



Concurrent versus Sequential Administration of CMF Chemotherapy and Radiotherapy after Breast Conserving Surgery in Early Breast Cancer: A Retrospective Comparative Study



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Background

- Breast conservative therapy achieves comparable local control and overall survival with mastectomy, and is a standard treatment in most cases of early breast cancer.
- Some investigators have made efforts to find out a subset of patients capable of omitting radiotherapy (RT) in the breast conservative therapy, rather they have shown the necessity of RT. Since patients with risk factors of distant metastases receive chemotherapy as well as RT, the integration of local and systemic treatment may cause conflicts in the multidisciplinary approach.
- On the optimal sequencing of chemotherapy and RT, most of the studies compared two different types of sequential chemoradiotherapy (SCRT), that is, chemotherapy first group and RT first group.
- As a third option, concurrent chemoradiotherapy (CCRT) in the adjuvant setting after breast conserving surgery has been evaluated in several single-arm studies. Among various chemotherapeutic agents tested, CMF regimen has been shown to be feasible even in full dosage.
- In this study, we performed a retrospective comparative analysis on the outcome of CCRT versus SCRT after breast conserving surgery for early breast cancer.

Methods and Materials

Eligibility

- Accrual Period: February 1992 – January 2002
- Newly diagnosed patients with stage I/II breast cancer who underwent CMF chemotherapy and radiotherapy after breast conserving surgery
- Number of patients: 156 women
- Median duration of follow-up: 89 months (range; 13-153)

Treatment Scheme of Chemoradiotherapy

- RT with concomitant CMF #2 + CMF #4 (n=88) → CCRT
 CMF #3 + RT + CMF #3 (n=26) → SCRT
 CMF #6 + RT (n=42) → SCRT
- CMF: cyclophosphamide (100 mg/m² orally on D1-14 or 600 mg/m² i.v. on D1, D8) methotrexate (40 mg/m² i.v. on D1, D8) fluorouracil (500-600 mg/m² i.v. on D1, D8)
- RT: 50.4 Gy/28 fx to whole breast + 10 Gy/5 fx to tumor bed

Patient Characteristics

Variables	No. of patients		p value
	CCRT	SCRT	
Age			
<40 yr	38 (43.2%)	20 (29.4%)	0.0776
≥40 yr	50 (56.8%)	48 (70.6%)	
T stage			
T1	43 (48.9%)	49 (72.1%)	0.0035
T2	45 (51.1%)	19 (27.9%)	
Resection margin			
Negative	79 (89.8%)	66 (97.1%)	0.2795
Close/Positive	5 (5.7%)	1 (1.5%)	
Unknown	4 (4.5%)	1 (1.5%)	
N stage			
N0	51 (58.0%)	49 (72.1%)	0.0686
N1	37 (42.0%)	19 (27.9%)	
Estrogen receptor [*]			
Positive	35 (52.2%)	23 (47.9%)	0.6476
Negative	32 (47.8%)	25 (52.1%)	
Histologic grade [†]			
1	5 (6.9%)	7 (12.7%)	0.1837
2	25 (34.7%)	26 (47.3%)	
3	32 (44.4%)	15 (27.3%)	
Non-ductal carcinoma	10 (13.9%)	7 (12.7%)	
Hormonal therapy			
Yes	19 (21.6%)	20 (29.4%)	0.2633
No	69 (78.4%)	48 (70.6%)	

^{*}In 41 patients, the estrogen receptor status was not available.
[†]In 29 patients, the histologic grade was not available.

Results

Delivery of CMF Chemotherapy according to Treatment Sequence

Cycles of chemotherapy	No. of patients		p value
	CCRT	SCRT	
6	84 (95.5%)	63 (92.6%)	0.5045
≤5	4 (4.5%)	5 (7.4%)	
5	2	2	
4	1	0	
≤3	1	3	

Univariate Analysis for Overall and Local-regional Relapse-free Survival

Variables	5-yr OS	p value	5-yr LRRFS	p value
Age				
<40 yr	89.6%	0.4269	96.6%	0.4417
≥40 yr	93.8%		95.8%	
T stage				
T1	93.4%	0.9187	94.4%	0.8072
T2	90.6%		98.4%	
Resection margin				
Negative	93.7%	0.0419	96.5%	0.3025
Close/Positive	66.7%		83.3%	
Unknown	80.0%		100.0%	
N stage				
N0	92.0%	0.8121	95.9%	0.9751
N1	92.9%		96.4%	
Estrogen receptor				
Positive	98.3%	0.0259	98.1%	0.6116
Negative	85.8%		94.7%	
Histologic grade				
1	100.0%	0.0547	100.0%	0.2207
2	96.1%		97.8%	
3	85.1%		91.5%	
Non-ductal carcinoma	100.0%		100.0%	
Hormonal therapy				
Yes	97.4%	0.3177	100.0%	0.4419
No	90.5%		94.7%	
Treatment sequence				
CCRT	92.1%	0.9768	97.7%	0.1688
SCRT	92.5%		93.8%	

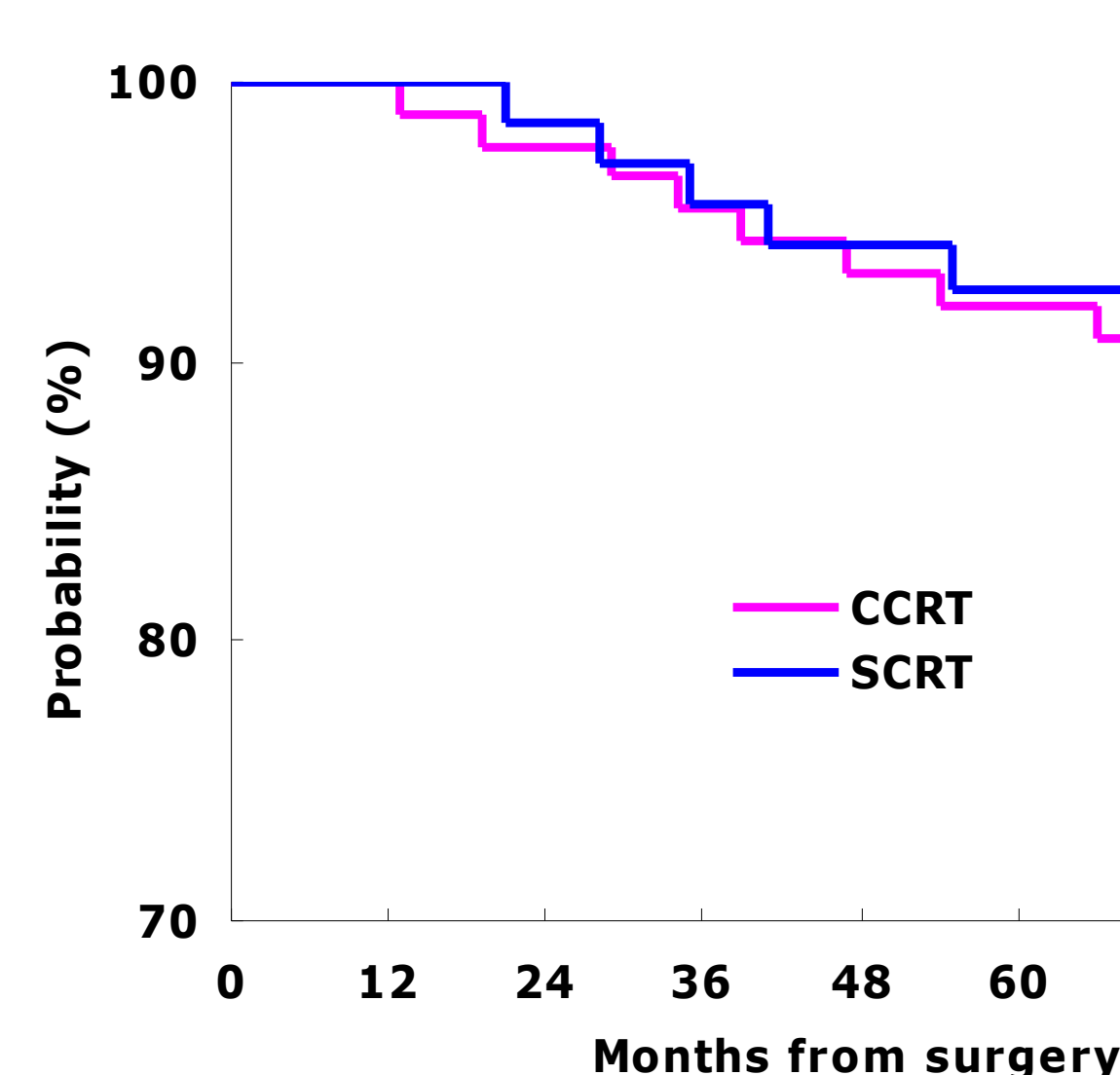
Abbreviations: OS=overall survival; LRRFS=local-regional relapse-free survival.

Multivariate Analysis for Overall and Local-regional Relapse-free Survival

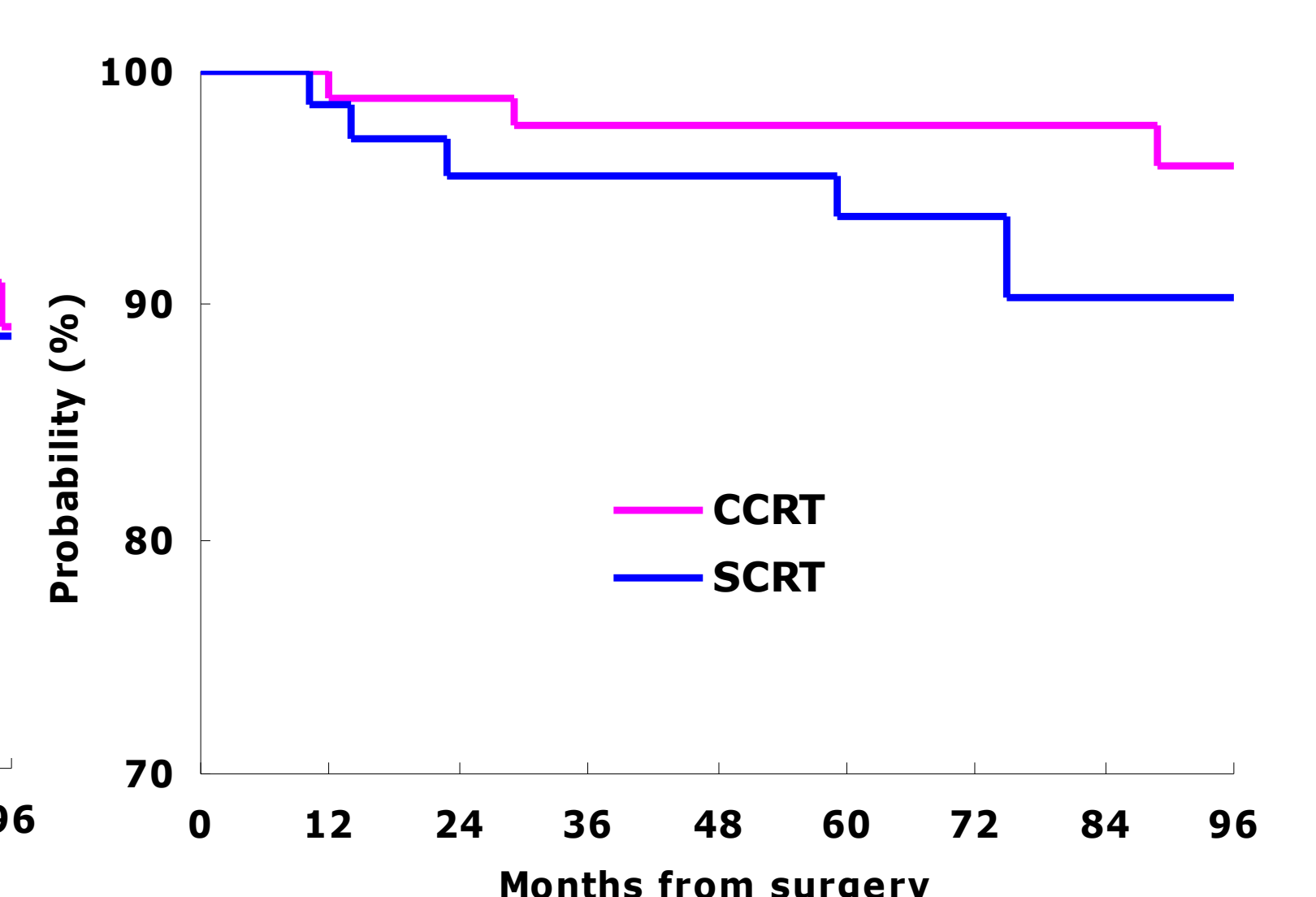
Variables	p value	
	OS	LRRFS
Age	0.2661	0.1905
TNM stage	0.3289	0.9235
Resection margin	0.4775	0.2949
Estrogen receptor	0.0604	0.5782
Hormonal therapy	0.5900	0.9953
Treatment sequence	0.3505	0.0463

Abbreviations: OS=overall survival; LRRFS=local-regional relapse-free survival.

Overall Survival



Local-regional Relapse-free Survival



Cosmetic Outcome according to Treatment Sequence

Cosmesis score [*]	CCRT	SCRT	p value
Excellent	10.5%	15.1%	0.5526
Good	60.5%	60.4%	
Fair	26.3%	18.9%	
Poor	2.6%	5.7%	

^{*}From Danoff et al. Int J Radiat Oncol Biol Phys 1983;9:1625-1630.

Late Toxicity according to Treatment Sequence

Toxicity	No. of patients	
	CCRT	SCRT
Skin fibrosis, Grade 2	2	0
Lymphedema, Grade 2	1	0
Radiation pneumonitis, Grade 3	0	1
Rib fracture	1	0

Conclusion

Concurrent administration of CMF chemotherapy and radiotherapy is a safe and effective regimen as an adjuvant treatment after breast conserving surgery for early breast cancer, and may enhance local-regional control for patients with high risk factors of local-regional recurrence.