clear cell carcinomas which was comparable to other studies.[1,2,4,10-13] It is notable that benign and borderline mucinous tumors had lower frequencies of bilaterality in this study than in Japan (2.4% and 3.3% versus 12.6% and 9.8%, respectively).[2] Benign cystic teratoma had bilateral involvement 8.4% which was also less than in Japan (14%).[2]

In summary, primary ovarian tumors in King Chulalongkorn Memorial Hospital during 1990-1997 had the following distinctive features: (1) the relative frequency of common epithelial tumors was the same as in other Asian countries (but lower than in western countries) but malignant common epithelial tumors were as frequent as in western countries (higher than in Asian ones) (2) the relative frequency of germ cell tumors was the same as in other Asian countries (but much higher than in western ones) but malignant germ cell tumors were less frequent as western reports (lower than Asian reports) (3) the relative frequency of sex cord stromal tumors was not significentally different from other reports but granulosa cell tumors occurred more frequently as in other reports in Thailand and which was much higher than in Japan and in western countries (4) the age distribution of the histological subtypes did not essentially differ from other reports (5) the relative frequency of bilaterality was the same as in previous reports except for a lower frequency of mucinous tumors.

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