A Study of Squamous Cell Carcinoma of the Cervix in a Young versus an Older Thai Population

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Abstract: *A retrospective clinico-pathologic review was undertaken of all cases of invasive cervical squamous cell carcinoma accessioned at Siriraj Hospital from 1980 to 1985 in women 35 years or less and 55 years or greater. After study criteria were applied, 635 women were eligible for inclusion: 152 younger and 483 older. Younger women tended to present with early (Stage IB) as opposed to advanced (Stage III) stage disease found in older women ($p<0.001$). An earlier stage at presentation may be attributed to their higher frequency of contact bleeding (22% versus 2%). No shift in age distribution of disease to a younger population was found ($p>0.05$). A self addressed questionnaire was mailed to the patient's last known address in an attempt to increase follow-up data but significant deficits in the data base regarding time to first recurrence, its location, and date of death persisted. These deficits precluded an analysis of possible differences in tumour behaviour and virulence between younger and older women. Continued monitoring of this disease is warranted in view of world-wide reports of changing patterns of epidemiology and biology. (Thai J Obstet Gynaecol 1992; 4: 43-50.)*

Key words: cervical carcinoma, prognosis, age, epidemiology

Squamous cell carcinoma (SCC) is the major cause of death from cancer in the female population of Thailand[1]. This may be attributed in large part to the absence of an organized, country-wide cytology screening program for the detection and treatment of preinvasive cervical lesions commonly called cervical intraepithelial neoplasia (CIN).

Despite the presence of organized cervical cytology screening pro-

grams in some Western countries, reports are emerging from some of those countries of an increasing incidence of invasive SCC of the cervix in younger women[2-5]. Further, there are numerous reports from those nations documenting the emergence of an aggressive form of this cancer in young women[6-9]. In the young woman, invasive SCC of the cervix may be characterized by a poor response to conventional treatment with a short interval from diagnosis and treatment, to recurrence and to death[10-11].

The purpose of this study was to determine if a similar pattern of cervical SCC is emerging in the young Thai population. For this purpose certain characteristics of invasive SCC of the cervix in young women, 35 years or less at diagnosis, have been determined and compared to those of older women, 55 years or more at diagnosis.

Materials and Methods

The medical records at Siriraj Hospital from 1980 to 1985 were searched for all diagnoses of invasive SCC of the cervix involving women 35 years or less, or 55 years or greater. 1985 was chosen as a cut-off date to allow five years of follow-up. This involved a search of the records in the Cytology Unit, the Pathology Unit and the Statistical Unit of the Department of Obstetrics and Gynaecology. In addition the records of the Radiotherapy Division and the Hospital Statistics Record were searched. Follow up information was obtained from all those records as well as the Outpatient Department Gynaecologic Cancer Unit's records. In addition a letter requesting follow up information was mailed to the patient's last known address if she had not been seen in the pervious 12 months unless the date of death was recorded. A stamped return envelope was included with the follow up questionnaire[12].

From the above sources the following data were recorded as available: age, stage, presenting complaint, tumour size, treatment modality, time interval to recurrence and its location, and time interval to death.

All patients were staged according to FIGO criteria except firstly, routine intravenous pyelograms were not obtained. Secondly, on review of the histopathology, a 3mm level of invasion was used to separate microinvasive(Stage IA) from invasive (Stage IB or greater) SCC as recommended by the Society of Gynecologic Oncologists (SGO). This criterion also allows for better comparison with other published data from Western societies. All histopathology slides were reviewed by one of the authors (D.I.R.).

The only patients excluded from this study were those whose diagnosis and treatment were not established and/or completed in the study period, or those for whom the diagnosis of invasive (Stage IB or greater) SCC could not be confirmed on pathology review. Reasons for the

latter included the following:

1. the histologic diagnosis was made elsewhere, the patient being referred to Siriraj Hospital for radiotherapy or follow up.
2. the diagnostic slides were missing from the file.
3. transcription errors of name or record numbers occurred.
4. using SGO criteria, some patients were restaged as Stage O or IA.
5. on review the diagnosis was revised to verrucous carcinoma, malignant carcinoid tumour, oat cell (small cell) carcinoma, lymphoma or adenocarcinoma (one patient each per revised diagnosis).

For statistical test of significance, the *Chi square test* was used.

Results

Of the 1220 patients originally identified for this study, 635 remained eligible for inclusion after the application of study criteria. Figure 1 shows the number and percent of women in each age group diagnosed in each year of the study. No trend is apparent to suggest that the incidence of invasive cervical SCC is shifting to a younger age population ($p>0.05$). The stage at diagnosis for both groups of women for the entire study period is shown in Figure 2. The stage distribution at the time of diagnosis differed between younger and older women: younger women were more likely to present with early (Stage IB) disease while older women were more likely to present with advanced (Stage III) disease ($p<0.001$).

The commonest symptoms at presentation are shown in Figure 3. Only three of the younger, and seven of the older patients were asymptomatic. Five of the younger, and 12 of the older patients had no recorded symptoms. Many patients presented with multiple symptoms, the commonest combination being abnormal vaginal bleeding with leukorrhea. The percent of younger versus older women complaining of abnormal vaginal bleeding was almost identical (78% versus 77%). However, within the

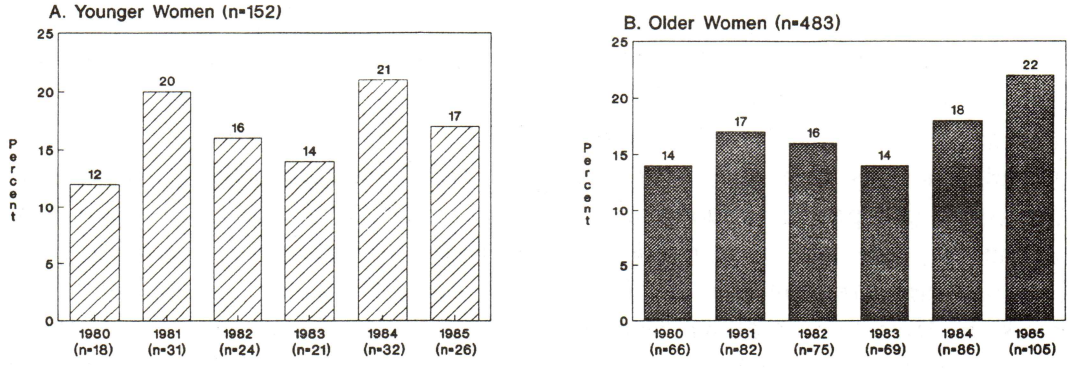

Fig. 1 Percent of women diagnosed by year.

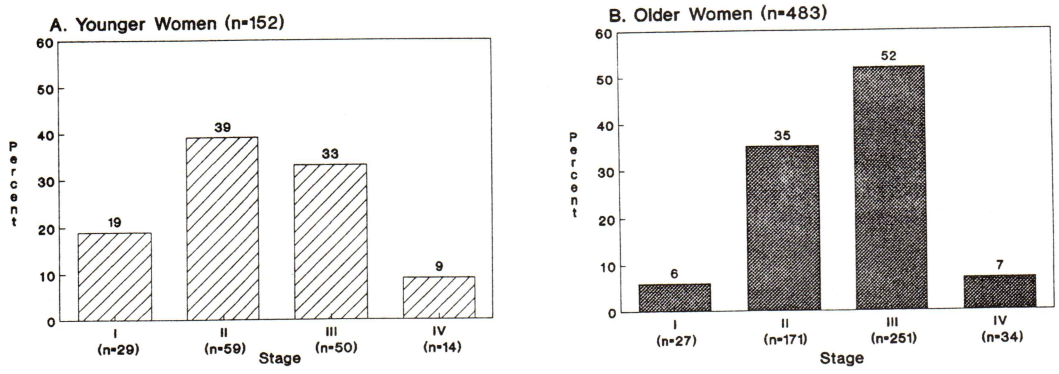

Fig. 2 Stage at diagnosis.

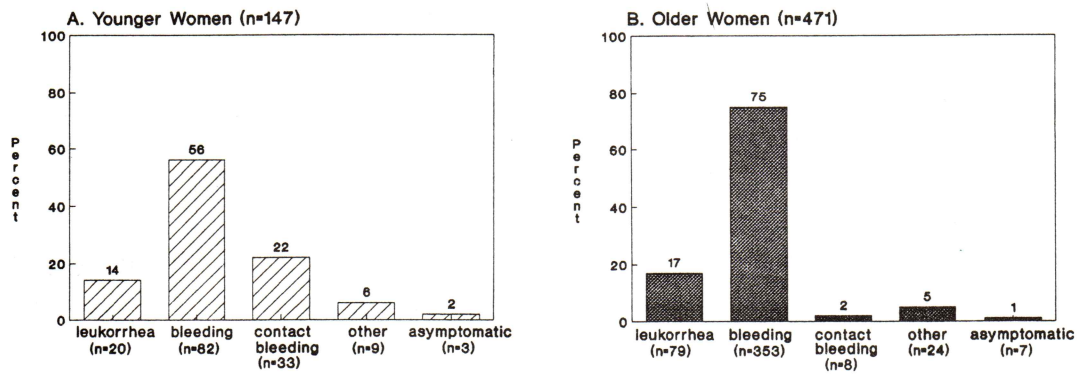

Fig. 3 Percent of women diagnosed by year.

category of abnormal vaginal bleeding, 22% of younger versus only 2% of older women complained of contact bleeding.

Other clinical or pathological features recorded during the review included lesion size, number of involved quadrants, tumour growth characteristics (exophytic, endophytic or ulcerative), presence of lymphatic or blood vessel invasion and depth of invasion. However, large amounts of missing data preclude comparison between age groups.

Some follow-up information was available on 556 patients (87.6%); the remaining 79 patients (12.4%) were not seen again at Siriraj Hospital after diagnosis (Table 1). Although the follow-up period ranged from 0 to 142 months, the majority of patients in both younger and older groups, were ultimately lost to follow-up. Follow-up to death was recorded (data for older women in parenthesis) in 0 of 29 Stage IB (4 of 27), 7 of 59 Stage II (26 of 171), 8 of 50 Stage III (51 of 251) and 4 of 14 Stage IV pa-

Table 1 Follw-up in months by stage

Stages	No.	Mean	Median	Range	No. with no Follow-Up
A. Younger women					
				14	
IB	29	70.7	62.0	0.5-136.0	4
II	59	47.2	26.0	1.0-129.0	6
III	50	31.1	11.0	1.0-121.0	1
IV	14	3.8	3.0	0.5-8.0	3
B. Older women					
				65	
IB	27	16.6	65.6	3.0-124.0	5
II	171	37.8	22.0	0.5-142.0	17
III	251	27.6	10.0	0.5-142.0	36
IV	34	21.4	8.0	0.5-133.0	7

tients (10 of 34). From the return of the questionnaire it was confirmed that an additional 5 younger and 18 older women were dead but no indication was given of the date or cause of death. The large amounts of missing data preculde a comparison of survival in each stage between younger and older women. Similarly, the absence of large amounts of data regarding time to recurrence and sites of recurrence prevent comparisons between groups of women.

Discussion

Although this is not a population based study, the analysis of data from Siriraj Hospital shows no trend to suggest that the incidence of invasive SCC of the cervix is shifting to a younger population. The ratio of younger to older patients remained relatively constant over the study period. The recently documented shift to a younger population reported from some Western countries is most likely related to changing female sexual habits with those women commencing sexual intercourse at a younger age and having multiple sex partners. The latter are well recognized major risk factors for the development of cervical cancer[13-14]. The absence of an apparent shift in this study suggests a more traditional and monogamous pattern of sexual behaviour exists for Thai women.

The analysis of data from Siriraj Hospital shows also that younger women tent to present with earlier stage disease than their older counterparts, a difference which was statistically significant ($p<0.001$). Why younger women tend to present earlier in the course of their disease is not entirely clear but may be related to the presenting symptom of contact

bleeding. If is can be assumed that older women are less likely to be sexually active than younger women, then contact bleeding from sexual intercourse might alert the younger women at an earlier stage to her disease. Thus, it is noteworthy that 22% of all younger women as opposed to only 2% of older women complained of contact bleeding.

It is also noteworthy that only three younger and seven older patients were asymptomatic at the time of presentation since a symptomatic presentation, especially in young women, correlates with recurrence and poor prognosis[11]. This may reflect with sampling bias of patients since Siriraj Hospital is a public hospital catering to the poor (as opposed to a private hospital) who have had limited access to health care. However, it almost certainly also reflects on the absence of a country-wide cervical cancer screening program which would increase the rate of detection of asymptomatic women.

This study emphasizes the necessity of a review of the original pathology specimens prior to the inclusion of any patient in a retrospective study. Of the original 1220 patients deemed eligible for inclusion, only 635 (52%) remained after pathology review. That exclusion rate is very similar to that reported recently from Canada where only 45 out of an original 83 (54%) patients remained eligible for inclusion[11]. Indeed, the exclusion rate as a direct result of pathology review from the Canadian Study was even greater since the first three reasons for exclusion in this study did not apply. Over the years diagnostic criteria are refined and/or changed. This is especially true in distinguishing Stage IA from IB cervical SCC. Some pathologists use the FIGO criterion of 5 mm invasion to separate the stages; others use the SGO's criterion of 3mm[15]. Still others do not recognize "microinvasive" as distinct from "invasive" disease. Since young women tent to present with early stage disease, the separation of Stage IA from IB disease is especially important. The inclusion of significant numbers of Stage IA tumours would tend to mask any difference in tumour virulence between younger and older patients. The importance of a standardized pathology review, especially in a retrospective study, has also been emphasized recently by Eifel and Hendrickson[16].

The large amounts of missing data preclude a valid statistical analysis of pathologic factors which might be indicative of a poor prognosis in both groups of women, or predictive of a difference in prognosis between younger and older women. Since invasive SCC of the cervix in older women presenting at Siriraj Hospital is preferentially treated by radiotherapy rather than radical surgery (as is the practice in many other hospitals), only small biopsies to confirm the diagnosis were available for review. Depth of invasion and the presence/absence of lymphvascular invasion cannot be assessed in such material.

Hysterectomies, which provide adequate specimens for such assessment, are only routinely performed in young women with early stage disease.

Similarly, a comparison of survival between younger and older women in each stage was not possible because of large amounts of missing data with respect to date of first recurrence, its location and the exact date of death. For example, in Stage IV disease which in almost all cases the patients might be expected to die of their tumour, no follow-up data was available for 3 of 14 younger and 7 of 34 older women and for only 4 of 14 younger and 10 of 34 older women was death known to have occurred. Although the response rate to our questionnaire was excellent[12], the replies were sometimes imprecise for they simply stated "dead", or "dead long ago". We have assumed in this study such patients died of tumour but especially for older women with early stage tumour with no documented evidence of recurrence, death from intercurrent disease could significantly alter the results.

Thus, the significant findings of this study are that younger women with cervical SCC tend to present at an earlier stage than their older counterparts. This is most likely the result of their noticing contact bleeding. Further, no shift of disease incidence to a younger population is apparent in this study. We are unable to determine if SCC of the cervix is becoming more virulent in the younger Thai patient as reported in some Western countries. However, a recent report form Japan[17], the first from an Asian country, confirms that age at diagnosis is also a prognostic factor in their study population. Continued monitoring of the incidence and biology of cervical SCC in Thailand would seem desirable.

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