

Cost Effectiveness of Concurrent Chemoradiation in Comparison with Radiation Alone in Locally Advanced Cervical Cancer

Sumonmal Manusirivithaya, MD, MSc*,
Manit Sripramote, MD, MSc*, Siriwan Tangjitgamol, MD*,
Nopawan Sanjareonsuttikul, MD, MSc**, Pagaporn Pisarnturakit, DBS, MSc***

* Department of Obstetrics and Gynecology,

Bangkok Metropolitan Administration Medical College and Vajira Hospital

** Department of Physical and Rehabilitation Medicine, Ramathibodi Hospital, Mahidol University

*** Department of Community Dentistry, Faculty of Dentistry, Chulalongkorn University

Introduction: Concurrent chemoradiation has been advocated to be more effective than radiation alone in the treatment of cervical cancer. However, it certainly has more side effects. Hence, it is worthwhile to investigate the cost-effectiveness (CE) of concurrent chemoradiation in comparison with radiation alone in locally advanced cervical cancer.

Material and Method: The treatment of cervical cancer was modeled using the decision tree where the treatment option would be either concurrent chemoradiation or radiation alone. Patients receiving each treatment had different risks of tumor recurrence. Costs in this analysis were separated into four major categories: costs for treatment of cervical cancer, costs for treatment of major side effects, costs for follow up cancer patients, and costs for diagnosis including supportive care of recurrent cervical cancer. Charges were used for the costs of chemotherapy, radiotherapy, drugs, and accessories. Unit cost was used for the costs of laboratory investigations, in-patient and out-patient services. Costs incurred after the first year were discounted at an annual rate of 5%. The benefit was measured as months of life survived. The present study evaluated the patients to 5 years after complete treatment.

Results: The CE ratio in the concurrent chemoradiation group was 2,855 and 1,835 Baht/month survived if the chemotherapy was given as in-patient and out-patient respectively. The CE ratio in the radiation group equaled 2,366 Baht/month survived. For the sensitivity analysis, in the situation that chemoradiation was not much better than radiation alone in terms that the recurrent rate from chemoradiation group was not more than 20% lower than the radiation group, radiation therapy alone would be more cost effective even if chemotherapy was given as an out-patient basis.

Conclusion: Radiation alone was more cost effective than chemoradiation in the treatment of cervical cancer. Nevertheless, if chemotherapy was administered on an out-patient basis, chemoradiation will be more cost effective only if the recurrent rate from the chemoradiation group was more than 20% lower than the radiation group.

Keywords: Cost-effectiveness, Cost-utility, Cervical cancer, Chemoradiation, Radiation

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Cervical cancer is the most common cancer in Thai women⁽¹⁾. This cancer is a major health problem in Thailand, which consumes the resources for taking

care of these patients. Despite the availability of a sensitive method in the screening of preinvasive cervical cancer, about 5,500 Thai women develop

Correspondence to : Manusirivithaya S, Department of Obstetrics and Gynecology, Bangkok Metropolitan Administration Medical College and Vajira Hospital, Bangkok 10330, Thailand.

invasive cervical cancer per year⁽¹⁾. This cancer is the principal cause of death from cancer in women⁽¹⁾. In addition, this cancer affects women at a younger age than other malignancies, therefore improvements of treatment resulting in a higher cure rate can have a profound impact on longevity.

The treatment of cervical cancer is dependent on the stage of disease at diagnosis. In the past, the standard treatment for most cases of the cervical cancer patients was radiotherapy, since 60-70% of cervical cancer were diagnosed in stage IIb - IVa⁽²⁾. Moreover, 10-20% of patients in stage Ib-IIa^(3,4) would have lymph node metastasis or parametrial invasion found during radical hysterectomy, and were also candidates for adjuvant radiotherapy.

Recently, many studies have reported the superior results of concurrent chemoradiation over radiation alone for the treatment of these groups of patients⁽⁵⁻¹⁰⁾. In February 1999, based on the results of these studies, the National Cancer Institute of the United States of America released an announcement that⁽¹¹⁾ "strong consideration should be given to incorporation of concurrent cisplatin based chemotherapy with radiation therapy in women who require radiation therapy for treatment of cervical cancer".

In the year 2002, the Cochrane Library reported the systematic review and meta-analysis of this issue⁽¹²⁾. They concluded that concomitant chemoradiation improved overall survival and reduced local and distant recurrent rates but with more cytotoxic effect.

Although, concurrent chemoradiation appeared to be more efficient, it certainly produced more side effects and complications. This, consequently necessitates more symptomatic and supportive treatments⁽¹³⁾. Since most cervical cancer patients in Thailand are not well-off, the budgets for the treatment of these patients are provided mostly from the national budgets. Hence, it is worthwhile to investigate the cost effectiveness of concurrent chemoradiation in comparison with radiation alone in the treatment of locally advanced cervical cancer.

Material and Method

Decision tree

The treatment of cervical cancer was modeled using the decision tree (Fig. 1). The decision tree began at the decision node where the treatment choice for locally advanced cervical cancer would be either concurrent chemoradiation or radiation alone. With different treatment, there were higher chances of grade

4 neutropenia (absolute neutrophil count \leq 500 cells/ML); 8.2% in chemoradiation group compared to 0% in the radiation alone group⁽⁵⁾. Grade 4 neutropenic patients might be febrile or nonfebrile, in which 50% was assumed to have febrile neutropenia. Approximately, about 5% of febrile neutropenic patients would have sepsis and die⁽¹⁴⁾. Patients in each treatment group would have different chances of tumor recurrence (including tumor progression); 33% in the chemoradiation group compared to 68% in the radiation alone group⁽⁵⁾. According to these clinical data, the probability of each branch was calculated by fold back technique as demonstrated in Fig. 1.

Cost

Since this economic analysis was conducted from the perspective view of the payer of health care, the authors used only direct medical costs as "costs". Costs in this analysis were separated into four major categories: costs for treatment of cervical cancer, which composed of cost for chemotherapy and radiotherapy administration, costs for treatment of major side effects, costs for follow up after complete treatment, and costs for diagnosis of recurrent cervical cancer including supportive care of these recurrent patients.

Charges were used for the costs of chemotherapy, other drugs, and accessories and radiotherapy. Unit cost was used for the cost for laboratory investigations. The authors did not calculate for the capital cost and labor cost because these costs have already been included in the unit cost for in-patient and out-patient services. The unit cost of laboratory investigations, in-patient and out-patient services were based on unit cost analysis of King Chulalongkorn Memorial Hospital⁽¹⁵⁾.

Cost for chemotherapy administration

The chemotherapeutic regimen in this analysis referred to cisplatin 75 mg/m² administered in day 1 followed by 5-fluorouracil (5-FU) 4000 mg infusion in 96 hours. The first cycle of chemotherapy was given within 16 hours of the first radiation fraction. Two additional courses of chemotherapy were scheduled at 3 week intervals. All chemotherapy were given in the hospital, so the patients were required to be admitted for about 5 days for each course. Break down of costs were as follows: (i) chemotherapy (1922.50 Baht/cycle for cisplatin 110 mg and 5FU 4g), (ii) 488.42 Baht/cycle for antiemetics (metoclopramide, dexamethasone, lorazepam, benedryl), and KCl, 50% MgSO₄, 20%

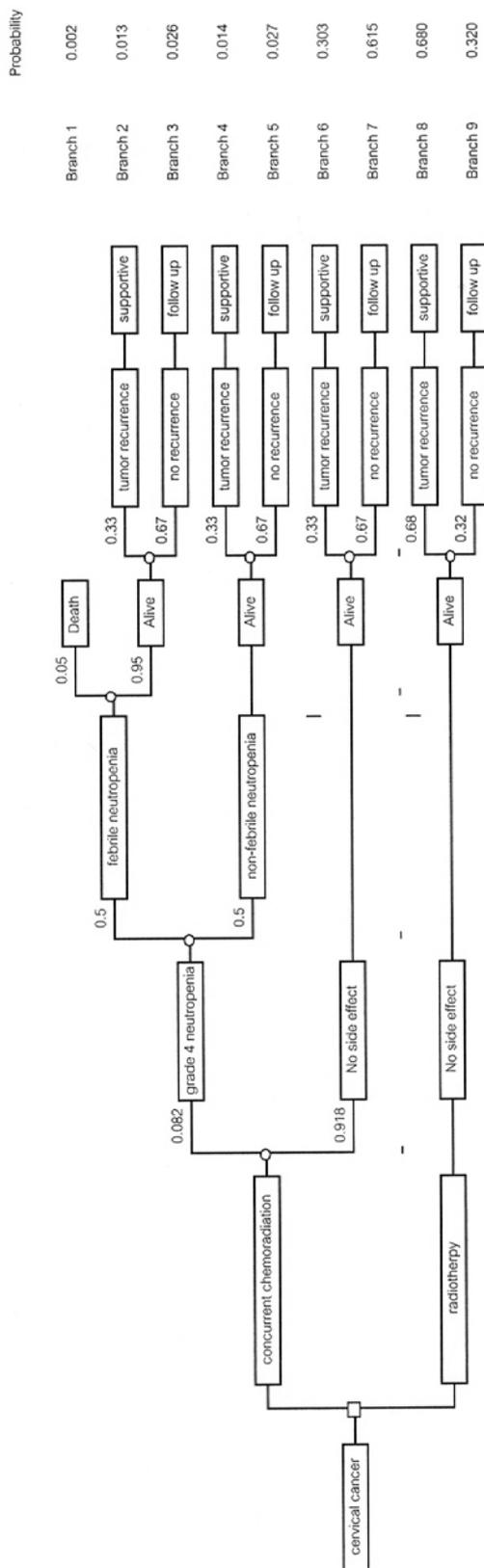


Fig. 1 Decision tree of cervical cancer treatment

Mannitol, IV fluid and IV set. In addition, the unit cost for in-patient service was 4207.35 Baht/day, laboratory investigations before chemotherapy was 181.18 Baht for CBC, renal function and liver function tests. Other supportive drugs were estimated at 200 Baht for each day of in-patient administration. Thus, the overall costs for chemotherapy administration were 24,628.84 Baht/cycle or 73,886.50 Baht for three cycles.

Cost for radiotherapy administration

The prescribed regimen of radiotherapy was identical in both groups of patients. External pelvic radiation was delivered with a fraction of 200 rads, 5 days a week for a total dose of 5,000 cGy. Four high doses intracavitary brachytherapy were given 1 week apart, started at the second week of external radiotherapy. Patients needed to see the physician once a week or about 6 times during radiotherapy.

Total costs of radiotherapy were calculated from the charges of radiotherapy [including X-ray simulator (200 Baht), external radiation (2 Baht/1 cGy), and brachytherapy (3,000 Baht for 1 brachytherapy), unit cost for out-patient service (896.07 Baht/visit), laboratory investigations (96.09 Baht for 3 times of CBC), and other supportive drugs, which were estimated to be 1,000 Baht during the whole course of radiotherapy. The total cost for radiotherapy administration was 28,672.51 Baht.

Cost for treatment of side effects

Costs for adverse events management were calculated from the most common and severe side effect, grade 4 neutropenia, which occurred more commonly in the chemoradiation treatment as compared to radiation treatment. This side effect was divided into febrile and nonfebrile neutropenia. Patients with febrile neutropenia were admitted for about 6 days for investigations and treatment, while nonfebrile patients were observed and treated on an out-patient basis.

Costs from febrile and nonfebrile neutropenia were calculated from the unit cost for in- and out-patient services, laboratory investigations (64.06 Baht in nonfebrile neutropenic patients for 2 times of CBC with platelet count and 1,493.56 Baht in febrile neutropenic patients for CBC with platelet count, renal and liver function tests, chest X-ray, hemoculture and other cultures as indicated), and other supportive drugs and antibiotics, which were approximated to be 100 Baht/visit for out-patient and 1500 Baht/day for in-patient. The overall costs for the management of nonfebrile

and febrile neutropenic patients was 2056.2 Baht and 37,729.80 Baht respectively.

Cost for follow up management during tumor free period

Costs of follow up in the tumor free period was calculated from the unit cost for out-patient services, laboratory investigations (752.44 Baht/year), and other supportive drugs, which were estimated to be 100 Baht for each visit. The costs were calculated for each year according to the number of visits and laboratory investigations. According to the standard surveillance programs, the patients should be examined every 3 months in the first 2 years, every 4 months during the third year, and every 6 months during the fourth and fifth year. After 5 years of uncomplicated follow-ups, the patients were seen annually thereafter. All patients received routine investigations (CBC, renal function and liver function tests) and chest X-ray once a year. Cost without discount rate for the first two years were 4,736.72 Baht/year, for the third year was 3,740.65 Baht/year and for the fourth and fifth year were 2,744.58 Baht/year.

Costs for follow up would be calculated depending on the period of disease free. Patients in the progression branches had 6 months of tumor free in the first year (median time to tumor recurrence or progression was 6 months according to the previous report on the results of treatment in BMA Medical College and Vajira Hospital)⁽¹⁶⁾. The costs were the costs in the first year (4,736.72 Baht) divided by two, which was equal to 2,368.36 Baht. For those branches without tumor recurrence, the costs for five-year follow up was the sum of yearly cost. Costs incurred after the first year of follow up were discounted at an annual rate of 5%. Cost of 5-year follow up in each nonrecurrent patient was 17,269.7 Baht [$4736.7 + (4736.7/1.05) + (3740.6/(1.05)^2) + (2744.6/(1.05)^3) + (2744.6/(1.05)^4)$].

Cost for diagnosis and supportive treatment in patients with tumor progression or recurrence

Costs for management of patients with tumor progression or recurrence were calculated in three categories as follows: costs for diagnosis of recurrence or progression (6,964.85 Baht), costs during supportive care (13,452.46 Baht), and costs of palliative care at terminal stage (55,825.94 Baht). These costs were calculated from the unit cost of out and in-patient services, investigations and supportive drugs.

Generally, patients with a recurrent of tumor

may be treated with either radiotherapy or chemotherapy or even surgery in some cases. However, even with these additional treatments, the prognosis remained quite poor^(17,18). Hence, in the present analysis, all the recurrent cases were assumed to receive only supportive care and were treated on an out-patient basis. They were also assumed to receive supportive care as in-patients during the end of life, for about 10 days. The costs for supportive care was calculated based on the survival time after recurrence. Costs incurred after the first year were discounted at an annual rate of 5%. In the present analysis, based on the authors' previous report⁽¹⁶⁾, the median time to tumor recurrence (including tumor progression) was assumed to be 6 months and the median survival time after recurrence was 14 months⁽¹⁶⁾. From these calculation, the total cost for management recurrent cancer in each patient was 68,435.04 Baht.

Benefit

For the cost effectiveness analysis in the present study, the benefit was measured as months of life survived. The authors assumed that all patients would be treated for about 2 months. The present study evaluated the patients up to 5 years after completion of treatment. Hence, patients in no recurrence branches were calculated as survival for 62 months. For those in recurrent branches, the survival time was calculated as 22 months (based on the treatment period of 2 months, the median time to recurrence of 6 months, and median survival time after recurrence of 14 months)⁽¹⁶⁾.

For the cost utility analysis, the authors had grouped the quality of life into two periods, ie the period during treatment and the period during follow up. The authors weighted the quality of life in these groups by the time trade-off method comparing to the best quality of life by asking the gynecologic oncologist.

The quality of life during treatment was weighted as 0.92 for radiation alone and 0.83, 0.75 and 0.67 for concurrent chemoradiation without serious side effects, with nonfebrile and febrile neutropenia respectively. The quality of life during the follow up period was weighted as 1.00 during the tumor free period and 0.58 during the tumor recurrence period.

Calculation of cost

The costs in each branch of the decision tree were calculated by summing up the costs of cervical cancer treatment (chemoradiation or radiation alone)

together with costs for treatment of neutropenia, costs for follow up and costs for diagnosis and supportive care of recurrent cervical cancer (Table 1).

Cost effectiveness analysis

The costs in each branch were multiplied by the probability of occurrence of each branch (from the decision tree). The survival was also multiplied by the probability of each branch (Table 2). Then the total costs, and total survival in the two treatment groups were summed up. The cost effectiveness ratio was calculated from total cost in each group (chemo-

radiation or radiation group) divided by total life gained in that group.

Cost Utility analysis

The authors calculated the quality adjusted life gain in each branch by multiplying the duration of treatment period, duration of tumor free period, duration of tumor recurrence period with the quality of life in that period. The authors then summed up the quality of life gained in these periods in each branch (Table 3). Thereafter, the authors multiplied the cost in each branch by the probability of each branch. The

Table 1. Cost of treatment in each branch

	Costs for					
	Chemo-therapy	Radio-therapy	Side effect	Follow up	Management of recurrent	Total
Concurrent chemoradiation branches						
Branch 1: FN - death	73886.52	28672.51	37729.80	-	-	140288.83
Branch 2: FN - recurrence	73886.52	28672.51	37729.80	2368.36	68435.04	211092.23
Branch 3: FN - no recurrence	73886.52	28672.51	37729.80	17269.61	-	157558.44
Branch 4: NFN - recurrence	73886.52	28672.51	2056.20	2368.36	68435.04	175418.63
Branch 5: NFN - not recurrence	73886.52	28672.51	2056.20	17269.61	-	121884.84
Branch 6: No side effect-recurrence	73886.52	28672.51	-	2368.36	68435.04	173362.43
Branch 7: No side effect-not recurrence	73886.52	28672.51	-	17269.61	-	119828.64
Radiation only branches						
Branch 8: No side effect-recurrence	-	28672.51	0.00	2368.36	68435.04	99475.91
Branch 9: No side effect-not recurrence	-	28672.51	0.00	17269.61	0.00	45942.12

FN = Febrile neutropenia; NFN = Nonfebrile neutropenia

Table 2. Total cost and survival in each branches

Branch	Probability	Cost	Cost x prob	Survival (months)	Survival x prob
Concurrent chemoRT					
Branch 1: FN - death	0.002	140288.83	287.59	0	0.0
Branch 2: FN - recurrence	0.013	211092.23	2713.27	22	0.3
Branch 3: FN- no recurrence	0.026	157558.44	4111.72	62	1.6
Branch 4: NFN - recurrence	0.014	175418.63	2373.41	22	0.3
Branch 5: NFN - not recurrence	0.027	121884.84	3348.18	62	1.7
Branch 6: No side effect - recurrence	0.303	173362.43	52518.41	22	6.7
Branch 7: No side effect - not recurrence	0.615	119828.64	73701.80	62	38.1
Total in concurrent chemoradiation branches	1		139054.39		48.7
Radiation					
Branch 8: No side effect-recurrence	0.680	299475.91	67643.616	22	15.0
Branch 9: No side effect-not recurrence	0.320	45942.12	14701.48	62	19.8
Total in radiation branches	1		82345.09		34.8

FN = Febrile neutropenia; NFN = Nonfebrile neutropenia

quality adjusted life years gained was also multiplied by the probability of each branch (Table 3). Then the total costs, and total quality life year gained in the two treatment groups were summed up. The cost utility ratio was calculated from total costs in each group divided by quality adjusted life gained in that group.

Results

The cost effectiveness ratio in the concurrent chemoradiation group and radiation only group equaled 2,855 Baht/month survived (13,9054.4 divided by 48.7) and 2,366 Baht/month survived (82,345.1 divided by 34.8) respectively (Table 2). Hence, the cost spent for 1 month-gained was 2,855 Baht from concurrent chemoradiation treatment and 2,366 Baht from radiation treatment. This demonstrated that radiation alone was more cost effective than concurrent chemoradiation.

The cost utility ratio in the concurrent chemoradiation group and radiation only group equaled to 2,996 Baht/month (13,9054.4 divided by 46.4) and 2,687 Baht/month (82,345.1 divided by 30.6) (Table 3) respectively. Hence, the cost used for 1-month of quality lifed gained was 2,996 Baht from concurrent chemoradiation treatment, and 2,687 Baht from radiation treatment. This also indicated that radiation alone was more cost utility than concurrent chemoradiation.

Since the unit cost of out-patient and in-patient services in the present study (King Chula-

longkorn Memorial Hospital) is quite expensive, the authors did the sensitivity analysis varying unit cost. The authors found that if the unit cost of other hospitals is only 0.3 times of King Chulalongkorn Memorial Hospital, the chemoradiation arm would be more cost effective (Fig. 2).

In the present study, all patients were assumed to receive chemotherapy on an in-patient basis. If the patients received chemotherapy on an out-patient basis, the cost effectiveness ratio of concurrent chemoradiation arm would be cheaper since the unit cost of out-patient service is much cheaper than in-patient service. As out-patient chemotherapy, the cost effectiveness ratio of concurrent chemoradiation arm would be 1,835 Baht/month, which was considerably cheaper than 2,366 Baht in the radiation arm. Hence, it seems that concurrent chemoradiation will be more cost effective if chemotherapy is administered on an out-patient basis.

In the present analysis, based on the study of Morris⁽⁵⁾, the recurrent rate in chemoradiation arm was much lower than in the radiation arm (33% vs 68%). Therefore, the authors performed the sensitivity analysis varying recurrent rates in both chemoradiation and radiation arms on the basis that chemotherapy was given as an out-patient (Fig. 3). The authors found that, if the result of concurrent chemoradiation is not good enough and the difference of recurrent rate between chemoradiation and radiation arm is less

Table 3. Calculation of quality adjusted life gained (QALG) in each branch

Branch	Probability	Duration (months)			Quality adjusted life gained (QALG, months)			Total QALG x probability	
		Rx	Fu s dis	Fu c dis	Rx	Fu s dis	Fu c dis		
Concurrent chemoradiation									
Branch 1: FN-death	0.002	2	0	0	1.34	0	0	1.34	0.003
Branch 2: FN-recurrence	0.013	2	6	14	1.34	6	8.12	15.46	0.201
Branch 3: FN- no recurrence	0.026	2	60	0	1.34	60	0	61.34	1.595
Branch 4: NFN-recurrence	0.014	2	6	14	1.5	6	8.12	15.62	0.219
Branch 5: NFN-not recurrence	0.027	2	60	0	1.5	60	0	61.50	1.661
Branch 6: No side effect-recurrence	0.303	2	6	14	1.66	6	8.12	15.78	4.781
Branch 7: No side effect-not recurrence	0.615	2	60	0	1.66	60	0	61.66	37.921
Total in concurrent chemoradiation branches	1								46.380
Radiation alone									
Branch 8: No side effect-recurrence		2	6	14	1.84	6	8.12	15.96	10.853
Branch 9: No side effect-not recurrence		2	60	0	1.84	60	0	61.84	19.789
Total in concurrent radiation branches	1								30.642

FN = Febrile neutropenia; NFN = Nonfebrile neutropenia; Rx = treatment
Fu s dis = follow up without disease; Fu c dis = follow up with disease

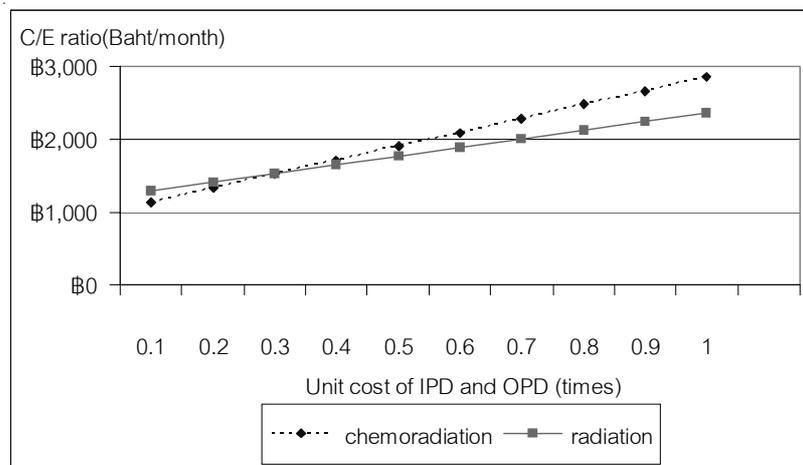


Fig. 2 Sensitivity analysis varying unit cost of in patient and out-patient services

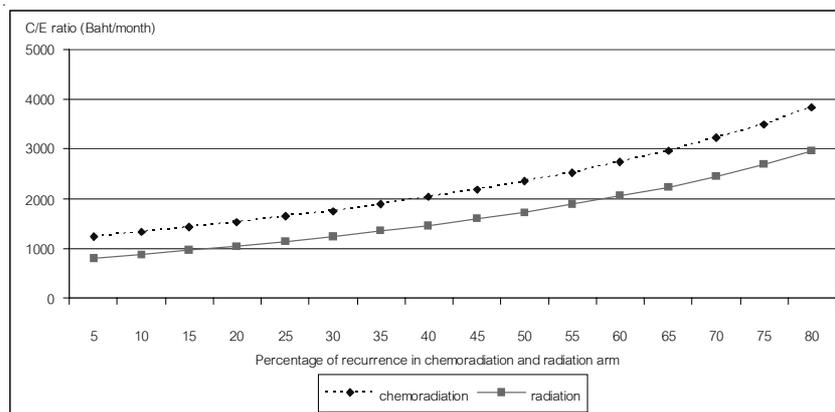


Fig. 3 Sensitivity analysis varying recurrence rate in radiation arm and chemoradiation arm (chemotherapy was given as an out-patient basis)

than 20%, radiation alone will be more cost effective, although the authors administered chemotherapy on an out-patient basis.

Discussion

Concurrent cisplatin based chemoradiation was reported to be more effective than radiation alone in cervical cancer. The systematic review^(12, 13) in this topic demonstrated a highly significant improvement of overall survival at 12% (95% CI= 8-16%); from 40% to 52%. However, the present systematic review also reported that patients receiving concurrent chemoradiation experienced more side effects especially hematologic side effects. To the authors' knowledge, only one article has reported the cost effectiveness of concurrent chemoradiation compared to radiation alone⁽¹⁹⁾. In that study, the authors calculating the

incremental cost per life year gained by calculating the cost for administration of chemotherapy and its side effects, then divided by the incremental survival rate. They concluded that cost per life-year gained from cisplatin-based chemoradiation regimens varied from US \$2,384 to US \$22,770 based on published survival. They ignored the costs for taking care of patients with tumor recurrence or progression.

In the present study, most of the clinical data were based on the study of Morris et al⁽⁵⁾. Morris's study was the randomized controlled trial comparing the concurrent chemoradiation with radiation alone in the treatment of locally advanced cervical cancer (stage Ib with bulky tumor to stage IVa) in 403 patients. The authors chose the clinical data from that study because the chemotherapy used in that study was the same as the one used in our institute, with regards

to the preparation, dose and schedule of administration. However, the median time of follow up in that study was only 43 months, which might not be long enough to detect all recurrences.

In the present study, the authors tried to use unit cost for all costs. However, the actual unit cost of radiotherapy was not available, and charges had to be used instead.

The authors calculated the costs of chemotherapy from the charges of local manufactured cisplatin and 5 fluorouracil, the costs of the original manufactured preparation are much higher than the local ones. Had the original preparations been used, radiotherapy would be even more cost effective. Moreover, in the present study the authors calculated the costs of antiemetics used for chemotherapy induced emesis from our standard antiemetic regimen, which comprised of metoclopramide, dexamethasone, benedryl and lorazepam. If the authors changed the antiemetics to serotonin antagonist (granisetron or ondansetron, or etc.), the costs for concurrent chemotherapy arm will be much higher and radiation will be much more cost effective. However, the quality of life during chemoradiation may be better, which might change the result of cost utility analysis.

Concerning the adverse effect from the treatment, there would be many types of side effects from chemoradiation and radiation, which required subsequent treatment and resulted in additional costs. However, in the present analysis, the authors only focused on the most severe and life-threatening side effects - grade 4 neutropenia. This may, therefore, underestimate the actual cost of treatment for overall side effects. The costs of late side effects were also excluded from the analysis, because they were not common and the authors considered these late side effects to occur equally in both chemoradiation and radiation groups⁽⁵⁾.

This cost effective analysis would be more accurate had the authors calculated the costs and survival of those who had distant or local recurrence separately. However, the authors do not have the clinical data on this issue and the analysis would be too complicated. Hence, total recurrence rate in this analysis was used.

One of the outcomes that affected the cost effectiveness of the treatment was the difference in recurrent rate between treatment groups. From Fig. 3, it can be seen that even when chemotherapy was given on an out-patient basis, the concurrent chemoradiation would be more cost effective only if the

recurrence rate from chemoradiation was lower than radiation for about 20-25%. For example, the cost per month gain was equal at about 1,340 Baht/month if the recurrent rate of chemoradiation was 10% and radiation was 35%, and the cost per month gain would be equal at about 1,886 Baht/month if the recurrent rate of chemoradiation was 35% and radiation was 55%. For the calculation of the present study, the difference of recurrent rate was 35% (68% for radiation and 33% for chemoradiation based on the study of Morris⁽⁵⁾) and the result showed that concurrent chemotherapy was more cost effective if chemotherapy was given on an out-patient basis. However, in some other randomized studies, the difference in recurrence rate between these two treatments was not as high as 20-25%, but ranged from only 10-18%^(6,7,10).

The other outcome that affects the cost effectiveness were the median time to recurrence and survival time after recurrence. Since no data of median time to recurrence and survival after recurrence has been reported from any randomized controlled trial, the authors used the data from our previous report⁽¹⁶⁾. In this model, the authors used the median time to recurrence and median survival time after recurrence equally in both treatment groups at 6 and 14 months⁽¹⁶⁾. Since the prognosis in recurrent cervical cancer is quite poor, it is reasonable to assume that the survival time after recurrence is equal in both treatment groups for recurrent patients. However, regarding the median time to recurrence, if the result of concurrent chemoradiation is better than radiation, the time to recurrence should be longer in the concurrent chemoradiation group. This would result in higher cost effectiveness of concurrent chemoradiation compared to radiation alone.

For cost utility analysis, it also demonstrated that radiation alone is more cost utility than concurrent chemoradiation. However, the weight of quality of life was obtained from the view point of the gynecologic oncologist. The view point of the patients might be different, and would affect the result of cost utility analysis.

The present study covered up to 5 year - follow up, since most recurrences occur within 5 years. Had the follow up period been extended to 10 years, it might turn out that chemoradiation is much more cost effective because life gained in nonrecurrence group might be much longer.

Conclusion

In conclusion, it appeared that radiation alone was more cost effectiveness than chemoradiation in

the treatment of cervical cancer. Nevertheless, if the unit cost of in-patient and out-patient was much cheaper or chemotherapy was administered as an out-patient basis, chemoradiation would be more cost effective. However, if the difference of recurrent rate from the radiation and chemoradiation group was less than 20%, the radiation therapy would be more cost effective even if chemotherapy were given as an out-patient basis.

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References

1. Deerasamee S, Martin N, Sontipong S, Sriamporn S, Sirplung H, Srivatanakul P, et al. Cancer in Thailand. IARC technical report No 34, 1999: 56.
2. Maunsirivithaya S. Gynecologic Oncology Annual Report: BMA Medical College and Vajira Hospital; 2001. Report No 3.
3. Maleemonkol S, Charoeniam V, Isariyodom P, Pantusart A. Risk factors for pelvic node metastasis in cervical cancer patients undergoing radical hysterectomy and pelvic lymphadenectomy. *Chiang Mai Med Bull* 1995; 34: 167-71.
4. Martimbeau P, Kijorstad K, Iversen T. State Ib carcinoma of the cervix, The Norwegian Radium Hospital II. Results when pelvic nodes are involved. *Obstet Gynecol* 1982; 60: 215-8.
5. Morris M, Eifel P, Lu J, Grigsby P, Levenback C, Stevens R, et al. Pelvic radiation with concurrent chemotherapy compared with pelvic and para-aortic radiation for high-risk cervical cancer. *N Engl J Med* 1999; 340: 1137-43.
6. Rose P, Bundy B, Watkin E, Thigpen T, Deppe G, Maiman M, et al. Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. *N Engl J Med* 1999; 340: 1144-53.
7. Keys H, Bundy B, Stehman F, Muderspach L, Chafe W, Suggs C III, et al. Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma. *N Engl J Med* 1999; 340: 1154-61.
8. Pearcey R, Brundage M, Drouin P, Jeffrey J, Johnstom D, Lukka K, et al. Phase III trial comparing radical radiotherapy with and without cisplatin chemotherapy in patients with advanced squamous cell cancer of the cervix. *J Clin Oncol* 2002; 20: 966-72.
9. Whitney C, Sause W, Bundy B, Malfetamo J, Hannigan E, Fowler W, et al. Randomized comparison of fluorouracil plus cisplatin versus hydroxyurea as an adjunct to radiation therapy in stage IB-IVA carcinoma of the cervix with negative para-aortic lymph nodes: A Gynecologic Oncology Group and Southwest Oncology Group Study. *J Clin Oncol* 1999; 17: 1339-48.
10. Peters III W, Liu P, Barrett II R, Stock R, Monk B, Berek J, et al. Concurrent chemotherapy and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early-stage cancer of the cervix. *J Clin Oncol* 2000; 18: 1606-13.
11. Thomas GM. Improved treatment for cervical cancer: concurrent chemotherapy and radiotherapy. *N Engl J Med* 1999; 340: 1198-200.
12. Green J, Kirwan J, Tierney J, Symonds P, Fresco L, Collingwood M, et al. Concomitant chemotherapy and radiation therapy for cancer of the uterine cervix. *The Cochrane Library* 2002(1).
13. Green J, Kirwan J, Tierney J, Symonds P, Fresco L, Collingwood M, et al. Survival and recurrence after concomitant chemotherapy and radiotherapy for cancer of the uterine cervix; a systematic review and meta-analysis. *Lancet* 2001; 358: 781-6.
14. Bodey F. Antibiotics in patients with neutropenia. *Arch Intern Med* 1984; 144: 1845-51.
15. Kamolrattanakul P, Srirattanabal J, Ngarmkieartpisarn S. Unit cost analysis of King Chulalongkorn Memorial Hospital. Research report; King Chulalongkorn Memorial Hospital 2002.
16. Sheanakul C, Manusirivithaya S, Tantiwattana T, Nakwong L. Results of invasive cervical cancer treatment at BMA Medical College and Vajira Hospital. *Vajira Med J* 2003; 46: 93-102.
17. Burke TW, Hoskins WJ, Heller PB, Shen MC, Weiser EB, Park RC. Clinical patterns of tumor recurrence after radical hysterectomy in stage IB cervical carcinoma. *Obstet Gynecol* 1987; 69: 382-5.
18. Alberts DS, Garcia DJ. Salvage chemotherapy in recurrent or refractory squamous cell cancer of the uterine cervix. *Semin Oncol* 1994; 21(4 Suppl 7): 37-46.
19. Rose P, Lappas P. Analysis of the cost effectiveness of concurrent cisplatin-based chemoradiation in cervical cancer: implications from five randomized trials. *Gynecol Oncol* 2000; 78: 3-6.

ความคุ้มค่าของการให้รังสีรักษาร่วมกับเคมีบำบัดเปรียบเทียบกับการให้รังสีรักษาอย่างเดียวในการรักษา มะเร็งปากมดลูก

สุนทรมาลัย มนัสศิริวิทยา, มานิต ศรีประโมทย์, ศิริวรรณ ตั้งจิตกมล, นพวรรณ แสนเจริญสุทธิกุล, ผกาภรณ์ พิศาลธุรกรกิจ

วัตถุประสงค์: เพื่อศึกษาความคุ้มค่าของการรักษามะเร็งปากมดลูกเปรียบเทียบระหว่างการให้รังสีรักษาร่วมกับเคมีบำบัดและการให้รังสีรักษาอย่างเดียว

วัสดุและวิธีการ: แบ่งกลุ่มผู้ป่วยมะเร็งปากมดลูกเป็นกลุ่มที่ได้รับการรักษาด้วยรังสีรักษาร่วมกับเคมีบำบัด และกลุ่มที่ได้รับรังสีรักษาอย่างเดียว แต่ละกลุ่มจะมีโอกาสเกิดภาวะแทรกซ้อน และอัตราการกลับเป็นซ้ำของมะเร็งต่างกัน แยกการคำนวณค่ารักษาออกเป็น 4 กลุ่ม คือ ค่ารักษาโรคมะเร็ง ได้แก่ค่าใช้จ่ายในการให้เคมีบำบัด และรังสีรักษา ค่ารักษาภาวะแทรกซ้อนที่สำคัญ ค่ารักษาเมื่อผู้ป่วยมีการกลับเป็นซ้ำของมะเร็ง และค่ารักษาในการตรวจติดตามผู้ป่วย ทั้งนี้การคำนวณค่าใช้จ่ายในการให้รังสีรักษา และค่ายา รวมทั้งอุปกรณ์ต่าง ๆ จะใช้ค่าใช้จ่ายจริง (charges) ส่วนค่าตรวจทางห้องปฏิบัติการ ค่าการให้บริการผู้ป่วยทั้งผู้ป่วยนอก และผู้ป่วยในใช้ unit cost การมีชีวิตรอดของผู้ป่วยจะคิดเป็นเดือน โดยจะคำนวณเป็นเวลา 5 ปี หลังให้การรักษาครบ

ผลการศึกษา: Cost effectiveness-ratio (CE ratio) ของกลุ่มที่ได้รับเคมีบำบัดร่วมกับรังสีรักษาคิดเป็น 2,855 บาท และ 1,835 บาท ต่อการมีชีวิตรอด 1 เดือน สำหรับการให้เคมีบำบัดแบบผู้ป่วยใน และ ผู้ป่วยนอก ตามลำดับ ส่วนในกลุ่มที่ให้รังสีรักษาอย่างเดียวนั้นมี CE ratio เท่ากับ 2,366 บาท ต่อการมีชีวิตรอด 1 เดือน เมื่อได้ทำ sensitivity analysis พบว่าถ้าอัตราการกลับเป็นซ้ำของมะเร็งในกลุ่มที่ได้เคมีบำบัดร่วมกับรังสีรักษาต่ำกว่ากลุ่มที่ได้รับรังสีรักษาอย่างเดียวไม่ถึงร้อยละ 20 การให้รังสีรักษาอย่างเดียวจะคุ้มค่ากว่า แม้จะให้เคมีบำบัดแบบผู้ป่วยนอก

สรุป: การให้รังสีรักษาอย่างเดียวจะมีความคุ้มค่ากว่าการให้เคมีบำบัดร่วมกับรังสีรักษาในการรักษามะเร็งปากมดลูก และแม้ว่าจะให้เคมีบำบัดแบบผู้ป่วยนอก การให้เคมีบำบัดร่วมกับรังสีรักษาจะคุ้มค่ากว่าก็ต่อเมื่ออัตราการกลับเป็นซ้ำของมะเร็งน้อยกว่ากลุ่มที่ได้รับรังสีรักษาอย่างเดียวเกินกว่าร้อยละ 20
