Present status of carcinoma of the uterine cervix and standardisation of its treatment in Thailand.

Puangtong Kraiphibul, M.D., Yaowalak Chansilpa M.D.***

*Ramathibodi Hospital, **Siriraj Hospital, Mahidol University Bangkok, Thailand.

ABSTRACT

In Thailand the most common female cancer was carcinoma of the uterine cervix. It's estimated national age-standardised incidence as 23.4 per 100,000. The peak age group was between 41-59 year old. The most important risk factors were among women with low socio-economic and who had been infected by HPV. The stage distributions of the disease were about 10-15%, 40-50%, 30-45%, and 3-5% in stage I, II, III and IV, respectively. Nearly 90% of cases were sequamous cell carcinoma. Adenocarcinoma about 10% and others were about 2-3%. The treatment of stage I was surgery, while stage II-IV main modality was radiotherapy. Chemotherapy was preserved for measurable residual tumor, recurrence or in study protocols. The 5 yr. survival rate in stage I, II, III and IV were about 75-90%, 50-80%, 30-50% and 0%, respectively. The most common acute effect was mild diarrhea. The common late effects cystitis and proctitis, but severe status was less than 5%.

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Introduction

Thailand is one among Southeast Asian countries. It covers the area of 512,115 square kilometres which devided into 76 provinces. Bangkok is the capital city which situated in the central region. The national religion is Buddhism. In 1990, the estimated population was around 55 million. The male to female ratio was about 1:1. Therefore the female population was around 27 million. One third of people were in the age group between 15-30 year old. About occupation, 70% were in agriculture and 11% were labourers[1].

Concerning with cancer, the top 4 of both genders were liver, lung, cervix and breast, respectively. The most common of male were liver, lung and head and neck while in female, they were cervix, breast, liver and lung. The national estimated crude rate (CR) and age standardised incidence rate (ASR) of all sites of cancer in male were 110.8 per 100,000 and 153.6 per 100,000, respectively, while in female were 107.3 and 128.5. The crude death rate and age standardised mortality rate (ASMR) for all site cancer in male were 35.6 per 100,000 and 58.1 per 100,000, respectively, while being 27.6 and 39.2 in female[1].

Carcinoma of the uterine Carvix

Introduction

Uterine cervical cancer was the most common female Thai cancer. It rank the first in every region. The overall ASR was 23.4 per 100,000 ; lowest in the south, 18.5 and highest in the north, 29.7[1]. The ASMR was between 0.61-1.04, varied from year to year[1]. The peak age group was among 41-59 year old, about 70% of the cases[1,2]. The incidence was low at the age below 30 and over 70, about 3%[1,2]. About 80% of patients had 3 or more than 3 of pregnancies. The incidence was low below 3 pregnancies, about 2-7%[2]. The high risk were among women with : a) history of repeated infections of vagina and

cervix[3], especially, human papilloma virus (HPV)[4] and low socioeconomic status[3]. Both factors had statistic significant.[3,4]. Other factors which had relation to but not reached statistic significant were : a) gonorrheal, syphilis[3] and herpes simplex virus (HSV)[4] ; b) familial history[3] ; c) high parity[3] ; d) age at first intercourse or number of sex partners[3]and e) oral contraceptive[5]

Natural history

The most common symptoms were leukorrhea and abnormal vaginal bleeding. Very few were detected by Pap's smear. Pap's smear was available throughout the country but limitted to a small group of population. The disease stage distributions were about 10-15% in stage I, 40-50% in stage II, 30-45% in stage III and 3-5% in stage IV[2,6,7]. The overall distant metastatic rate was ranged between 10-30%[7-13].

Pathology

Most of the cases had histologic diagnosis. Nearly 90% were squamous cell carcinoma. Adenocarcinoma was around 10%. The others such as lymphoma or adenoidcystic carcinoma were around 2-3%[6-8, 10-14].

Staging work up.

Each case had complete history and physical examination included per vagina and rectum. And each case, these were done routinely ; CBC, U/A, BUN or Cr, FBS, LFT, PA chest, IVP or renography. Cystoscopy and proctoscopy, despite available in every center, not done routinely in each stage but all agreed to perform in every case of late stage II and III. Others, such as CT-scan or MRI of the lower or whole abdomen or bone scan, etc, had been done as indicated clinically.

Treatment

Management of cervical cancer throughout Thailand was in the same policy and this was true in the radiation techniques as well. The standard treatment according to stages were :

Stage O : conservative surgery by mean of conization, TAH or TAH + BSO, depends on their indications.

Stage IA : TAH ± BSO or hysterectomy ± bilat. SO + bilateral pelvic lymphadenectomy or Radiation therapy by Brachytherapy. Brachytherapy.

Stage IB : Radical Hysterectomy ± belat SO + bilateral pelvic lymphadenectomy. on curative radiotherapy by mean of Brachytherapy alone or combined with external radiation. If the lymph node was positive for metastasis or more advanced stage by surgical or pathological finding, postoperative radiation was recommended.

Stage II : Curative radiotherapy by mean of combination external radiation XRT to whole pelvis and brachytherapy by low dose rate (LDR), medium dose rate (MDR) or high dose rate (HDR). In some center, TAH ± BSO has been added 4-8 weeks after completed radiation in these situation. a) barrel shape or huge cervical mass, b) endometrial extension or enlarged uterus, c) residual tumor, and d) improper Brachytherapy.

Stage III : Curative radiotherapy by mean of XRT and brachytherapy (LDR, MDR or HDR). Chemotherapy, mostly CDDP single agent or CDDP in combination with others were used in the cases of measurable residual tumor or in protocols.

Stage IV : Various treatments, depended on clinical indications. Some hospitals had protocol treatment by mean of radiation in combination with chemotherapy but some prefered radiation alone.

Recurrence tumor : Various treatments, depended on clinical indications. As in stage IV, some hospitals has ongoing protocol studies.

Details of Radiation Therapy.

A. Radiation therapy Centers : At this moment, we have 14 radiation therapy centers throughout Thailand, 1 in the north (Chiengmai), 2 in the northeast (Kornkhan and Nakornrajasima), 1 in the south (Songkla). But, in near future, more 4 new centers are in the plan of being instituted throughout country.

B. Machines : Each center has at least one cobalt unit, while linear accelerators has installed in the university hospitals or big hospitals. There are, throughout Thailand, 17 units of cobalt and 9 linear accelerators of 4, 6 and 10 MV.

C. Isotopes : LDR : each hospital has radium or cesium and most using Fletcher's applicator.

MDR : 3 units of Selectron (cesium)

HDR : 5 units (4 of Cobalt and 1 Iridium).

D. Treatment regime : We have the standard treatment in LDR but in HDR the treatment protocol has been depended on each center (table 1). No adequate datas concerning with HDR, therefore no any conclusion on outcome or standard treatment regime of HDR at this moment.

Result

Treatment status : Due to many problems, such as, socioeconomic, accomodation, transportation, poor distribution of radiotherapy centers or misunderstanding about disease or treatment, only around 60% of patients had their treatment completely, about 20% refused the treatment since the begining, about 10%, had incompleted and other 10% were referred to other centers near their home[2].

Survival Rate At 5 years, the survival rate in stage I, II, III and IV were about 75-90%, 50-80%, 30-50% and 0%, respectively[8-11, 13-17].

Disease free survival : The factors which had statistic significant influenced on disease free survival (DFS) were staging, tumor size and time interval between external irradiation (XRT) and brachytherapy[7]. While the following factors also had relationship but not reached the statistic significant, total dose at the point A[18] and histology[7].

Complication : During the treatment, the most common effect was mild diarrhea. After treatment, most common effects were cystitis and proctitis but less than 5% had them in severe[16,19,20]. The time to the occurrence of the symptoms were usually within 3 years after treatment. The proctitis occurred earlier than cystitis[17,19,20]. The factors which had statistic significant influenced on these events were the total dose at point A[19,20]. The others, as age, weight and history of pelvic surgery had no statistic significant relationship[20].

Follow up

Rate of follow up was varied from hospital to hospital due to many problems. The main, were poor socioeconomic and lack of knowledge on the disease. However the rate was ranged between 30-80%. By the way, there was higher follow-up rate in early stage patients especially stage I (94%)[2].

The policy of followup was the same in each hospital. Doctors prefered to see patients every month at the first 6 months of post treatment, every 1-2 months at the last 6 month of the first year. The visit was changed to be every 2-3 months during the second and third year and then every 3-6 months. After 5 years, the followup was annually. The procedures performed during followup were history, physical examination, per vaginal and rectal examination. Routine laboratory tests by CBC, U/A, LFT, FBS, Cr or BUN and chest X-ray were performed annually. First pap smear was usually at the 4-6 th month after treatment, then annually. IVP or other special investigations had been performed according to indicate by clinically.

Conclusion & Recommendation.

1. pap smear should be performed at least once a year in high risk women in order to get cancer control and early detection.

2. Survival rate in stage III was quite low by conventional method of treatment, therefore new modality should be considered.

References :

1. V. Vatanasapt et al. Cancer in Thailand 1988-1991. IARC Technical Reporting No. 16, Lyon, 1993.
2. Somkeart Srisupundit, Somsak Tangtrakul, Puangtong Kraiphibul, Lucksana Pochanukul, Carcinoma of cervix at Ramathibodi Hospital from cancer registry 1978-1982. J Med Assoc. Thai 1984, 67 : 68-72.
3. Wangsuphachart V. et al. Risk by Pap's smears in Thai women int J Epidemiology 1987 ; 16 : 362-366.
4. Thanapatra S et al. Common Specific cervical infection in cytology study. Thai Cancer J 1992 ; 18 : 1-8.
5. Thanapat S et al. Relationship between oral contraceptives and cervical carcinogenesis. Thai cancer J 1988 ; 14 : 36-4.
6. Paiwuti S. Cancer of female genital organ. Thai Cancer J, 1989 ; 15 : 135-145.
7. Montien P. et al. Radiotherapy alone in the treatment of carcinoma of uterine cervix in Srinagarind Hospital : Analysis of treatment failure. Thai J Radiology 1989 ; 26 : 67-70.
8. Pisit Sirisuk. Adenocarcinoma of the cervix uteri. Thai Cancer J 1990 ; 16 : 88-95.
9. Supatra Sangruchi et al. Result of treatment of squamous cell carcinoma of cervix stage II and III by telecobalt and Selectron LDR at Siriraj Hospital during 1981-1986. Thai cancer J 1989 ; 15 : 123-129.
10. Puangtong Kraiphibul et al. Result of treatment in old age carcinoma of the uterine cervix. Thai Cancer J. 1990 ; 16 : 115-118.
11. Puangtong Kraiphibul et al. Results of treatment of young age group of the uterine cervix. Thai cancer J 1990 ; 16 : 119-122.

12.Puangtong Kraiphibul et al. Pattern of treatment failure among patients who died of invasive carcinoma of the uterine cervix. J Med Assoc Thai 1990 ; 73 : 20-22.
13.Sirisak Buributh et al. ผลการรักษามะเร็งปากมดลูกด้วยรังสี. Thai Cancer J. 1984 ; 10 : 155-121.
14.Pairat Tepmongkol. Radiation therapy for carcinoma of cervix uteri : A clinical study in Siriraj Hospital. J Med Assoc Thai 1980 ; 63 : 512-517.
15.Somkeart Srisupundit, Puangton Kraiphibul, Somsak Tangtrakul, Yaovalak Bhumarapravati : Cervical cancer survival at Ramathibodi Hospital 1979-1983. J Med Assoc Thai 1990 ; 73 : 15-19.
16.Puangtong Kraiphibul et al. Combined radiotherapy and hysterectomy in the treatment of high risk stage II invasive carcinoma of the uterine cervix : A preliminary report. J Med Assoc Thai 1990 ; 73 : 23-27.
17.Puangtong Kraiphibul et al. Result of treatment in stage IIB squamous cell carcinoma of the uterine cervix : Comparison between two and one intracavitary insertion. Gynecol Oncol 1992 ; 45 : 160-163.
18.Lalida Tuntipumi-amorn, et al. Local failure in radiation treatment of cervical carcinoma. Thai J Radiology 1991 ; 288 : 31-36.
19.Lalida Tuntipumi-amorn, et al. Bladder and rectal complication from radiation treatment of cervical cancer. Thai J Radiology 1991 ; 28 : 53-59.
20.Varadom Soonvisuth et al. Radiotherapy alone in the treatment of carcinoma of uterine cervix in Srinagarind Hospital : Amalysis of complication. Thai J Radiology 1989 ; 26 : 139-146.

Table 1 *Detail of treatment by radiotheray*

		XRT (Whole pelvis)	**Brachytherapy**	
		Gy	**LDR**	**HDR**
			Fletcher's applicator	**Total TDF**
			mg-hr.	**AT PT.A**
stage I	small lesion	-	10,000 (2 insertions)	
				84-135
	large lesion	40	7,200 (2 insertions)	
stage II		40	7,200 (2 insertions)	
			or.	138-147
		50	5,400 (1 insertions)	
stage III		50-55	5,400 (1 insertions)	150-163
stage IV		varied		