

- :
* , † , ‡ , §
* , † , ‡ , §
* , † , ‡ , §

_____ :
_____ : 1999 6 2002 4 T3 T4 가 ,
가 40
- 37 가
1.8 Gy 5 45 Gy UFT Leucovorin
(LV)(12), 5 - fluorouracil (FU) LV (10), 5 - FU (10 , 5)
4 ~ 6 35
_____ : (92.5%, 37/40).
가 2 35 , 22 (62.9%)
가 , 2 (5.7%) 33 30
, 1 2
45.5% (15/33), 78.8% (26/33)
Grade 3 ~ 4 가 4 (10.8%)
12.1%(4/33), 21.6% (8/37) , 3
87%
_____ :
,

가
5
가 5 ~ 15%,
가 10 2 2000 50% ,²⁻⁶⁾
4,500 II 20 ~ 30%, III 20 ~ 50%
2/3 ,¹⁾ 30% ,⁷⁻¹¹⁾
가 가 ,

*
2003 3 5 2003 5 28

1950 가

Sandwich 가 40

CT 40

3 (7.5%) , 1

가 , 1 가

1

1.8 Gy 5 , 25

45 Gy 32

38 35 35

(94.6%) - 3 ,

가 가 가

(5.4%) - 2

가

3 가

가

가 2 cm 3 cm

¹³⁾

12 (32.4%) UFT (Uracil+Tegafur)

LV (Leucovorin) , 10 (27.0%)

5 - FU (5 - fluorouracil) LV (bolus infusion) , 가 15 (40.5%) 5 - FU 10

1 5 3

(500 mg/m²) , 5

(continuous infusion)

RTOG/EORTC ¹⁴⁾

1999 6 2002 4 4 CT

CEA 가 4 6
 가 4
 CT
 X -
 CEA
 Table 1
 가 27 , 가 10 ,
 30 70 53 ,
 ECOG 1 36
 2 cm 15 cm 4 cm ,
 5 cm (89.2%, 33/37).
 2/3 (64.9%,
 24/37). CEA 1/3 CEA
 가 (33.3%, 11/33).
 25% 가 10 ,
 25 ~ 50% 15 , 12 50%
 . Thomas Jefferson III 9
 (24.3%), IV가 8 (21.6%) , 2002 AJCC ¹²⁾
 T T3가 25 (67.6%), T4가 12 (32.4%)
 , 가 23 (62.2%)
 , 3 37
 12
 40
 1 ,
 (92.5%, 37/40).
 4 CT
 3/4 가
 (73.0%, 27/37). 24
 CEA
 CEA
 CEA 가 7

CEA 가 , 5 CEA 가
 Table 1. Patient and Tumor Characteristics

Characteristics	No. of pts
Age	
Range (median)	30 ~ 70 (53) years
Gender	
Male	27
Female	10
ECOG performance status	
1	36
2	1
Tumor distance from anal verge	
Range (median)	2 ~ 15 (4) cm
3 cm	9
3 ~ 4 cm	10
4 ~ 5 cm	14
> 5 cm	4
Circumference of tumor by digital rectal examination	
25%	10
25 ~ 50%	15
> 50%	12
Histologic type	
Adenocarcinoma	33
Well differentiated	4
Moderately differentiated	24
Poorly differentiated	3
Unknown	2
Mucinous ca.	4
Serum CEA level	
Normal (0 ~ 7 ng/ml)	22
High	11
Not checked	4
Thomas Jefferson Clinical Stage	
I (mobile, movement in all direction)	14
II (partially fixed: tethered, movable in one direction)	6
III (fixed, deep ulceration, obstructed, circumferential)	9
IV (advanced fixation, unresectable, invasion of pelvic sidewall and/or sacrum)	8
Clinical T stage	
T3	25
T4	12
Clinical N stage	
N+	23
N-	14
Clinical AJCC stage (6th Edition)	
II	14
III	23

CEA 가 17 13
 CEA 가 , 4
 CEA 가

가 , 3
 가 , 1 가 .
 CEA 가 가
 CT
 가 . 37
 2 (5.4%)
 가
 , 2 CT
 가
 35
 12 (34.3%) 가 , -
 11 (31.4%), Hartmann 9
 (25.7%), 1 (2.9%) ,
 2 (5.7%)
 가 가
 33
 가 30 (90.9%),
 가 1 (3.0%) ,
 2 (6.1%)
 . 가 30
 4 (13.3%)
 , T4 .
 78.8% (26/33) (Table 2).
 cT3 21 3 pT2 , cT4 12
 6 pT3 , T
 T4가 36.3% 18.2% , T3
 63.7% 72.7% 가
 가 19 11
 가
 63.3%
 33.3% , 2002 AJCC
 45.5% (15/33) (Table 3).
 35
 5 cm 가 32 , 32
 가
 20 62.5% (20/32) .
 20
 가 16 , 4

Table 2. Resectability after Preoperative Concurrent Radio-chemotherapy for Rectal Cancer (n=33)

Resection	No. of pts
Complete resection	26 (78.8%)
Incomplete resection	7 (21.2%)
+Resection margin	4
Distal	1
Radial	3
Gross residual	1
Open & Closure	2

Table 3. Impact of Preoperative Concurrent Radio-chemotherapy on Down-staging by Comparisons of Initial and Postsurgical AJCC Stages (6th Edition)

A) T stage

Initial Stage	Post-surgical stage			
	pT2	pT3	pT4	Total
cT3	3	18	-	21 (64%)
cT4	-	6	6	12 (36%)
Total	3 (9%)	24 (73%)	6 (18%)	33 (100%)

B) N stage

Initial stage	Post-surgical stage		
	pN (+)	pN (-)	Total
cN (+)	8	11	19 (63%)
cN (-)	2	9	11 (37%)
Total	10 (33%)	20 (67%)	30 (100%)

C) AJCC stage

Initial stage	Post-surgical stage					
	I	IIA	IIB	IIIA	IIIB	Total
I	1	5	-	-	1	7
IIA	-	2	1	-	1	4
IIB	1	9	1	1	7	19
Total	2	16	2	1	9	30

가
 11 , Hartmann 4
 가
 가 1
 4 3

(radial) , 1 (distal)

Table 4. Acute Toxicities during Preoperative Concurrent Radio - chemotherapy

Organ/Tissue	RTOG/EORTC grade				
	0	1	2	3	4
Upper gastrointestinal	27	5	5	-	-
Lower gastrointestinal	12	20	5	-	-
Genitourinary	33	4	-	-	-
Body weight	26	11	-	-	-
Skin	0	34	3	-	-
Hematologic					
White blood cell	22	12	2	1	-
Absolute neutrophil count	26	6	1	2	2
Platelet	37	-	-	-	-
Hemoglobin	31	5	1	-	-

Pahlman ¹⁶⁾

가
(12% vs. 21%; p=0.02),

가

¹⁷⁻¹⁹⁾

가

²⁰⁻²²⁾

50%

가

5%

40 ~ 86%

1/4 ~ 1/2

가

가

²³⁻²⁷⁾

40

4

.RTOG/EORTC

1

가

1

Grade 3

4 (10.8%)

38

1

(Table 4). Grade 3

2

5 - FU LV

, Grade 4

92.5%

2

1

5 - FU

LV

, 1

Grade 3

11%

²⁸⁻³⁰⁾

5 - FU

. Grade 3

4

5 - FU

5 - FU LV

10

3

Grade 3

LV

가 3

, 5 - FU LV

10

3 (30%)

Grade 3

33

4 (12.1%)

(pre - sacral)가 3

MSKCC³⁰⁾

28%

intergroup 0114

37

8 (21.6%)

^{31,32)}

5 - FU LV

가

5 - FU

가

1

4

, 3

87%

5 - FU

LV

가

^{27,33-36)}

Grade 3

0%

15%

5 - FU

²⁸⁾

LV

가

가

sandwich

가

, Camma

86 ~ 100%

¹⁵⁾

Meta - analysis

가

(Table 5, 6). ^{27-30,33-36)}

가
가

Table 5. Comparison of Results after Preoperative Concurrent Radio-chemotherapy for Locally Advanced Rectal Cancer

	Grann ('01) ³⁰	Sanfilippo ('01) ²⁸	Janjan ('99) ²⁹	Shin (Current study)
Total no. enrolled	72 (uT3)	45 (cT4)	117 (uT3: 96%)	40 (cT3: 68%, cT4: 34%)
RT dose (Gy)	46.8+3.6	45	45	45
Chemotherapy	IV, 5 - FU+LV	PVI, 5 - FU	PVI, 5 - FU	3 type*
Resectability	68/68 (100%)	32 [†] /32 (100%)	117/117 (100%)	33/37 (89%)
Pathologic CR	13%	6%	27%	0% (near CR 6%)
Down staging	56%	56%	62%	45%
Sph. preservation	31/35 (89%)	11/32 (34%)	29/69 (42%)	20/32 (63%)
Toxicity (Gr 3)	28%	9%	NA	11%
Local failure	2% (3 yr)	20% [‡] (4 yr)	13% [§] (3 yr)	13%
Distant failure	21% (3 yr)	44% [‡] (4 yr)	27% [§] (3 yr)	19%
Overall survival	95% (3 yr)	69% [‡] (4 yr)	97% [§] (3 yr)	87% (3 yr)

Grann ('01) at Memorial Sloan - Kettering Cancer Center, Sanfilippo ('01) and Janjan ('99) at MD Anderson Cancer Center, and Shin at Smaung Medical Center. *: oral UFT+LV (12 pts), IV 5FU+LV (10 pts), IV 5FU (bolus 10, continuous infusion 5 pts), †: multivisceral resection (21), pelvic exenteration (11), ‡: for resected cases, §: for uT3 lesions

Table 6. Comparison of Results after Preoperative Concurrent Radio-chemotherapy for Rectal Cancer in Korea

	Kim ('95) ²⁷	Cho ('00) ³³	Kang ('02) ³⁴	Seong ('01) ³⁵	Kim ('02) ³⁶
Total no. enrolled	27 (B2)	37 (cT3-4)	15 (cT2-3)	23 (cT3: 67%)	45 (cT3: 89%)
RT dose (Gy)	45+5.4	45	45+5.4	45	45+5.4
Chemotherapy	5 - FU+LV	5 - FU+LV	5 - FU+LV	oral 5 - FU* +LV	Capecitabine+LV
Resectability	NA	29/31 (94%)	15/15 (100%)	18/21 (86%) [†]	38/40 (95%) [†]
Pathologic CR	11%	6%	7%	10%	31%
Down staging	NA	68%	73%	71%	84%
Sph. Preservation	NA	NA	15/15 (100%) [‡]	8/13 (62%)	13/18 (72%)
Toxicity (Gr 3)	4%	15%	0%	10%	7%
Local failure	NA	18% (3 yr)	13%	NA	NA
Distant failure	NA	NA	7%	NA	NA
Overall survival	NA	NA	NA	NA	NA

Kim ('95) and Kim ('02) at Chungnam National University Hospital, Cho ('00) and Seong ('02) at Yonsei Medical Center, and Kang ('02) at Catholic Medical Center. *: Doxifluridine, †: Complete resection rate, ‡: Laparoscopic sphincter preserving surgery

Heriot³⁷⁾

가 T 4 가 , N
4 ~ 83% 가 T 67 ~ 93%, N 62 ~ 88% 가 가 T ,
가 T 가 , T2 20% . CT MRI T4 가
T3 가
79%
T4 가 T4 MDACC
T4²⁸⁾

15 : -

4 4 (p=0.001)

2 가

44 Table 5 6 34 ~ 100%

6 ~ 31% 56 ~ 84% MDACC²⁹⁾

(Table 5, 6). MDACC²⁹⁾

T3 5 - FU (> 40),

45 Gy 27% (3 cm), (< 6 cm), , T

가 62% (< T4),

가 6% 45% 63% 가

가 , T4 가

, T4 MDACC²⁸⁾

6% , Mohiuddin³⁸⁾

55 Gy 44% (8/18) 50 Gy 2 ~ 20%

13% (2/15) 7 ~ 44% 가

가 5 ^{28 ~ 30,33)} 13% 19%

Mayo/NCCTG³⁹⁾ 12

5 - FU 3 , 5 - FU

가 (47% vs. 37%, 가

p=0.01), 가 (60% vs. 70%, 가

p=0.005) . Mohiuddin³⁸⁾ 가

(55Gy) 5 - FU 가

67% (8/12) 가

0% (0/6) ^{25,26)} 가

Berger⁴⁰⁾ 가 가 가

(p=0.04). 가 가

11% (4/37) 가 가

65% (24/37) 가

. Berger⁴⁰⁾ 가 2 ^{35,36)}가

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system. *Dis Colon Rectum* 2002;45:1051 - 1056

Abstract

**Preoperative Concurrent Radio - chemotherapy for Rectal Cancer:
Report of Early Results**

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Purpose: To report the early results of preoperative concurrent radio - chemotherapy (CRCT) for treating rectal cancer.

Materials and Methods: From June 1999 to April 2002, 40 rectal cancer patients who either had lesions with a questionable resectability or were candidates for sphincter - sacrificing surgery received preoperative CRCT. Thirty - seven patients completed the planned CRCT course. 45 Gy by 1.8 Gy daily fraction over 5 weeks was delivered to the whole pelvis in the prone position. The chemotherapy regimens were oral UFT plus oral leucovorin (LV) in 12 patients, intravenous bolus 5 - FU plus LV in 10 patients, and intravenous 5 - FU alone in 15 patients (bolus infusion in 10, continuous infusion in 5). Surgery was planned in 4 ~ 6 weeks of the completion of the preoperative CRCT course, and surgery was attempted in 35 patients.

Results: The compliance to the current preoperative CRCT protocol was excellent, where 92.5% (37/40) completed the planned treatment. Among 35 patients, in whom surgery was attempted after excluding two patients with new metastatic lesions in the liver and the lung, sphincter - preservation was achieved in 22 patients (62.9%), while resection was abandoned during laparotomy in two patients (5.7%). Gross complete resection was performed in 30 patients, gross incomplete resection was performed in one patient, and no detailed information on the extent of surgery was available in two patients. Based on the surgical and pathological findings, the down - staging rate was 45.5% (15/33), and the complete resection rate with the negative resection margin 78.8% (26/33). During the CRCT course, grade 3 ~ 4 neutropenia developed in four patients (10.8%). Local recurrence after surgical resection developed in 12.1% (4/33), and distant metastases after the preoperative CRCT start developed in 21.6% (8/37). The overall 3 - years survival rate was 87%.

Conclusion: Preoperative CRCT in locally advanced rectal cancer is well tolerated and can lead to high resection rate, down - staging rate, sphincter preservation rate, however, longer term follow - up will be necessary to confirm these results.

Key Words: Rectal cancer, Preoperative treatment, Concurrent radio - chemotherapy