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Radiation therapy for carcinoma of theendometrium : our experience duringthe period 1977-1983

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Radiation therapy for carcinoma of the endometrium : our experience during the period 1977-1983.

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The authors evaluated 106 cases of endometrial carcinoma. The median age at presentation was 57 years. Seventeen patients (16%) were hypertensive and 13 (12%) were diabetic. The most common presenting symptom was abnormal vaginal bleeding which constituted 76% of the patients. The distribution of the disease by stage was : stage I = 59%, stage II = 15%, stage III = 12%, stage IV = 3%, unknown stage = 11%. The most common histology was adenocarcinoma which accounted for 85.9% of the patients. Thirty-five patients (36%) were treated by radiation alone. Pre-and post-operative radiation was used in 28 patents (29%) and 33 patients (34%), respectively. Overall five-year survival was 78.6%. The survival rates for stages I, II, III and IV were 88.8%, 79.4%, 36.9% and 0%, respectively. Statistical analysis showed the age of the patients at presentation significantly influenced survival (p 0.025). Radiation method, histologic grade and uterine length could not be shown to influence survival. Measures to prevent patients lost to follow-up were proposed.

Key words: *Endometrial carcinoma, Radiation therapy.*

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ประยุทธ์ โรจน์พรประดิษฐ์, สุรีย์ ฐิตะฐาน, ประเสริฐ เลิศสงวนสินชัย, ประภัสสร รัชตะปิติ, เติมศักดิ์ พึ่งรัศมี. การรักษามะเร็งเยื่อบุโพรงมดลูกด้วยรังสี-ประสบการณ์ของเราในปี 2520-2526. จุฬาลงกรณ์เวชสาร 2536 มีนาคม; 37(3) : 173-182

*ได้ศึกษาผู้ป่วยมะเร็งเยื่อบุโพรงมดลูก ย้อนหลังตั้งแต่ 1 มกราคม 2520 ถึง 31 ธันวาคม 2526 ที่มารับการรักษาที่สาขารังสีรักษา ภาควิชารังสีวิทยา จุฬาลงกรณ์มหาวิทยาลัย เป็นจำนวน 106 ราย เกณฑ์อายุผู้ป่วยอยู่ระหว่าง 21-74 ปี อายุเฉลี่ย 57 ปี ร้อยละ 16 ของผู้ป่วยเป็นโรคความดันโลหิตสูง และ 12% เป็นเบาหวาน อาการที่ผู้ป่วยมาพบแพทย์บ่อยที่สุด คือ เลือดออกจากช่องคลอด (76%) ระยะของโรคแบ่งได้ดังนี้ ระยะที่ 1 = 59% ระยะที่ 2 = 15% ระยะที่ 3 = 12% ระยะที่ 4 = 3% ไม่ทราบระยะ = 11% ผลทางพยาธิที่พบบ่อยที่สุดคือ **Adenocarcinoma** ซึ่งพบได้ 85.9% ผู้ป่วยได้รับการรักษาด้วยรังสีอย่างเดียว = 36% รักษาด้วยรังสีและผ่าตัด = 64% อัตราการอยู่รอด 5 ปี ของผู้ป่วยทั้งหมด = 78.6% อัตราการอยู่รอดของผู้ป่วยในระยะที่ 1, 2, 3 และ 4 = 88.8%, 79.4%, 36.9% และ 0% ตามลำดับ การวิเคราะห์ทางสถิติพบว่าอายุของผู้ป่วยเป็นตัวแปรที่สำคัญต่ออัตราการอยู่รอด ผู้ป่วยที่มีอายุน้อยกว่า 60 ปี มีอัตราการอยู่รอด = 88.1% ผู้ป่วยที่มีอายุตั้งแต่ 60 ปีขึ้นไป มีอัตราการอยู่รอด = 60.9% ไม่พบความแตกต่างในอัตราการอยู่รอดอย่างมีนัยสำคัญทางสถิติ ในด้านวิธีการรักษา **histologic grade** และขนาดของมดลูก ได้เสนอวิธีการป้องกันผู้ป่วยไม่มาติดตามผลการรักษา*

Although the optimum method of treatment for stages I and II endometrial carcinoma is still a subject of controversy,[1-5] our treatment programme has been total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH-BSO) in both stages I and II, adding adjunctive radiation therapy in patients with certain risk factors (high-grade histology, deep myometrial invasion, cervical extension or metastasis to regional lymph nodes). For stages III and IV, radiation therapy is the mainstay of treatment.

This study is a retrospective review of our experience in treating 106 cases of endometrial cancer with radiation alone or adjunctive radiation during the years 1977-1983. It must be stressed that this group of patients, referred by gynecologists at their own discretion, comprised only a fraction of all endometrial cancers and do not, therefore, represent the whole range of endometrial cancer seen at Chulalongkorn Hospital.

Materials and Methods

The records of all endometrial cancer patients who were treated in the Department of Radiology, Faculty of Medicine, Chulalongkorn University from 1977 to 1983 were reviewed. There were 106 patients. The patients were staged according to International Federation of Gynecology and Obstretics (FIGO, 1971) guidelines. The policies of treatment have not been standardized but they generally fall into the following categories: patients with stage IAG1 disease were treated by TAH-BSO alone; other stage I and stage II patients received radiation treatments in addition to TAH-BSO. Pre-or post-operative radiation was utilized according to our staff's preference. Patients with stages III and IV of disease received radiation treatment alone or in conjunction with systemic chemotherapy or hormonal treatment.

Radiation treatments were given by external irradiation and/or intracavitary insertion. External irradiation was given by telecobalt-60 to the pelvis, using anterior and posterior opposing fields. Radium-226 was used for intracavitary insertion.

Patients were considered to have local or regional failure depending on whether they had clinical or histopathologic evidence of disease within the uterus, cervix, vagina, pelvic side-wall or other pelvic structures. Patients were considered to have distant metastasis if they had upper abdominal disease or hematogenous metastases.

The following patients were excluded from calculation of survival: three patients with uterine sarcoma and 15 patients who were lost to follow up, but included in the study of clinical features. Because of incomplete information regarding myometrial involvement and lymph node status, they were also exculded from this study. Eighty-eight patients were left for survival analysis. The median follow-up time was 4.8 years with the minimum being 1 month and maximum 12 years.

Five-year survival was determined by the life-table method.[6] Differences between survival curves and nominal measurement were tested by the logrank test and Chi-square analysis, respectively.[6,7] A p-value less than 0.05 was considered significant.

Results

The age of the patients ranged from 12 to 74 years, whith the median being 57 years (Fig. 1). Seventeen patients (16%) were hypertensive and 13 (12%) were diabetic. Nineteen patients (18%) were nulliparous (Table 1).

Fifteen patients (14%) were lost to follow-up. The median age of this group of patients was 53 years (range 21 to 73 years). Stages of disease were: stage I = nine patients, stage II = two patients, stage III = one patient, and unknown stage = three patients.

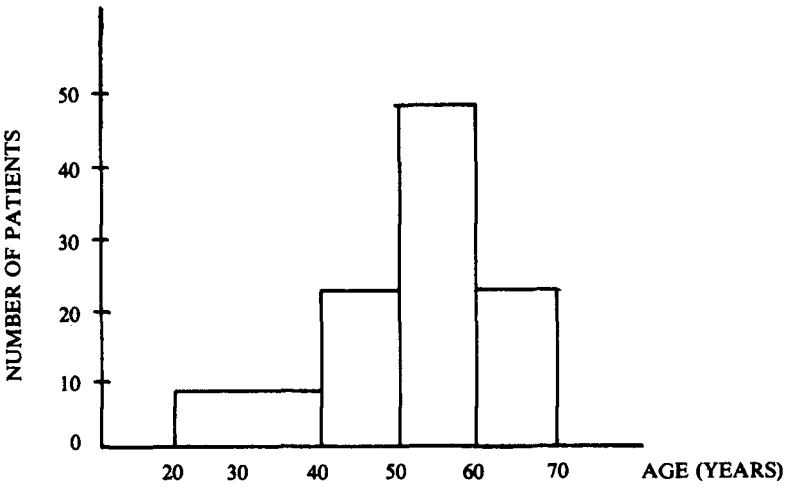

Figure 1. Age distribution of patients.

The most common presenting symptom was abnormal vaginal bleeding which accounted for 76% of the patients (Table 1).

Table 1. General Charcteristics of Patients.

Characteristic	**No. (%)**
Parity	
Multiparous	78 (74)
Nulliparous	19 (18)
Unmarried	9 (8)
Presenting symptoms	
Abnormal vaginal bleeding	81 (76)
Leukorrhea	8 (7)
No record	17 (16)
Associated diseases	
Hypertension	17 (16)
Diabetes	13 (12)
Ovarian diseases	5 (4)
Total patients	**106 (100)**

The Percentage distribution of endometrial cancer by stage at initial presentation was : stage I = 59%, stage II = 15%, stage III = 12%, stage IV = 3% and unknown stage = 11% (Table 2).

Table 2. Stage of Disease.

Stage	No. (%)
Stage I	62 (59)
IA	24 (23)
IB	36 (34)
I?	2 (2)
Stage II	16 (15)
Stage III	13 (12)
Stage IV	3 (3)
Unknown stage	12 (11)
Total	**106 (100)**

Note : I? = Stage I with unknown uterine size.

Histopathological types and grades are shown in Table 3. Adenocarcinoma was the most common histology, comprising 85.9% of the patients (Table 3).

Table 3. Correlation of Histologic Grade with Stage

Histology/ Grade	Stage No. (%) I	II	III	IV	?
Adenocarcinoma	54	15	12	3	7
Well	37	6	5	1	2
Moderately	8	1	2	-	1
Poorly	5	3	2	-	1
Unknown grade	4	5	3	2	3
Adenoacanthoma	2	-	-	-	1
Adenosquamous	1	1	-	-	-
Undifferentiated	1	-	-	-	1
Clear cell	3	-	1	-	-
Sarcoma	-	-	-	-	3
No record	1	-	-	-	-
Total	**62**	**16**	**13**	**3**	**12**

Thirty-seven percent of the patients were treated by radiation alone, 28% received pre-operative radiation and 35% received post-operative radiation (Table 4).

Table 4. Treatment Method.

Method	No. (%)
Radiation alone	35 (36)
Pre-op. radiation	28 (29)
Post-op. radiation	33 (34)
Total	**106**

The actuarial survival rate at five year for all patients was 78.6%. When the patients were classified by stage of the disease, the actuarial survival rates at five years were: stage I = 88.8%, stage II = 79.4% and stage III = 36.9%. There were only three patients in stage IV: one patient was lost to follow-up one month after treatment, and the other two patients died at two months and one year, respectively, after treatment (Table 5, Figure 2)

Table 5. Survival by Stage.

Stage	No. of patients	5-year survival
Overall	81	78.6%
I	53	88.8%
II	13	79.4%
III	12	36.9%
IV	3	0%

Pathologic grade and survival are shown in Table 6, and figure 3. For all stages, patients with grades 1 and 2 had a better five-year survival (82.5%) than grade 3 patients (76.7%), but it was not statistically significant ($p>0.05$). The survival rate for stage I grade 1,2 was 79% versus 100% for stage I grade 3.

Table 6. Survival by Grade.

Stage	No. of	5-year survival
All Stages		
grade 1,2	50	82.5%
grade 3	11	76.7%
I, grade 1,2	37	79.0%
I, grade 3	5	100.0%

The survival at five years for stage I patients with uterine size less than 8 cm (IA) was 100% versus 72.8% for patients with uterine size greater than 8 cm (IB). This observed difference is not significant statistically, even having controlled for confounding variables (histologic grades) (Table 7, Figure 4)

Table 7. Survival by Uterine Length.

Stage	No. of patients	5-year survival
IA	16	100%
IB	31	72.8%

Table 8 and figure 5 show the survival according to methods of irradiation. The survival rates for patients receiving RT alone, pre-operative RT and post-operative RT were 91.7%, 82.6% and 90%, respectively, which are not statistically significant ($p>0.05$). When the groups of pre-and post-operative RT were combined and analysed as a single modality of combined treatment, it showed a survival of 87.6%, again not statistically significant as compared with RT alone ($p>0.05$).

Table 8. Survival of Stage I by RT Method.

RT Method	No. of patients	5-year survival
RT alone	16	91.7%
Pre-op. RT	16	82.6%
Post-op. RT	21	90.0%
Pre + post – opRT	37	87.6%

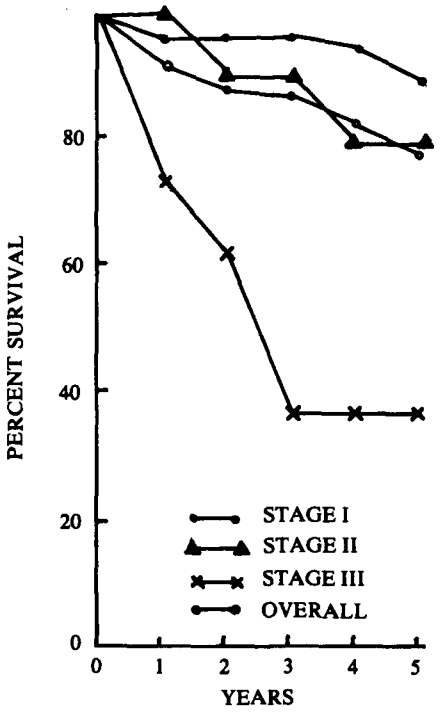

Figure 2. Survival by stage.

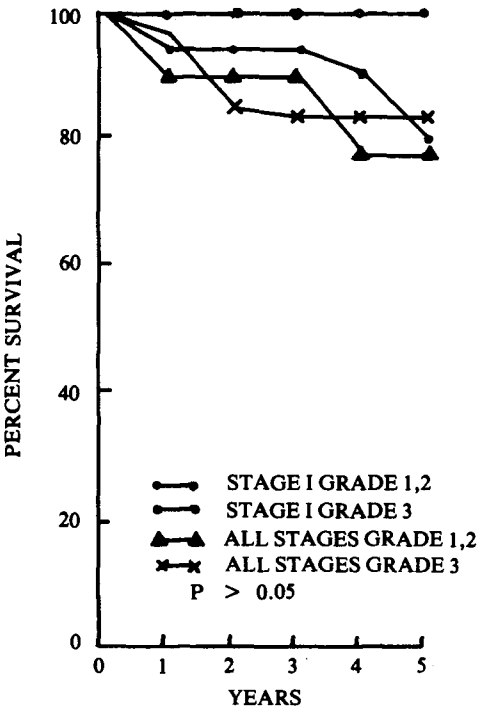

Figure 3. Survival by grade.

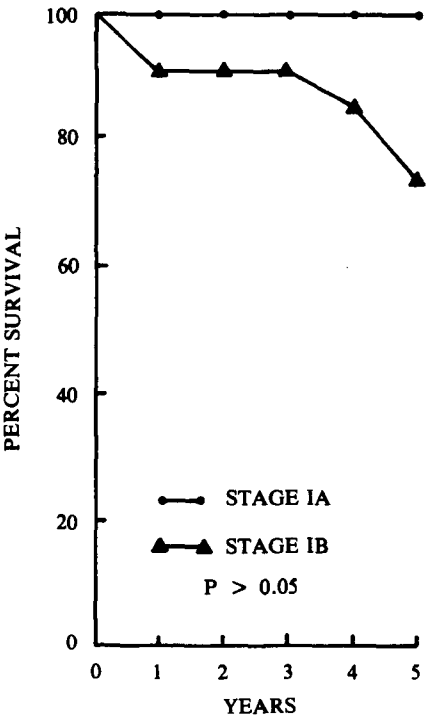

Figure 4. Survival by uterine length.

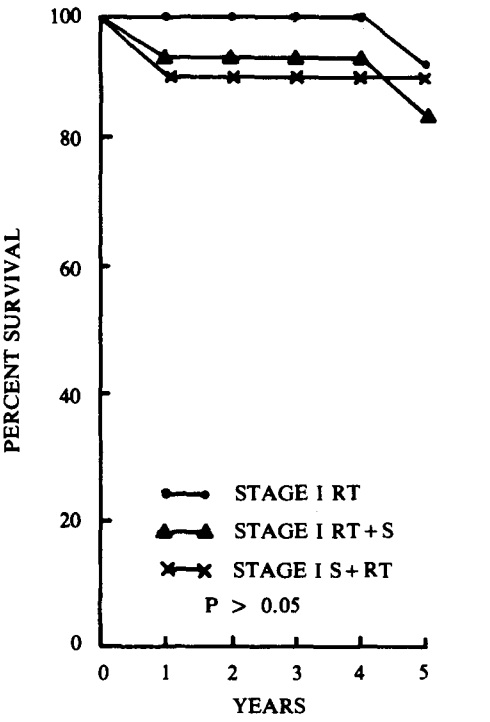

Figure 5. Survival by radiation method.

Age of the patients had a strong correlation with survival in our study, as shown in Table 9. Patients aged under 60 had a significantly better survival rate (88.1%) than patients 60 or more years of age (60.9%) ($p<0.025$). Similarly, 33.3% of patients 60 or more year of age presented with stage III and IV disease as compared with 9.4% of patients aged under 60 ($p<0.025$) (Table 10, Figure 6).

Table 9. Survival by Age.

Age (yrs.)	No. of	5-year survival
60	62	88.1%
60	25	60.9%

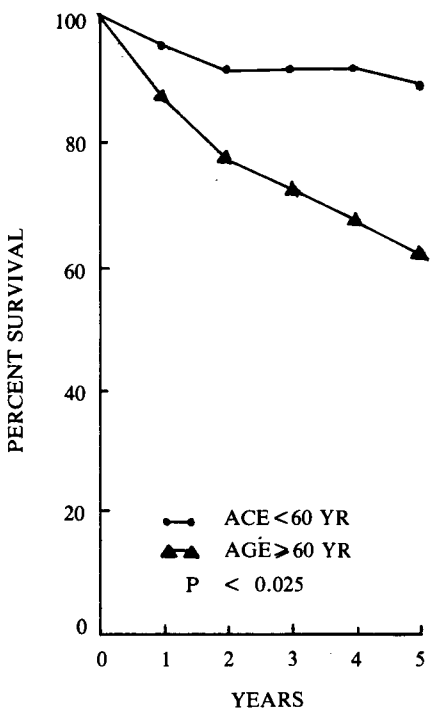

Figure 6. Survival by age.

Table 10. Stage III, IV Presentation by Age.

Age (yrs.)	No. of Patients	Percentage
60	63	88.1
60	25	60.9

In seven Patients (8%) the disease recurred: loco-regionally in five patients (5.7%) and distantly in two patients (2.3%).

Discussion

This study was undertaken to review the clinical characteristics and radiation treatment results of endometrial cancers in our Unit. The median age of presentation was 57 years. Abnormal vaginal bleeding was the presenting complaint in 76% of our patients. This stresses the importance of thorough investigation for post-menopausal women with abnormal vaginal bleeding. Nulliparity accounted for 18%, hypertension and diabetes were frequent associated diseases. The most common histology was adenocarcinoma comprising 85.9% of the patients. The actuarial five-year survival of our patients compares favorably with other studies.[8-11] The overall survival was 78.6%. For stages I, II and III the survival rate were 88.8%, 97.4% and 36.9%, respectively. There was no five-year survival for stage IV disease.

Despite universal reports of histologic grade as an important prognostic factor that influences survival,[12-14] the number of patients with poorly differentiated tumors in our series was not sufficient to established this relationship, particulaly in stage I patients. But for all stages, patients with well or moderately differentiated tumors had better survival (82.5%) than poorly differentiated patients (76.7%). However this observed difference was not significant. Within stage I disease, patients with a uterine cavity length of less than 8 cm had better survival (100%) than patients with uterine length of more than 8 cm (72.8%), this was not statistically different even after having controlled for confounding variables (histologic grade).

Choice of treatment for stage I adenocarcinoma of the endometrium still remains controversial.[1-5] RT alone, pre-or post-operative RT have all been advocated. In this study, there was no difference in suvival for patients receiving RT alone (91.7%), pre-operative RT (82.6%) or post-operative RT (90%).

There was a strong correlation between age and survival in our study, as have been reported in other series.[15,16] Patients less than 60 years of age had an obvious better survival rate (88.1%) than those aged 60 or more (60.9%) ($p<0.025$). Similarly the latter group of patients also presented clinically with more advanced diseases (stages III, IV), 33.3% versus 9.4% for patients aged less than 60 years ($p<0.025$).

The rate of recurrence was 8% : loco-regional failure was seen in five patients (5.7%), and two patients (2.3%) were associated with distant metastases.

One of the problems in reporting clinical trials is the loss of patient information in patients who are lost to follow-up. In this study, 14% of the patients were lost completely. We accepted that such was a high percentage and could influence treatment outcome. We would like to propose some measures to prevent patients from becoming lost to follow-up. Firstly, patients should be clearly and fully informed about the importance of attending follow-up clinics. Radiotherapy dose not stop with the completion of treatment. Patients are seen regularly at follow-up clinics; they may receive further treatment or rehabiliation they terminal doses may need help or palliation. Secondly, all patient data should be recorded by computer, frequently generating lists of patients due for follow-up. Patients who have been lost to follow-up or are overdue must be contracted promptly before all patient data are lost completely. Thirdly, on a national scale, a well-organized system of patient referral should be set up so that patients will not have to travel a long distance from rural areas to attend an urban follow-up clinic, District or provincial general hospitals should be able to provide facilities for continued follow-up of cancer patients, keeping all information available for analysis of treatment results.

Conclusion

This retrospective study examined the outcome of adjuvant radiation or radiation alone in treating 106 patients with endometrial carcinoma during period 1977-1983. Excluding patients who were lost to follow-up and whose histology was other than adenocarcinoma, 88 patients were left for survival analysis. Patients were staged according to FIGO (1971) guidelines. The median time of follow up was 4.8 years. The median age of the patients was 57 years. Eighty-one patients (76%) presented clinically with abnormal vaginal bleeding. Twenty-eight patients (26%) were nulliparous and unmarried. Seventeen patients (16%) were hypertensive and 13 of them (12%) were diabetic.

Sixty-two patients (59%) were stage I, 16 patients (15%) were stage II, 13 patients (12%) were stage III, and three patients (3%) were stage IV. Adenocarcinoma was the most common histology, accounting for 85.9% of the patients. Thirty-five patients (36%) were treated by radiation alone, 28 of them (29%) by pre-operative radiation, and 33 (34%) by post-operative radiation. The overall five-year survival rate was 78.6%, and the survival rates of stages I, II, III, and IV were 88.8%, 79.4%, 36.9% and 0%, respectively. Age of the patients at presentation was the only prognostic factor found in this study to significantly affect survival. Patients less that 60 years of age had a better survival rate (88.1%) than patients aged 60 or more (60.9%). However, we could not established a positve correlation between histologic grade, method of RT, or uterine length and survival. Measures to prevent patients lost to follow-up were suggested.

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