Effect of Total Mesorectal Excision on the Outcome of Rectal Cancer after Standardized Postoperative Radiochemotherapy

Do Randomized Studies Translate into Clinical Routine?

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Purpose: To compare local control, disease-free survival and overall survival after postoperative radiochemotherapy with or without total mesorectal excision (TME) in a retrospective analysis.

Patients and Methods: Between 1993 and 2002, 103 patients with UICC stage II and III rectal cancer were treated by surgery and postoperative chemoradiation. Group B (n = 50; 1993–1998) were operated before TME era without using TME and group A (n = 53; 1998–2002) with TME; both groups received identical radiochemotherapy to a total dose of 50.4 Gy (median) and two courses of continuous 5-fluorouracil infusion.

Results: Patients in group A (TME) showed a significant improvement in 5-year disease-free survival (71.1%; 46.8%) and freedom from distant metastases (76.3%; 46.9%) and a marked improvement of local control (85.2%; 62.5%). Acute and late toxicity were significantly less frequent in group A.

Conclusion: Radiochemotherapy cannot compensate an insufficient surgical procedure. These data confirm that TME is the standard. High outcome quality can be achieved in daily practice compared to results of randomized studies without patient selection.

Key Words: Rectal cancer · Radiochemotherapy · Total mesorectal excision

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Effekt der totalen mesorektalen Exzision auf die Therapieergebnisse beim Rektumkarzinom nach standardisierter postoperativer Radiochemotherapie. Können die Ergebnisse randomisierter Studien im klinischen Alltag reproduziert werden?

Ziel: In einer retrospektiven Analyse werden die lokale Kontrollrate, das krankheitsfreie Überleben und das Gesamtüberleben nach postoperativer simultaner Radiochemotherapie mit oder ohne totale mesorektale Exzision (TME) verglichen.


Ergebnisse: Die Patienten der Gruppe A (TME) zeigten eine signifikante Verbesserung des krankheitsfreien 5-Jahres-Überlebens (71,1%; 46,8%) und des metastasenfreien Überlebens (76,3%; 46,9%) sowie einen Trend zu einer verbesserten lokalen Kontrollrate (85,2%; 62,5%). Akut- und Spätnebenwirkungen traten in Gruppe A signifikant seltener auf als in Gruppe B.

Schlussfolgerung: Die Radiochemotherapy kann eine insuffiziente Operationstechnik nicht kompensieren. Standard ist die TME. Im Vergleich zu Ergebnissen randomisierter Studien lässt sich eine hohe Behandlungsqualität auch in der klinischen Routine ohne studientypische Patientenselektion erreichen.

Schlüsselwörter: Rektumkarzinom · Radiochemotherapy · Totale mesorektale Exzision

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Introduction
International randomized studies in the 1980s and 1990s have shown significant improvements of long-term survival and decreased recurrence rates after concurrent radiochemotherapy following radical surgery of rectal cancer UICC stage II and III [5, 7, 18, 27, 29]. In these studies, local recurrence rates of 11–16%, freedom from distant metastases of 67–74% and survival rates of 50–64% were reported. Surgery alone, postoperative radiotherapy or chemotherapy alone did not produce satisfactory results [20]. In 1994, the consensus meeting of the German Cancer Society recommended adjuvant concurrent radiochemotherapy of rectal cancer UICC stage II and III [16, 21]. After the introduction and establishment of total mesorectal excision (TME) as the standard surgical technique for rectal cancer, local recurrence rates < 10% were reported [1, 2, 4, 9, 13, 15].

The aim of this retrospective study was to analyze whether the results of prospective trials can be achieved in daily practice of a regional therapy center without “selection criteria” or prospective monitoring. This retrospective analysis evaluated the results of postoperative treatment of rectal cancer in a Northern Bavarian institution and should prove the reproducibility of treatment quality compared to international standard.

Patients and Methods
Between 04/1993 and 03/2002, 103 patients with rectal cancer UICC stage II and III were registered. All patients were treated in the surgical department of the same institution in curative intention and received postoperative radiochemotherapy in the radiotherapeutic department. All patients were staged according to the UICC-TNM classification of 1997, with 53 patients in group A (TME) and 50 patients in group B (non-TME; Table 1).

Surgery
TME has been used since 1998 in our surgical department; therefore, the patient collective was divided into two groups. Group A consisted of 53 patients who were operated using the TME technique from 1998 to 2002. Group B comprised 50 patients who underwent surgical treatment without TME from 1993 to 1998. A total of 62.5% of patients had low anterior resection (LAR), 32.8% abdominoperineal resection (APR), and 3.1% a Hartmann procedure.

Radiotherapy
Patients were irradiated in prone position on a belly board with 1.8 Gy per fraction, five fractions per week to a total dose of 45 Gy. In a second series, the tumor bed was boosted to a total dose of 50.4 Gy (median; range 11–70 Gy). From 1993 to 2001, two-dimensional, and since 2001, three-dimensional radiation treatment planning was applied with a linear accelerator, using three- or four-field beam arrangements.

Chemotherapy
5-fluorouracil (5-FU) was applied concurrently to radiotherapy as continuous infusion for 120 h during weeks 1 and 5 (d1–5; d29–34) at a dose of 1,000 mg/m²/d with four courses of additional 5-FU chemotherapy subsequently.

Follow-Up
Median follow-up of the patients was 1,269 days. Data were evaluated from radiotherapeutic department charts, regional cancer register, general practitioners, and institutions. Survival data were updated using governmental registers. The starting point of time event analyses was the date of surgery. Events were diagnosed radiologically and confirmed pathologically. The Common Toxicity Criteria (CTC) were used to classify therapy-related acute side effects and the RTOG/EORTC LENT-SOMA criteria for classification of chronic side effects.

Statistical Analysis
For statistical analysis of local control, freedom from distant metastases, disease-free and overall survival, the Kaplan-Meier method was used. Statistical significance was calculated by the log-rank test. Categorical variables were analyzed using Fisher’s