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An epidemiological study of endometrial cancer at King Chulalongkorn Memorial Hospital

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Worasethsin P, Triratanachat S, Termrungruanglert W, Vasuratna A, Sittisomwong T, Tresukosol D. An epidemiological study of endometrial cancer in King Chulalongkorn Memorial Hospital. Chula Med J 2000 Dec; 44(12): 907 - 15

Objective : *To study the epidemiology of endometrial cancer at King Chulalongkorn Memorial Hospital between 1994-1998.*

Setting : *Department of Obstetrics and Gynecology, Faculty of Medicine, King Chulalongkorn Memorial Hospital*

Research design : *Retrospective descriptive study*

Material & Method : *A review of medical records of endometrial cancer patients treated at the Department of Obstetrics and Gynecology, King Chulalongkorn Memorial Hospital between 1994-1998 was undertaken.*

Results : *Median age of the women was 55 years (range 24-83). Most of these were postmenopause, had a BMI over 25 kg/m^2, nulliparity, and had no underlying medical diseases i.e., including hypertension and/or diabetes mellitus. The main presenting symptom was abnormal uterine bleeding. The most common pathology was well-differentiated endometrioid carcinoma with minimal myometrial invasion. Primary surgery was done in nearly all cases. Seventy-nine point six percent were diagnosed as clinical stage I, compared with 73.5 % found to be in surgical stage I. Most adjuvant treatment was chemotherapy.*

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Conclusion : *An epidemiological study of endometrial cancer was shown. The incidence in lower age group of patients was higher than previous reports. Stage I disease was the majority of cases. Forty-one point five percent were high-risk cases, which needed adjuvant treatment.*

Key words : *Epidemiology, Obesity, Postmenopause, Endometrial cancer.*

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Received for publication : July 10, 2000.

พงษ์เกษม วรเศรษฐสิน, สุรางค์ ตรีรัตนชาติ, วิชัย เติมรุ่งเรืองเลิศ, อภิชัย วสุรัตน์, ตุลย์ สิทธิสมวงศ์, ดำรง ตรีสุโกศล. ระบาดวิทยาผู้ป่วยมะเร็งเยื่อบุโพรงมดลูก ในโรงพยาบาลจุฬาลงกรณ์. จุฬาลงกรณ์เวชสาร 2543 ธ.ค; 44(12): 907 - 15

วัตถุประสงค์ : *เพื่อศึกษาระบาดวิทยาของมะเร็งเยื่อบุโพรงมดลูกในโรงพยาบาลจุฬาลงกรณ์ ระหว่าง พ.ศ. 2537 ถึง 2541*

สถานที่ทำการศึกษา : *ภาควิชาสูติศาสตร์-นรีเวชวิทยา คณะแพทยศาสตร์ โรงพยาบาลจุฬาลงกรณ์*

รูปแบบการวิจัย : *การศึกษาบรรยายแบบย้อนหลัง*

วัสดุและวิธีการ : *ศึกษาย้อนหลังจากเวชระเบียนผู้ป่วยมะเร็งเยื่อบุโพรงมดลูก ที่เข้ารับการรักษาที่ภาควิชาสูติศาสตร์-นรีเวชวิทยา โรงพยาบาลจุฬาลงกรณ์ ระหว่าง พ.ศ. 2537 ถึง 2541*

ผลการศึกษา : *อายุของผู้ป่วยอยู่ในช่วง 24-80 ปี มัธยฐานเท่ากับ 55 ปี ผู้ป่วยส่วนใหญ่อยู่ในวัยหมดระดู ดัชนีมวลกายมากกว่า 25 กิโลกรัมต่อตารางเมตร ไม่มีบุตร ไม่มีโรคความดันโลหิตสูง และ/หรือ เบาหวานร่วมด้วย อาการนำสำคัญส่วนใหญ่เป็นเลือดออกผิดปกติทางช่องคลอด พยาธิสภาพส่วนใหญ่เป็นชนิด Well-differentiated endometrioid carcinoma ซึ่งมีการลุกลามลงสู่กล้ามเนื้อมดลูกน้อยกว่าครึ่งหนึ่งของความหนา ร้อยละ 79.6 ของผู้ป่วยอยู่ในระยะที่ 1 จากการประเมินทางคลินิก และ ร้อยละ 73.5 อยู่ในระยะที่ 1 จากการประเมินโดยการผ่าตัด การให้เคมีบำบัดเป็นการรักษาเสริมที่ใช้บ่อยที่สุด*

สรุป : *ผลการศึกษาทางระบาดวิทยาของผู้ป่วยมะเร็งเยื่อบุโพรงมดลูกที่โรงพยาบาลจุฬาลงกรณ์ พบอุบัติการณ์ในกลุ่มผู้ป่วยที่อายุน้อยเพิ่มขึ้นมากกว่าการศึกษาอื่น ผู้ป่วยส่วนใหญ่อยู่ในระยะที่ 1 ร้อยละ 41.5 ของผู้ป่วยทั้งหมด อยู่ในกลุ่มเสี่ยงซึ่งต้องได้รับการรักษาเสริม*

Endometrial cancer is the forth most common cancer in Thai females. Worldwide incidence varies geographically, the highest rates being from the United States and Canada, while the incidences are four to five times lower among Asian countries. The areas with the lowest rates are in India and South Asia.[1] Endometrial cancer usually occurs in postmenopausal women, although 25 % of cases are premenopausal women, with 5% occurring in patients younger than 40 years of age.[2-4] It is also associated with obesity, nulliparity, unopposed estrogen, late menopause, hypertension and diabetes mellitus.[1] Unlike other cancers, endometrial cancer is often detected in the early stage. Its favorable prognosis makes it a readily treatable disease.[5-7] The purpose of this study was to report the epidemiological features of endometrial cancer in the Department of Obstetrics and Gynecology, Faculty of Medicine, King Chulalongkorn Memorial Hospital.

Materials and Methods

During the years 1994-1998, 152 women diagnosed with endometrial cancer were treated at the Department of Obstetrics and Gynecology, Faculty of Medicine, King Chulalongkorn Memorial Hospital. Patient age, body mass index (BMI), parity, menopausal status, presenting symptoms, underlying diseases, last Papanicolaou smear results, cancer staging, histologic type and grading, depth of myometrial invasion, type of primary and adjuvant treatment were recorded.

Tumors were staged according to the International Federation of Gynecology and Obstetrics (FIGO) guidelines, which compared both clinical and surgical staging. The BMI was calculated as body weight (kg) divided by the square of height (m^2); values above 25 kg/ m^2 were regarded as overweight, and those above 30 kg/ m^2 were regarded as obese.

Results

The median age at diagnosis was 55 years (range 24-80). Twenty-five (16.4 %) women were 40 years or younger. Eighty-four (55.2 %) women had a BMI more than 25 kg/m^2 with 47 (30.9 %) patients being overweight and, 37 (24.3 %) obese. Sixty-three (41.1 %) women were nulliparous, while 62 (40.8 %) women had at least 3 children, with the highest parity of 10 (Table 1). Fifty-four (35 %) women were

Table 1. The characteristics of endometrial cancer patients in King Chulalongkorn Memorial Hospital, 1994-1998.

Characteristics	N	%
Age (years)	152	100
< = 40	25	16.4
41 - 45	15	9.9
46 - 50	19	12.5
51 - 55	20	13.2
55 - 60	30	19.7
61 - 65	23	15.1
66 - 70	9	5.9
> 70	11	7.2
Body mass index (kg/m^2)	152	100
< 20.0	14	9.2
20.0 - 25.0	54	35.5
25.1 - 30.0	47	30.9
> 30.0	37	24.3
Parity	152	100
None	63	41.4
1	12	7.9
2	15	9.9
> = 3	62	40.8

premenopausal status. Eighty-two (53.9 %) women had no underlying disease (Table 2).

Table 2. Underlying medical diseases of the women.

Disease	N	%
None	82	53.9
Hypertension	29	19.1
Diabetes mellitus	10	6.6
Diabetes mellitus	10	6.6
Hypertension & Diabetes mellitus	20	13.2
Others	11	7.2
Total	152	100.0

The main presenting symptoms (95.4 %) were abnormal uterine bleeding. The mean duration of bleeding was 6 months (range 2 weeks - 72 months). Others presented with pelvic mass (3), abdominal pain (2), secondary amenorrhea (1), or abnormal Pap smear (1).

Of the 152 women, eighty-four (55.3 %) had had a Papanicolaou smear check up within the last 6 months. Fifty-seven (67.9 %) women had negative (class I) results. Sixteen (19 %), nine (10.7 %), and two (2.4 %) women had negative atypical (class II), suspicious (class III), and positive (class V) results, respectively.

On histologic review showed that most of them (78.9%) had endometrioid adenocarcinoma. Twenty-nine(19.1 %) had endometrioid adenocarcinoma with squamous differentiation, two and one were clear-cell carcinoma and mucinous carcinoma, respectively. One hundred and fifty tumors were graded, excepting the clear-cell carcinoma. Eighty-four (56.0 %), thirty-seven (24.7 %) and twenty-nine (19.3 %) were G1, G2 and G3, respectively. The grading of twenty-nine endometrioid adenocarcinomas with squamous differentiation were twelve (G1), eleven (G2), and six (G3).

One hundred forty-seven women underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH+BSO). Pelvic and/or para-aortic lymph node sampling (LNS) were performed in ninety (59.2 %) women. Four patients were treated with radiation alone, one was inoperable due to advanced disease (Table 3).

Table 3. Treatment modalities of endometrial cancer.

Treatment	N	%
TAH + BSO + LNS	90	59.2
TAH + BSO	53	34.9
Preoperative radiation	4	2.6
Preoperative radiation	4	2.6
Radiation alone	4	2.6
Radiation alone	4	2.6
Inoperable	1	
Total	152	100.0

In the 147 women who received TAH+BSO, the level of myometrial invasion was evaluated. Almost half of them, seventy-two (47.4 %), had minimal myometrial invasion (less than 50 % of the total myometrial thickness). Thirty-eight (25.9 %) had deep myometrial invasion (more than 50 % of the total myometrial thickness) and the remainder (25.2 %) had no myometrial invasion.

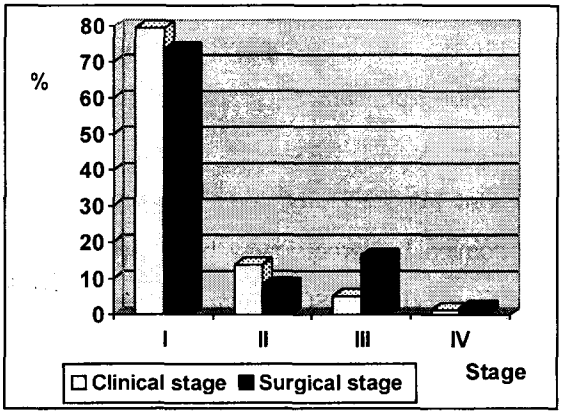

Figure 1. Clinical and surgical staging of endometrial cancer.

The FIGO clinical staging was compared to the surgical staging of the endometrial cancer. Of the 152 women, one hundred twenty-one (79.6 %) were clinical stage I. Twenty-one (13.8 %), 8 (5.3 %), and 2 (1.3 %) women were clinical stage II, III, and IV, respectively. Surgical staging was evaluated in the 147 women who underwent TAH+BSO +/- LNS. One hundred eight (73.5 %) women were surgical stage I. Twelve (8.2 %), 24 (16.3 %), and 3 (2 %) women were surgical stage II, III, and IV, respectively (Figure 1).

Adjuvant therapy was given to 61 (41.5 %) women. Twenty-two (36.1 %) women received adjuvant chemotherapy, 18 receiving carboplatin and 4 cisplatin. Twenty (32.8 %) women received adjuvant radiation therapy consisting of vault cesium and/or external beam irradiation to the pelvis. Sixteen (26.2 %) women received adjuvant hormonal treatment, 13 received goserelin, 2 megestrol, and 1 tamoxifen. The others received combined chemotherapy and hormonal treatment, carboplatin plus goserelin.

Discussion

Although endometrial cancer is the disease occurred mainly in postmenopausal women, the disease is increasing in premenopausal age group, especially in patient of less than 40 years. In this report, the incidence found was 16.4 %, as compared to previous studies, which have reported between 2-14 %.[3,8,9] Obesity is one of the major risk factors of endometrial cancer, which may increase the risk 3-10 fold.[10,11] Fifty-five point two percent of the women in this study had a BMI more than 25 kg/m^2, of whom 24.3 % were defined as obese. The other major risk factor is nulliparity, which has a 2-fold increase in risk of endometrial cancer.[11] Nearly half (41.4 %) of women in this study were nulliparous. However, up to 40 % of the women had at least three children. In this point, nulliparity has to be further evaluated to determine whether it is indeed an important risk factor in Thai women. Diabetes mellitus and hypertension are also associated with endometrial cancer. It may be true that both conditions are associated with obesity and age, which are usually found in women with endometrial cancer.

Abnormal uterine bleeding is the most common presenting symptom in endometrial cancer, seen in 90 % or more of patients, especially in postmenopausal women. The standard procedure for diagnosis of endometrial cancer is fractional curettage. Cytologic detection of endometrial cancer in the routine Pap smear is less accurate than cytologic screening in cervical cancer. Only one-third to one-half of cases may show abnormal papsmear results.[12] About thirteen percent of Pap smear in this study were abnormal; but only 2.4 % showed positive adenocarcinoma cells.

The International Society of Gynecologic Pathologists has proposed a classification for endometrial cancer. Endometrioid adenocarcinoma is the most common form of carcinoma, comprising 75-85 % of the cases.[13, 14] It is differentiated into three grades; well (G1), moderately (G2), and poorly (G3) differentiated tumors. Adenocarcinoma with squamous differentiation was formerly divided into adenoacanthoma and adenosquamous carcinoma. The new pathologic classification classifies the tumor by grading according to the adenocarcinoma part, because this is the best prognostic indicator.[15] In this study, most of cases (78.9 %) were endometrioid carcinoma, fifty-six percent were well-differentiated tumors, which was at variance with the 29 %-42 % in other reports.[5, 7] Nearly all cases were initially treated with primary surgery, i.e., TAH+BSO with or without lymph node sampling (pelvic and/or para-aortic lymph node).[16] Three-fourths were stage I disease and most of these had minimal myometrial invasion. Adjuvant treatment in endometrial cancer is given only to high-risk cases. The standard adjuvant treatment is radiation therapy, which is used to prevent recurrent disease, especially locally recurrence, but no study has yet determined whether it improves the survival rates of patients with high risk factors.[17-22] Abdominal recurrence may occur in these cases.[23] Adjuvant chemotherapy is becoming an option as a systemic control for advanced or recurrent disease.[24-28] Agents with at least a 20 % response rate include doxorubicin, carboplatin, cisplatin, epirubicin and paclitaxel. Up to forty per cent of the patients in this report received adjuvant treatment, which was adjuvant chemotherapy in most cases. The results of the adjuvant therapy have yet to be further investigated.

This study differs from our previous one,[2] that involved 117 patients during the period of 1982-1987. A higher rate of poorly differentiated endometrioid adenocarcinoma and relative tumor aggressiveness were observed in this current study. This may be due to the different treatment approach employed at that time. Since one-third of patients received preoperative radiation treatment, the surgicopathologic result might have been influenced by the effect of radiation- induced tumor regression and biased these data concerning tumor grade and myometrial invasion. We have no explanation why this cancer is found more commonly in younger patients. Later marriage or infertility may exert some cancer risk but this is still unclear. Further reports of treatment outcome in this group of patients is awaited.

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