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Personalized Radiotherapeutic Approaches for Elderly Patients with Epidural Cord Compression from Gastric Cancer

DIRK RADES[1], STEVEN E. SCHILD[2], AMIRA BAJROVIC[3], STEFAN JANSSEN[1,4] and TOBIAS BARTSCHT[5]

Departments of Radiation [1]Oncology, and [5]Hematology and Medical Oncology, University of Lübeck, Lübeck, Germany;
[2]Department of Radiation Oncology, Mayo Clinic, Scottsdale, AZ, U.S.A.;
[3]Department of Radiation Oncology, University Medical Center Eppendorf, Hamburg, Germany;
[4]Medical Practice for Radiotherapy and Radiation Oncology, Hannover, Germany

Abstract. *Aim: To facilitate personalization of radiotherapy (RT) for elderly patients with epidural cord compression (ECC) from gastric cancer. Patients and Methods: Several factors were analyzed for survival in 20 elderly patients including age, gender, time period from gastric cancer diagnosis to ECC, metastatic spread, additional osseous lesions, vertebral bodies afflicted by ECC, ambulatory function, dynamic of motor dysfunction, performance status and RT fractionation. Results: Four factors had a significant influence on survival: metastatic spread ($p<0.001$), ambulatory function ($p=0.001$), dynamics of motor dysfunction ($p=0.002$) and performance status ($p=0.003$). Points were assigned according to factors present for each patient. To avoid confounding variables, performance status was not incorporated into the scoring system. Based on 3-month survival rates, patients were divided into four groups according to the total score: 6, 12-13, 19 and 26 points. Three-month survival rates for these groups were 0%, 50%, 75% and 100%, respectively ($p<0.001$). Conclusion: This score is of great assistance when assigning the appropriate RT approach to an elderly patient with ECC from gastric cancer.*

In adult patients with epidural cord compression (ECC), gastric cancer accounts for approximately 2% of all primaries (1). About 50% of these patients are elderly patients, meaning age 65 years or more according to the definition of the World Health Organization (2). Because elderly patients are different from younger and middle-aged patients, they deserve specific consideration in the field of oncology (3, 4). Elderly patients generally have a lower metabolic rate, a different distribution of fat tissue, a less competent immune system and are more likely to suffer from chronic diseases. Anticancer treatment must take into account a patient's age and the fact that many elderly patients are not capable of tolerating aggressive therapies. In general, elderly patients require personalized treatment approaches to a greater extent than younger ones. Such approaches can be much more easily realized with the application of prognostic indices. Due to the differences between elderly and younger patients with cancer, such indices should be separately designed for each age group. Furthermore, separate indices should be available for single tumor entities that differ considerably regarding outcomes and prognoses. In order to achieve optimal personalized care of elderly patients with ECC from gastric cancer, the major goal of this study was the development of a prognostic index customized specifically for the specific patient group.

Correspondence to: Professor Dirk Rades, MD, Department of Radiation Oncology, University of Lübeck, Ratzeburger Allee 160, 23538 Lübeck, Germany. Tel: +49 4515006661, Fax: +49 4515003324, e-mail: rades.dirk@gmx.net

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Patients and Methods

Twenty patients conventionally irradiated for ECC from gastric cancer were included. All patients were 65 years of age or older and, according to the World Health Organization defined as "elderly". The primary end-point was survival. Several factors were analyzed for this end-point including age at radiotherapy (RT) (≤72 *versus* ≥73 years, median=72.5 years), gender, time from gastric cancer diagnosis to ECC (≤15 *versus* >15 months, median=15 months), metastatic spread to organs other than bone at RT (no *versus* yes), additional osseous lesions at RT (no *versus* yes), number of vertebral bodies afflicted by ECC (1 or 2 *versus* 3 or more), ambulatory function at RT (not able *versus* able to walk), dynamics of motor dysfunction (≤14 *versus* >14 days, median=14 days), performance status [more favorable: Eastern Cooperative Oncology Group (ECOG) score 1, 2 *versus* 3, 4], and type of RT (1×8 Gy/5×4 Gy *versus* 10×3 Gy/15×2.5 Gy/20×2 Gy).

Table I. *Survival analyses (Kaplan-Meier method plus log-rank test).*

	Survival rate (%)		
	At 3 months	At 6 months	*p*-Value
Age at RT			
≤72 Years (n=10)	60	30	
≥73 Years (n=10)	30	20	0.51
Gender			
Female (n=10)	40	30	
Male (n=10)	50	20	0.89
Time from gastric cancer diagnosis to ECC			
≤15 Months (n=11)	45	18	
>15 Months (n=9)	44	33	0.70
Metastatic spread to organs other than bone at RT			
No (n=4)	100	100	
Yes (n=16)	31	6	<0.001
Additional osseous lesions at RT			
No (n=7)	43	29	
Yes (n=13)	46	23	0.60
Number of vertebral bodies afflicted by ECC			
1 or 2 (n=8)	38	25	
3 or more (n=12)	50	25	0.92
Ambulatory function at RT			
Able to walk (n=10)	10	0	
Not able to walk (n=10)	80	50	0.001
Dynamic of motor dysfunction			
≤14 Days (n=11)	18	0	
>14 Days (n=9)	78	56	0.002
Performance status			
ECOG 1-2 (n=7)	86	57	
ECOG 3-4 (n=13)	23	8	0.003
Type of radiotherapy			
1×8 Gy/5×4 Gy (n=5)	40	20	
10×3 Gy/15×2.5 Gy/20×2 Gy (n=15)	47	27	0.86

RT: Radiotherapy, ECC: epidural cord compression, ECOG: Eastern Cooperative Oncology Group.

The survival analyses were carried-out with the Kaplan–Meier method supplemented by the log-rank test. The factors that achieved a significant association with survival after Bonferroni adjustment for multiple tests ($p<0.005$ corresponds to an alpha-error of 5%) were incorporated in the scoring system.

Points for significant factors were derived by dividing the 3-month survival rates by 10. A patient's score was calculated by adding up their points for all factors.

Results

Four out of the 10 investigated factors had a significant influence on survival: metastatic spread to organs other than bone at RT ($p<0.001$), ambulatory function at RT ($p=0.001$), dynamics of motor dysfunction ($p=0.002$) and performance status ($p=0.003$). The complete survival analysis is shown in Table I. In order to avoid redundancy and confounding variables, the performance status was not incorporated into the scoring system. Performance status and ambulatory function are very similar. Patients who are able to walk generally have an ECOG score of 1 or 2 and those unable to walk an ECOG score of 3 or 4.

Table II. *Scoring as obtained from the survival rates at 3 months.*

	Survival rate at 3 months (%)	Points
Metastatic spread to organs other than bone at RT		
No (n=4)	100	10
Yes (n=16)	31	3
Ambulatory function at RT		
Able to walk (n=10)	10	1
Not able to walk (n=10)	80	8
Dynamics of motor dysfunction		
≤14 Days (n=11)	18	2
>14 Days (n=9)	78	8

RT: Radiotherapy.

The 3-month survival rates and the related points are summarized in Table II. The addition of the points resulted in possible total patient scores of 6, 12, 13, 19 or 26 points. The 3-month survival rates related to these points were 0%, 50%, 50%, 75% and 100%, respectively. Taking into account these 3-month rates, the patients were divided into four groups: 6 points, 12-13 points, 19 points and 26 points. The 3-month survival rates of these groups were 0%, 50%, 75% and 100%, respectively ($p<0.001$), and the 6-month rates were 0%, 0%, 25% and 100%, respectively ($p<0.001$).

Discussion

Outcomes of patients with metastatic gastric cancer are generally poor, despite the introduction of novel targeted therapies (5-8). Another option for improving the treatment results for these patients is personalization of the treatment approach. For appropriately tailoring of the treatment approach to patients with metastatic gastric cancer, it is mandatory to have an idea of the patient's expected survival duration. These times can be predicted with the aid of independent predictive factors and prognostic scoring systems that are available for several tumor types (9). In patients with gastric cancer, Ohi *et al*. identified tumor morphology and histopathology plus a pre-clinical marker and the lymphocyte count as clinical factors independently predictive of peritoneal metastasis (10). In another study of patients with gastric cancer, the nuclear expression of a chemokine receptor was associated with a worse prognosis (11).

In the current study, we aimed to identify predictors of survival in elderly patients with ECC from gastric cancer. According to the results, metastatic spread to organs other than bone at RT, ambulatory function at RT, dynamics of motor dysfunction and performance status showed a significant association with the patient's remaining life time. The negative outcomes in patients with widely spread metastatic disease and a poor performance status appear quite obvious. Furthermore, a poor performance status has a strong correlation with inability to walk, which explains the prognostic significance of the ambulatory function at RT. In the present study, the dynamics of motor dysfunction was also a significant predictor of survival. A faster development of dysfunction was associated with a worse survival. This can be explained by the fact that a faster development of motor weakness reflects a more aggressive tumor and more rapidly growing metastases, which likely translates into a worse survival prognosis (12, 13).

Three out of the four significant predictors were included in the scoring system. The performance status was not included to avoid redundant information and confounding variables due to the correlation with ambulatory function. Based on the 3-month rates, four groups were created: 6 points, 12-13 points, 19 points and 26 points. Out of the patients with 6 points, none survived for 3 months following RT. Therefore, these patients appear best treated with a single fraction of RT such as 1×8 Gy or 1×10 Gy, since these programs are similarly effective with respect to pain relief and functional outcomes compared to multifraction programs. In selected patients of the 6-points group, best supportive care alone may also be appropriate (14, 15). In the group with 12-13 points, half of the patients survived for 3 months but none for 6 months. Therefore, to avoid unnecessarily long overall treatment times, these patients should receive single-fraction RT or short-course multifraction RT such as 4×5 Gy in 4 days or 5×4 Gy and 5×5 Gy in a week. Out of the patients with 19 points, 75% survived for 3 months and 25% for 6 months. Since at 6 months following RT, local control of EEC becomes more important, these patients appear to be good candidates for 10×3 Gy in 2 weeks, which leads to less in-field recurrence of EEC (16, 17). Patients with 26 points had the most favorable survival; all patients of this group survived longer than 6 months. According to a matched-pair study of 382 patients with EEC from different primary tumor types and favorable survival prognoses, 15×2.5 Gy in 3 weeks and 20×2 Gy in 4 weeks were superior to 10x3 Gy with respect to local control of EEC, progression-free and overall survival (18). The 2-year rates were 92% *versus* 71% (p=0.012), 90% *versus* 68% (p=0.013) and 68% *versus* 53% (p=0.032), respectively. Therefore, patients with 26 points should be treated with 15×2.5 Gy or 20×2 Gy. Highly selected patients achieving 19 or 26 points may also be candidates for upfront decompressive surgery, which should be discussed with neurosurgeons or orthopedic surgeons prior to delivery of the first RT fraction (19).

In conclusion, in the present study, it was possible to identify four different survival groups of elderly patients with EEC from gastric cancer. The fractionation program of RT ranging from single-fraction RT to multi-fraction RT with overall treatment times of a few weeks must be adapted to the patient's remaining life span to ensure optimal personalization of this treatment.

Conflicts of Interest

On behalf of all Authors, the corresponding Author states that there is no conflict of interest related to this study.

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