Concurrent Chemo-Hyperthermia for recurrent cervix cancer after previous CCRT

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Concurrent Chemo-Hyperthermia for recurrent cervix cancer after previous CCRT

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Introduction

Survival in patients with recurrent cervical cancer after irradiation remains very poor. Chemotherapy combined with hyperthermia has been shown to improve the response rate. This study was performed to evaluate the effect of electro-modulated hyperthermia combined with conventional chemotherapy vs. chemotherapy alone on recurrent cervical cancer previously treated with irradiation.

Methods

Twenty patients were treated with chemotherapy alone, and 18 were treated with chemotherapy combined with electro-modulated hyperthermia. One patient was treated with chemo-radiotherapy as a primary treatment and then relapsed; the tumor was inoperable and radio-refractory after recurrence. Nearby metastases were included, such as metastasis of the para-aortic lymph nodes (PANs) and adjacent pelvic lymph nodes (PLNs), but distant metastases were excluded. Electro-modulated hyperthermia was performed three times per week beginning at chemotherapy initiation; patients underwent a total of 36 sessions.

Results

The overall response (CR+PR+SD/PD) to treatment was significantly greater in the group of patients who underwent chemotherapy combined with electro-modulated hyperthermia ($p=0.0461$), and at the evaluation conducted at the last follow-up examination, the reaction results were significantly greater in this group ($p=0.0218$). Additionally, severe complications were not reported.

Conclusion

In this study, for patients with recurring cervical cancer previously treated with irradiation, the overall response rate for patients treated with chemotherapy combined with electro-modulated hyperthermia was significantly greater than that for the group of patients who were treated with chemotherapy alone.

Keywords: concurrent chemo-modulated electro-hyperthermia, chemotherapy alone, recurrent cervix cancer, treatment outcome

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Introduction

Survival in patients with recurrent cervix cancer in previously irradiation remains very poor. Chemotherapy combined hyperthermia has been shown to improve response rate, occasionally.

This study is devoted to evaluate the effect of electro-modulated hyperthermia with conventional chemotherapies on recurrent cervical cancer previously irradiation; analyzing of chemotherapy alone vs chemotherapy combined electro-modulated hyperthermia.

Materials and Methods

Materials

Inclusion Indications

1. para-aortic lymph node alone or pelvic lymph node and or cervix bed recurrent.
2. No distance metastasis (exclude PAN).
3. Not possible radiotherapy
   - because previous RT field recurrent.
4. above 6 months follow up periods

Materials and Methods

Materials

Chemotherapy alone (n=20)

Chemotherapy combined hyperthermia (n=18)

Age(year)	CTx	CTx + HT
Range	36~71	36~71
Mean	53	50.8

FIGO stage	CTx	CTx + HT
Ib	2	3
IIa	3	3
IIb	3	3
IIIa	5	2
IIIb	4	4
IVb	3	3

Materials and Methods

Materials

Pathology	CTx	CTx+HT
Squamous cell carcinoma	15	15
adenocarcinoma	5	3

Materials and Methods

Materials

Recurrent lesions

Recurrent lesions	CTx	CTx + HT
Cervix bed alone	4	6
PAN alone	4	4
Iliac LN alone	4	5
Iliac LN+cervix bed	8	3

Materials and Methods

Materials

Chemotherapy agents

Agent	CTx		CTx+HT	
	1st	2nd	1st	2nd
Cisplatin	12	0	11	2
Cisplatin+5-FU	1	6	1	6
Cisplatin+adriamycin	3	0	3	0
Cisplatin+paclitaxel	4	8	0	6
Cisplatin+paclitaxel	0	6	0	4

Materials and Methods

Materials

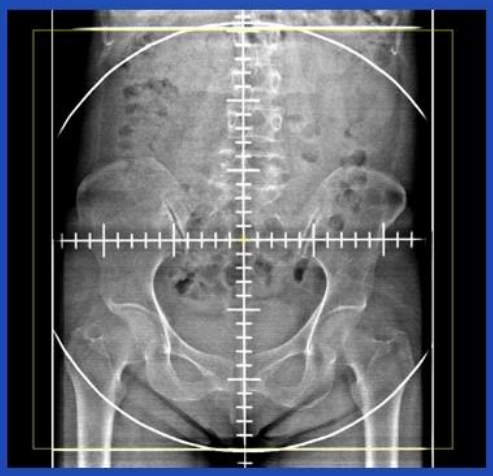
Chemotherapy cycles

Chemotherapy cycles	CTx		CTx+HT	
	1st	2nd	1st	2nd
3	0	0	0	1
4	0	3	0	3
5	1	4	1	3
6	15	11	14	10
7	0	1	0	0
9	4	1	3	1

Materials and Methods

Methods (Hyperthermia)

1.All patients performed 2-dimensional simulation.->Treatment field encompassed the mass over 3 cm margin from X, Y, Z dimension.



Materials and Methods

Methods (Hyperthermia)

2.The hyperthermia was performed for 60 min.

3.The hyperthermia was performed three times a week, starting at the same time as chemotherapy and performed 36 sessions.

Materials and Methods

Methods (Hyperthermia)

4. The power output was 80 W for the first 10 min, 120 W over the next 10 min and 150 W for the remaining treatment time.

5.The body and skin temperature, blood pressure, and pulse rate of each subject were measured before, during and after the experiment.

Materials and Methods

Methods (Hyperthermia)

6. Body temperature was measured using an infrared ear thermometer (Infrared Thermometer IRT 4020, Braun, Germany), and temperature of the abdominal skin surface below the circular upper electrode probe was measured using a non-contact infrared thermometer transmitter (Thermo Checker DT-060, Easytem, Republic of Korea).

Materials and Methods

Statistics

The time to event variable was estimated using Kaplan-Meier analysis.

P-values less than 0.05 were considered significant.

Statistical analysis was conducted using SAS software (version 9.3, SAS Institute Inc., Cary, NC, USA).

Results

Response Rate

Follow up periods

Periods (month)	CTx	CTx+HT
Range	7~21	7~28
Mean	11	13.5

The overall response rate (CR+PR+SD/PD) to treatment

	Complete remission	Partial response	Stable disease	Progressive disease	P-value
chemotherapy alone (n=20)	4	3	1	12	0.0461
chemotherapy combined hyperthermia (n=18)	9	2	2	5	

Results

Response Rate

The last follow up response rate (CR+PR+SD/PD) to treatment

	Complete remission	Partial response	Stable disease	Progressive disease	P-value
chemotherapy alone (n=20)	3	3	1	13	0.0218
chemotherapy combined hyperthermia (n=18)	9	2	2	5	

Results

Chemotherapy alone

only to recur when the cervix bed is therapeutic response was statistically significant (p=0.0456)

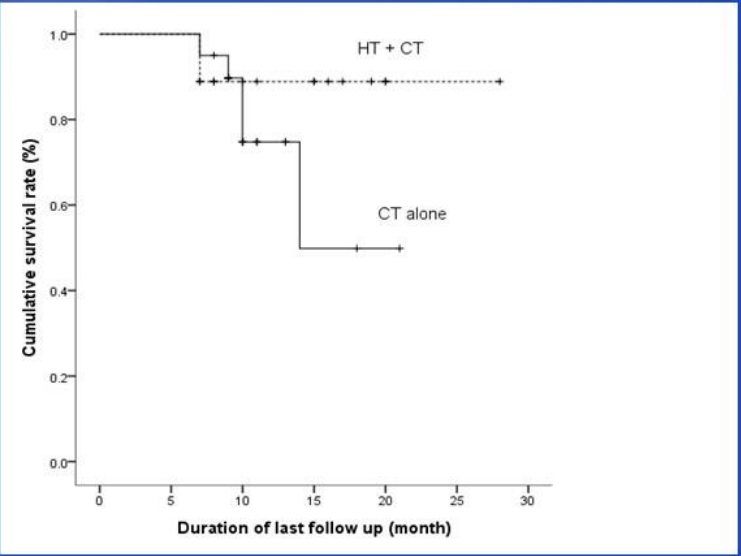
Chemotherapy combined hyperthermia

not observed any significant differences in abdominal lymph nodes and cervix bed recurrence (0.6199)

Results

Overall survival Kaplan-Meier plot

Chemotherapy combined hyperthermia was not significantly increased overall survival (p=0.235).



Results

Body temperature

before : 36.4~36.9°C (mean 36.5 °C)

after : 36.9~38.2 °C (mean 37.6 °C)

Abdominal skin temperature

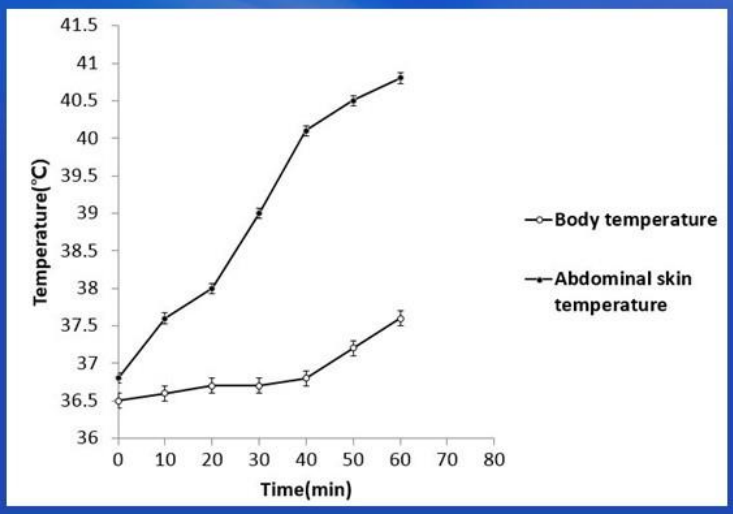
before: 36.4~37.3 °C (mean 36.8 °C)

after: 39.8 ~41.9 °C (mean 40.8 °C)

Results

Body temperature

Abdominal skin temperature



Results

Pathological characteristics

chemotherapeutic regimens, cycles, dosages age

There were no statistically significant difference at treatment response.

Results

Complications

Chemotherapy alone : nausea, vomiting, pancytopenia, and peripheral neuropathy

Chemotherapy combined hyperthermia : hot-sensation and abdominal discomfort at 8/18 (44%) patients, no other side effects (burn or blisters) were observed

Conclusion

In this study, the overall response rate (CR+PR+SD/PD) to treatment was significantly greater in the group of patients who underwent chemotherapy combined with electro-modulated hyperthermia ($p = 0.0461$).

For the evaluation conducted at the last follow-up examination, the results were significantly greater in the group who underwent chemotherapy combined with electro-modulated hyperthermia ($p = 0.0218$).

Conclusion

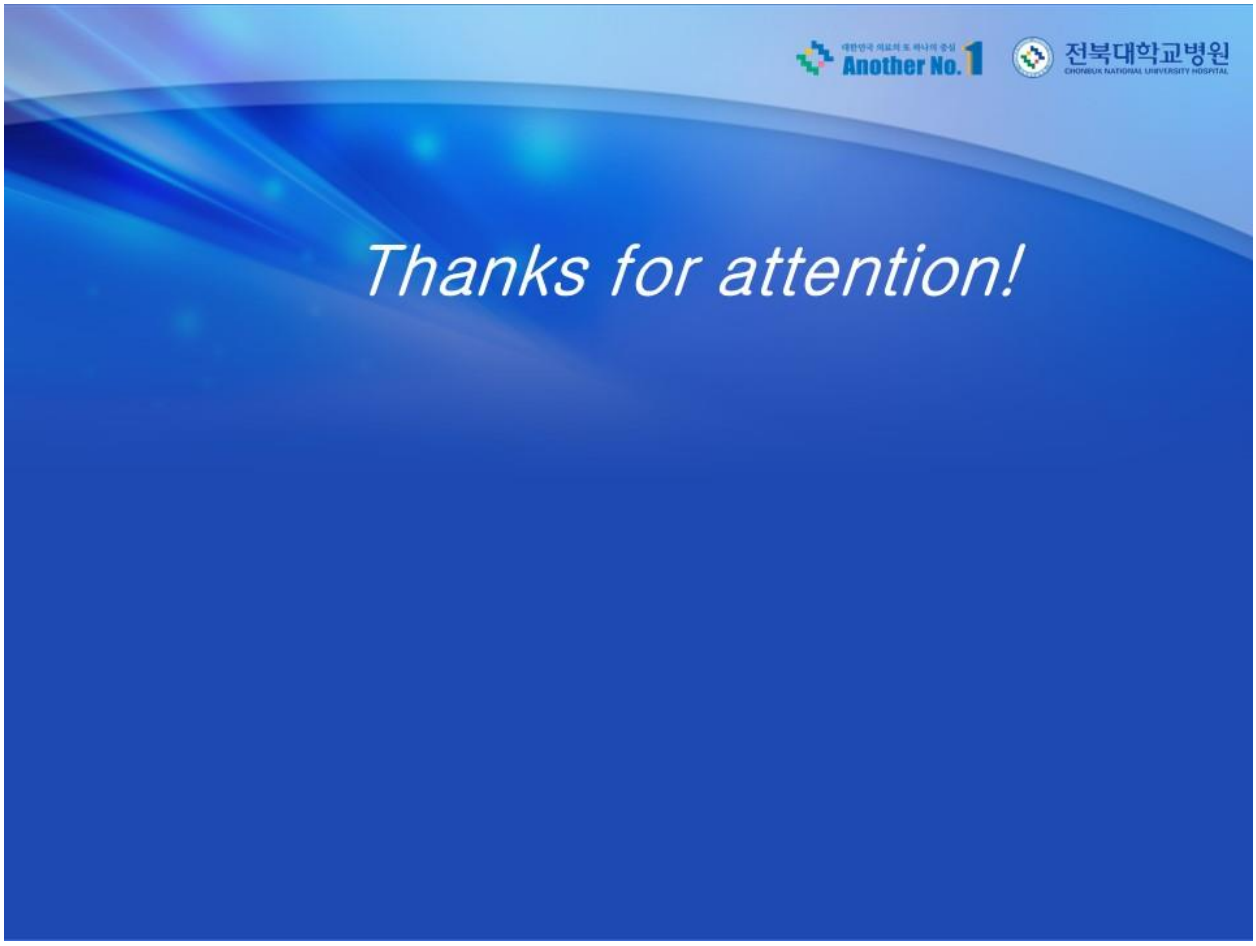
Specifically, in the case of chemotherapy alone, significant recurrence was observed only when the cervix was the target of the therapeutic response ($p = 0.0456$), but in the chemotherapy combined with electro-modulated hyperthermia group, no significant differences in abdominal lymph node and cervical recurrence were observed ($p = 0.6199$).

Hyperthermia may be slightly more effective for the treatment of abdominal lymph node metastasis.

Conclusion

This study clearly demonstrates the feasibility and advantages of chemotherapy combined with hyperthermia, concurrent with the application of platinum derivatives, for recurrent cervical cancer patients who specifically have regional lymph node metastasis.

Additionally, longer-term follow-up is needed to compare the disease-free survival rates of patients.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Thanks for attention!