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# Bladder preservation after radiochemotherapy for muscle invasive bladder cancer

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*To determine efficacy of radio-chemo-therapy (RCT) with platin-derivatives compared to radiotherapy (RT) alone in patients with bladder cancer. From May '82 to May '96, 333 patients with bladder cancer were treated at the University Hospital of Erlangen. 282 of them, who presented with muscle-invasive or high risk T1 (e.g. G3/4, R1/2, N+) bladder cancer, were treated either by radiotherapy (RT) or concomitant radiochemotherapy with platinum derivatives (RCT-Cis or RCT-Carbo) after preceding transurethral resection of bladder (TUR), with curative intent. Median doses of 50.4 Gy and 41.4 Gy in fractions of 1.8 Gy (once a day, 5 times per week) were applied to the bladder and pelvic lymphnodes. 54 patients recieved 45 Gy to the paraaortal lymphnodes. 128 patients received irradiation alone, while 205 patients received it simultaneously with either cisplatin or carboplatin in the 1st and 5th treatment weeks. Uni- and multivariate analyses were performed in order to assess the impact of age, sex, grading, T-category, R-status, and treatment modality on patients' survival and bladder preservation. Complete remissions were noted in 57%, 70% and 85% of patients after RT, RCT-Carbo or RCT-Cis, respectively ($p<0.05$). The strongest impact on CR was exerted by R-status ($p<0.0003$) and T-category ($p<0.0001$). 79% of survivors have a functional bladder. Concerning survival, RT, and RCT differed significantly only after univariate analysis. For survival with preserved bladder, only initial R-status was significant in multivariate analysis ($p<0.04$). Bladder cancer can be effectively treated by RT/RCT following TURB.*

*Key words:* bladder neoplasms-radiotherapy-chemotherapy; treatment outcome.

## Introduction

Until now, radical cystectomy has been the standard treatment for muscle-invasive bladder cancer. This procedure involves removal of the bladder, uterus, upper vagina and adnexa in women, or the bladder, prostate and seminal vesicles in men. Though perioperative mortality seems to be low, an artificial bladder can never replace the original organ in view of its functionality. For this reasons, we tried to establish a method which would avoid primary cystectomy and result in bladder conservation.

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## Patients and methods

From May '82 to May '96, 333 patients suffering from bladder cancer were treated either by radiotherapy (RT) alone or by concomitant radiochemotherapy (RCT) after preceding TUR-bladder (TURB). For a detailed description of our treatment schedule see Dunst *et al.* 1994.[1] Only patients with muscle invasive bladder cancer or high-risk T1 bladder cancer were analyzed. Patients with a total dose of less than 40 Gy and histology other than urothelial carcinoma (e.g. squamous cell carcinoma) were excluded from the analysis. So 282 patients were eligible for evaluation.

In conventional fractions median doses of 51.4 Gy (40.0 - 69.4 Gy) and 45.0 Gy (40 - 59.4) were applied to the bladder and pelvic lymphnodes, respectively (10 MV photons, 4-field-box); 54 patients received 45 Gy to paraaortal lymphnodes. After TURB

98 patients received irradiation alone and 184 patients simultaneously with either cisplatin (RCT-CIS, 115 patients) or carboplatin (RCT-CARBO, 69 patients) in the first and fifth treatment weeks. 64/92 patients received more than 200 mg/m² cisplatin, 40/69 patients more than 535 mg/m² carboplatin, which was more than 80% of the dose prescribed. Within 8 weeks after RT/RCT a second TURB was performed. In the case of a persistent tumor or invasive relapse cystectomy was recommended.

## Results

Initial complete remission rates (CR) were 57%, 70% and 85% after RT, RCT-Carbo or RCT-Cis. This difference was significant in multivariate analysis. The strongest impact was exerted by R-status and pT-category (Table 1).

Five-year-survival rates were 88%, 58% and 24% for R0, R1 and R2-status, respectively. This difference was significant again ($p<0.001$). In univariate analysis a significant advantage for those patients who had been treated by RCT could be shown ($p<0.05$). After five years, 47%, 69% and 57% of patients survived after RT alone or RCT-Cis and RCT-Carbo, respectively.

## Discussion

Recently, Jung and Jakse reported on five year survival rates of 56-75% for T2, 26-78% for T3a and 11-29% for pT3b tumors.[2] For our population the corresponding rates are 55%, 50% and 41%. Considering the T2 and T3a category, our data are within the same range, while for T3b and T4 tumors they are even better. A 79% rate of preserved bladder needs no further comment. The strongest prognostic factor for all endpoints was R-status after initial TURB. This emphasizes the importance of as radical as possible TURB before the start of RCT. Though chemotherapy seemed to have a positive influence on survival in univariate analysis its impact on survival was not significant in multivariate analysis due to worse prognosis of patients who did not receive chemotherapy. Nevertheless, the advantage for those patients who received chemotherapy has been proven with respect to initial response. Therefore we recommend RCT to be performed instead of RT alone if the patient's general condition allows this procedure.

**Table 1.** Univariate and multivariate analysis of factors related to complete response after transurethral resection and survival

| | CR after 1st TURB | | Survival | |
|---|---|---|---|---|
| | univ. p | multiv. p | univ. p | multiv. p |
| Age | <0.01 | n.s. | 0.001 | 0.005 |
| pT-category | <0.0001 | <0.0001 | 0.005 | 0.033 |
| Grading | 0.03 | n.s. | n.s. | – |
| R-Status | <0.0001 | 0.0003 | <0.001 | 0.002 |
| RT vs. RCT-Cis | 0.0002 | 0.003 | 0.04 | n.s. |
| RCT-Cis vs. RCT-Carbo | 0.025 | 0.02 | 0.045 | n.s. |

R = resection; RT = radiotherapy; RCT = radio-chemotherapy; Cis = Cisplatin; Carbo = Carboplatin; CR = complete response; TURB = transurethral resection of bladder

## Conclusion

Organ sparing treatment of bladder cancer is effective. Survival is as good as after radical cystectomy, but 80% of survivors have a functional bladder. The strongest impact on response and survival was exerted by R-status after the first TURB. Consequently, R0 resection is recommended before starting RT/RCT. Major prognostic factors for initial response are age, R-status and pT-category. Concurrent cisplatin (carboplatin) improves the CR rate by 1/3. Cisplatin is superior to carboplatin with respect to CR rate and survival.

## References

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