Dose Escalation of Radiotherapy for Metastatic Spinal Cord Compression (MSCC) in Patients with Relatively Favorable Survival Prognosis

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Background and Purpose: Local control of metastatic spinal cord compression (MSCC) is particularly important for long-term survivors. Radiotherapy alone is the most common treatment for MSCC. The most frequently used schedule world wide is 30 Gy/10 fractions. This study investigated whether patients with favorable survival prognoses benefit from a dose escalation beyond 30 Gy.
Patients and Methods: Data from 191 patients treated with 30 Gy/10 fractions were matched to 191 patients (1:1) receiving higher doses (37.5 Gy/15 fractions or 40 Gy/20 fractions). All patients had favorable survival prognoses based on a validated scoring system and were matched for age, gender, tumor type, performance status, number of involved vertebrae, visceral or other bone metastases, interval from tumor diagnosis to radiotherapy, ambulatory status, and time developing motor deficits. Both groups were compared for local control, progression-free survival, overall survival, and functional outcome.
Results: Local control rates at 2 years were 71 % after 30 Gy and 92 % after higher doses (p = 0.012). Two-year progression-free survival rates were 68 % and 90 %, respectively (p = 0.013). Two-year overall survival rates were 53 % and 68 %, respectively (p = 0.032). Results maintained significance in the multivariate analyses (Cox proportional hazards model; stratified model) with respect to local control (p = 0.011; p = 0.012), progression-free survival (p = 0.010; p = 0.018), and overall survival (p = 0.014; p = 0.015). Functional outcome was similar in both groups. Motor function improved in 40 % of patients after 30 Gy and 41 % after higher doses (p = 0.98).
Conclusion: Escalation of the radiation dose beyond 30 Gy resulted in significantly better local control, progression-free survival, and overall survival in patients with favorable survival prognoses.

Key Words: Metastatic spinal cord compression · Survival prognosis · Radiotherapy · Dose escalation

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Dosiseskalation bei der Strahlentherapie metastatisch bedingter Rückenmarkkompression (MSCC) bei Patienten mit vergleichsweise guter Überlebensprognose

Hintergrund: Die lokale Kontrolle der metastatisch bedingten Rückenmarkkompression (MSCC) ist von besonderer Bedeutung für Patienten mit vergleichsweise guter Überlebensprognose. Die alleinige Strahlentherapie ist die häufigste Behandlungsform der MSCC; das am meisten verwendete Fraktionierungsschema ist 30 Gy/10 Fraktionen. Diese Studie untersuchte, ob Patienten mit vergleichsweise guter Überlebensprognose von einer Dosiseskalation über 30 Gy hinaus profitieren.
Patienten und Methoden: 191 Patienten, die 30 Gy/10 Fraktionen erhielten, wurden mit 191 Patienten, die höhere Dosen (37,5 Gy/15 Fraktionen oder 40 Gy/20 Fraktionen) erhielten, verglichen (Matched-Pair-Analyse). Alle Patienten hatten nach einem validierten Score eine vergleichsweise gute Überlebensprognose. Die Paarbildung erfolgte unter Berücksichtigung folgender Faktoren: Alter, Geschlecht, Art des Primärtumors, Allgemeinzustand, Anzahl betroffener Wirbelkörper, viszerale Metastasen, weitere Knochenmetastasen, Intervall von der Erstdiagnose der Tumorerkrankung bis zur Bestrahlung, Gehfähigkeit, Entwicklungszeit motorischer Defizite. Beide Grupen wurden hinsichtlich lokaler Kontrolle, progressionsfreiem Überleben, Gesamtüberleben und motorischer Funktion verglichen.
Ergebnisse: Die Raten für die lokale Kontrolle nach 2 Jahren betrugen 71 % nach 30 Gy und 92 % nach höheren Dosen (p = 0,012). Die Raten für das progressionsfreie Überleben waren 68 % und 90 % (p = 0,013), die Raten für das Gesamtüberleben 53 % und 68 % (p = 0,032). Die Ergebnisse blieben in den Multivarianzanalysen (Cox proportional hazards model; stratified model) signifikant

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für die lokale Kontrolle (p = 0,011; p = 0,012), das progressionsfreie Überleben (p = 0,010; p = 0,018) und das Gesamtüberleben (p = 0,014; p = 0,015). Eine Verbesserung der motorischen Funktion war bei 40 % der Patienten nach 30 Gy und bei 41 % nach höheren Dosen zu verzeichnen (p = 0,98).

Schlussfolgerung: Eine Dosiseskalation über 30 Gy hinaus führt zu einer signifikanten Verbesserung von lokaler Kontrolle, progressionsfreiem Überleben und Gesamtüberleben.

Schlüsselwörter: Metastatisch bedingte Rückenmarkkompression · Überlebensprognose · Strahlentherapie · Dosiseskalation

Introduction

Metastatic spinal cord compression (MSCC) occurs in 5–14 % of all cancer patients during the course of their disease [9, 10]. World wide, radiotherapy alone is the most common treatment for these patients [1, 6–8, 12, 16]. A retrospective study suggested that a shorter course of radiotherapy such as 20 Gy in 5 fractions resulted in similar posttreatment motor function as longer-course radiotherapy such as 30 Gy in 10 fractions or 40 Gy in 20 fractions [15]. However, longer-course radiotherapy resulted in better local control of MSCC than shorter-course radiotherapy [14, 15].

In a large retrospective study, the three longer-course programs did not result in different local control rates [15]. This particular study included both patients with poor and favorable prognoses. In patients with a more favorable survival, local control becomes more important, because these patients often live long enough to experience recurrent MSCC. In the previous retrospective study, the local control results may have been biased because many patients died before local recurrence could occur [15]. Therefore, it appeared reasonable to investigate whether patients with more favorable prognoses benefit from an escalation of radiation dose beyond the "standard" 30 Gy in 10 fractions.

The survival prognoses of MSCC patients can be predicted with a scoring system, which included the prognostic factors tumor type, interval between tumor diagnosis and MSCC, other bone metastases, visceral metastases, ambulatory status before radiotherapy, and time developing motor deficits before radiotherapy [11]. The total score ranged between 20 and 45 points. The patients were divided into five groups based on this score, A: 20–25 points, B: 26–30 points, C: 31–35 points, D: 36–40 points, and E: 41–45 points. The 6-month survival rates of the five groups were 4 %, 11 %, 48 %, 87 % and 99 %, respectively ($p < 0.001$).

In the present matched-pair analysis, only patients with a favorable survival score of ≥ 36 points were included. The matched-pair (1:1) design was chosen to provide the highest level of evidence apart from a randomized trial. The major goal of this study was to investigate a potential benefit in local control of MSCC with escalating the radiation dose beyond 30 Gy in 10 fractions. Secondary endpoints were progression-free survival, overall survival, and posttreatment motor function. The biologically effective radiation dose is represented by the equivalent doses in 2 Gy fractions (EQD2). The EQD2 assuming an α/β ratio of 10 Gy for tumor cell kill were 32.5 Gy for 30 Gy in 10 fractions, 39.1 Gy for 37.5 Gy in 15 fractions, and 40.0 Gy for 40 Gy in 20 fractions [3]. Thus, this study investigated an escalation of the biologically effective radiation dose by 20–23 %.

Table 1. Patients' characteristics.

Tabelle 1. Patientencharakteristika.

	30 Gy/10 fractions n (%)	Higher doses n (%)
Age		
≤ 63 years (n = 194)	97 (51)	97 (51)
> 63 years (n = 188)	94 (49)	94 (49)
Gender		
Female (n = 200)	100 (52)	100 (52)
Male (n = 182)	91 (48)	91 (48)
Tumor type		
Breast cancer (n = 158)	79 (41)	79 (41)
Prostate cancer (n = 82)	41 (21)	41 (21)
Myeloma/lymphoma (n = 56)	28 (15)	28 (15)
Lung cancer (n = 22)	11 (6)	11 (6)
Other tumors (n = 64)	32 (17)	32 (17)
ECOG Performance Score		
1–2 (n = 302)	151 (79)	151 (79)
3–4 (n = 80)	40 (21)	40 (21)
Number of involved vertebrae		
1–2 (n = 196)	98 (51)	98 (51)
≥ 3 (n = 186)	93 (49)	93 (49)
Visceral metastases		
No (n = 356)	178 (93)	178 (93)
Yes (n = 26)	13 (7)	13 (7)
Other bone metastases		
No (n = 198)	99 (52)	99 (52)
Yes (n = 184)	92 (48)	92 (48)
Interval from tumor diagnosis to radiotherapy		
≤ 15 months (n = 94)	47 (25)	47 (25)
> 15 months (n = 288)	144 (75)	144 (75)
Ambulatory status		
No (n = 56)	28 (15)	28 (15)
Yes (n = 326)	163 (85)	163 (85)
Time developing motor deficits		
1–7 days (n = 18)	9 (5)	9 (5)
> 7 days (n = 364)	182 (95)	182 (95)

Patients and Methods

The goal of this study was to perform a matched-pair analysis and evaluate whether favorable MSCC patients benefit from higher dose therapy. From 2,296 MSCC patients treated with radiotherapy alone, 191 patients treated with 30 Gy in 10 fractions were matched to 191 patients treated with higher doses (37.5 Gy in 15 fractions or 40 Gy in 20 fractions). The patients were matched for ten potential prognostic factors: age (≤ 63 versus > 63 years), gender, Eastern Cooperative Oncology Group (ECOG) performance score (1–2 versus 3–4), tumor type (breast cancer versus prostate cancer versus myeloma/lymphoma versus lung cancer versus other tumors), number of involved vertebrae (1–2 versus ≥ 3), other bone metastases (no versus yes), visceral metastases (no versus yes), interval from tumor diagnosis to MSCC (< 15 versus ≥ 15 months), ambulatory status before radiotherapy (not ambulatory versus ambulatory), and time developing motor deficits before radiotherapy (1–7 versus > 7 days). All ten factors should match. Further criteria for inclusion were MSCC of the thoracic or lumbar spine, no prior surgery or radiotherapy to the involved sites, confirmation of MSCC by MRI, and administration of dexamethasone (12–32 mg/day) during radiotherapy. Patients were usually presented to a neurosurgeon before radiotherapy. Data were obtained from the patients, their general practitioners, treating oncologists, and patient files. Patient characteristics are summarized in Table 1.

Table 2. Univariate analysis of local control.

Tabelle 2. Univariate Analyse für die lokale Kontrolle.

	At 6 months (%)	At 12 months (%)	At 18 months (%)	At 24 months (%)	p
Radiation schedule					
30 Gy/10 fractions (n = 191)	98	87	83	71	
Higher doses (n = 191)	98	92	92	92	*0.012*
Age					
≤ 63 years (n = 194)	98	91	88	80	
> 63 years (n = 188)	98	88	88	88	0.92
Gender					
Female (n = 200)	98	90	87	81	
Male (n = 182)	98	89	89	86	0.99
Tumor type					
Breast cancer (n = 158)	99	90	87	80	
Prostate cancer (n = 82)	99	89	89	89	
Myeloma/lymphoma (n = 56)	98	96	96	88	
Lung cancer (n = 22)	95	90	90	90	
Other tumors (n = 64)	96	85	85	85	0.45
ECOG Performance Score					
1–2 (n = 302)	99	90	88	81	
3–4 (n = 80)	97	90	90	90	0.62
Number of involved vertebrae					
1–2 (n = 196)	98	93	91	89	
≥ 3 (n = 186)	98	87	85	77	0.057
Visceral metastases					
No (n = 356)	98	91	89	84	
Yes (n = 26)	100	74	74	74	*0.040*
Other bone metastases					
No (n = 198)	98	94	92	88	
Yes (n = 184)	98	86	84	78	0.057
Interval from tumor diagnosis to radiotherapy					
≤ 15 months (n = 94)	99	92	92	85	
> 15 months (n = 288)	98	89	87	82	0.73
Ambulatory status					
No (n = 56)	96	89	89	89	
Yes (n = 326)	99	90	88	82	0.84
Time developing motor deficits					
1–7 days (n = 18)	100	100	83	83	
> 7 days (n = 364)	98	90	88	83	0.97

Local control of MSCC, the primary study endpoint, was defined as absence of a recurrence of MSCC within the irradiated spinal area. The latter was defined either as local recurrence of motor deficits, if radiotherapy led to an improvement in motor function, or as progression of motor deficits, if radiotherapy resulted in no change of motor deficits. The diagnosis of local failure of MSCC was confirmed by MRI. Patients who experienced deterioration of motor function during radiotherapy and their corresponding matched pair patients were excluded from the analysis of local control. This was done because patients who fail during radiotherapy can confound the analysis of dose response in terms of local control. A total of 356 patients (178 matched pairs) remained for the analysis of local control. Secondary endpoints were progression-free survival, overall survival, and functional outcome. Progression-free survival was defined as lack of progressive motor deficits during radiotherapy or of local recurrence of MSCC in the irradiated spinal area following radiotherapy. Motor function was evaluated before and after radiotherapy with a 5-point scale: grade 0: normal strength; grade 1: ambulatory without aid, grade 2: ambulatory with aid, grade 3: not ambulatory, grade 4: paraplegia. Improvement or deterioration of motor function was defined as a change of at least one point [17].

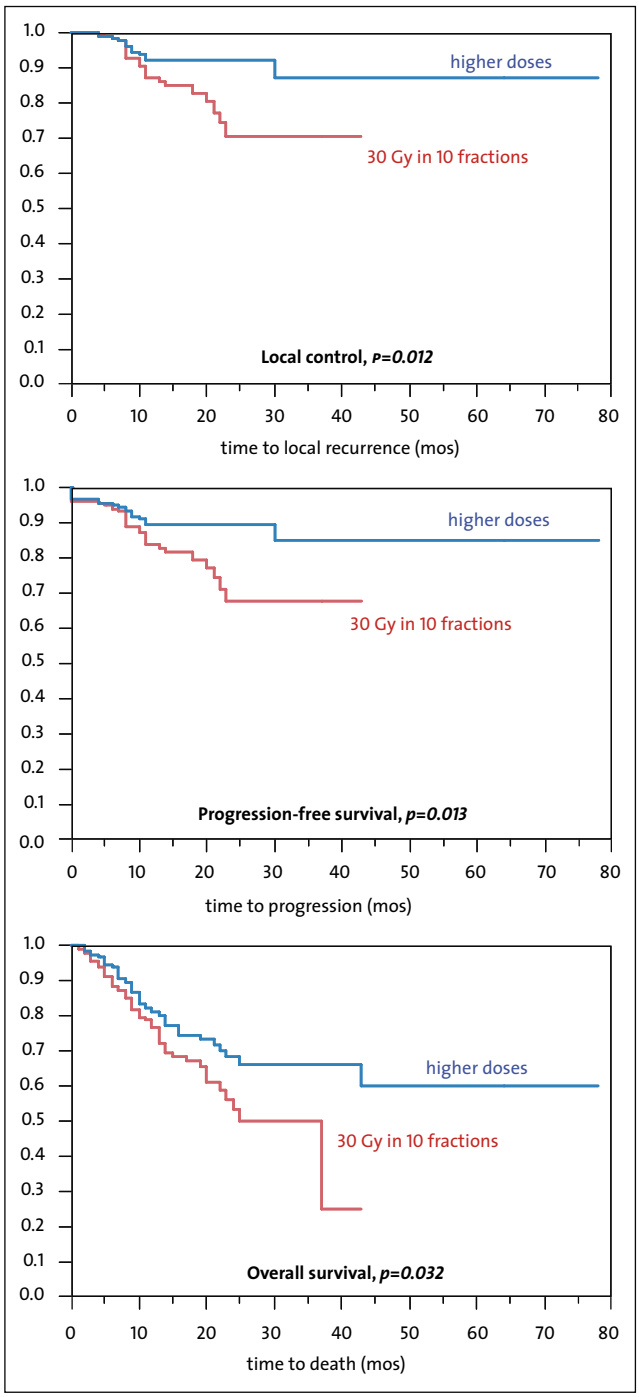

Figure 1. Comparison of 30 Gy in 10 fractions to higher doses with respect to local control of MSCC (*top*), progression-free survival (*middle*), and overall survival (*bottom*). mos: months.

Abbildung 1. Vergleich von 30 Gy in 10 Fraktionen und höheren Dosen hinsichtlich lokaler Kontrolle (*oben*), progressionsfreiem Überleben (*Mitte*) und Gesamtüberleben (*unten*). mos: Monaten.

Table 3. Univariate analysis of progression-free survival.

Tabelle 3. Univariate Analyse für das progressionsfreie Überleben.

	At 6 months (%)	At 12 months (%)	At 18 months (%)	At 24 months (%)	p
Radiation schedule					
30 Gy/10 fractions (n = 191)	94	84	80	68	
Higher doses (n = 191)	95	90	90	90	*0.013*
Age					
≤ 63 years (n = 194)	95	88	85	77	
> 63 years (n = 188)	95	85	85	85	0.92
Gender					
Female (n = 200)	97	89	86	80	
Male (n = 182)	92	84	84	81	0.22
Tumor type					
Breast cancer (n = 158)	98	89	86	79	
Prostate cancer (n = 82)	91	82	82	82	
Myeloma/lymphoma (n = 56)	98	96	96	88	
Lung cancer (n = 22)	91	86	86	86	
Other tumors (n = 64)	89	79	79	79	0.09
ECOG Performance Score					
1–2 (n = 302)	95	87	84	78	
3–4 (n = 80)	95	88	88	88	0.46
Number of involved vertebrae					
1–2 (n = 196)	94	89	87	85	
≥ 3 (n = 186)	96	85	83	75	0.27
Visceral metastases					
No (n = 356)	94	88	86	81	
Yes (n = 26)	100	74	74	74	0.24
Other bone metastases					
No (n = 198)	93	89	88	83	
Yes (n = 184)	96	84	82	76	0.38
Interval from tumor diagnosis to radiotherapy					
≤ 15 months (n = 94)	91	86	86	79	
> 15 months (n = 288)	96	87	85	80	0.38
Ambulatory status					
No (n = 56)	94	88	88	88	
Yes (n = 326)	95	87	85	79	0.55
Time developing motor deficits					
1–7 days (n = 18)	67	67	56	56	
> 7 days (n = 364)	96	88	86	81	*<0.001*

Local control, progression-free survival, and overall survival rates were calculated with the Kaplan–Meier method [4]. The differences between the Kaplan–Meier curves were calculated with the log-rank test. The prognostic factors found to be significant ($p < 0.05$) in the univariate analysis were included in a multivariate analysis performed with the Cox proportional hazards model. In addition to account for the matched-pair design, a stratified model was used. The stratified model was a Cox regression model with backward stepwise selection of variables using the likelihood ratio test. Regarding functional outcome, univariate and multivariate analyses were performed with the ordered logit model, as the data for functional outcome are ordinal (–1 = deterioration, 0 = no change, 1 = improvement). In a previous study, the local control rate at 1 year was 81 % for longer-course radiotherapy. A total of 356 patients allowed detection of an improvement in clinical efficacy of 10 % with a statistical power of 82.5 % (level of significance = 5 %). The statistical power was 85 % to detect a difference of 10 % (level of significance = 5 %) for progression-free survival and overall survival which were evaluated for the entire cohort of 382 patients. All patients were followed until death or for median of 14 months (range: 6–78 months) in those 278 patients alive at their last follow-up.

Table 4. Univariate analysis of overall survival.

Tabelle 4. Univariate Analyse für das Gesamtüberleben.

	At 6 months (%)	At 12 months (%)	At 18 months (%)	At 24 months (%)	p
Radiation schedule					
30 Gy/10 fractions (n = 191)	88	76	67	53	
Higher doses (n = 191)	94	81	75	68	*0.032*
Age					
≤ 63 years (n = 194)	94	82	74	65	
> 63 years (n = 188)	88	76	68	58	*0.11*
Gender					
Female (n = 200)	95	83	76	68	
Male (n = 182)	87	75	65	54	*0.012*
Tumor type					
Breast cancer (n = 158)	94	85	78	72	
Prostate cancer (n = 82)	84	73	63	63	
Myeloma/lymphoma (n = 56)	88	83	75	60	
Lung cancer (n = 22)	91	86	86	86	
Other tumors (n = 64)	95	62	53	25	*0.001*
ECOG Performance Score					
1–2 (n = 302)	96	84	76	66	
3–4 (n = 80)	71	61	51	46	*<0.001*
Number of involved vertebrae					
1–2 (n = 196)	94	79	76	67	
≥ 3 (n = 186)	88	79	66	56	0.10
Visceral metastases					
No (n = 356)	92	81	74	64	
Yes (n = 26)	81	52	30	30	*<0.001*
Other bone metastases					
No (n = 198)	95	80	77	67	
Yes (n = 184)	86	78	64	56	*0.049*
Interval from tumor diagnosis to radiotherapy					
≤ 15 months (n = 94)	90	75	73	60	
> 15 months (n = 288)	91	80	71	62	0.55
Ambulatory status					
No (n = 56)	71	67	55	47	
Yes (n = 326)	94	81	74	64	*0.002*
Time developing motor deficits					
1–7 days (n = 18)	89	59	47	47	
> 7 days (n = 364)	91	80	72	63	0.07

Results

The results of the univariate analysis of local control are summarized in Table 2. Local control was significantly better following doses greater than 30 Gy in 10 fractions ($p = 0.012$, Figure 1 top). Improved local control was also associated with absence of visceral metastases at the time of radiotherapy ($p = 0.040$). On multivariate analysis, local control remained significantly associated with the radiation schedule (relative risk [RR]: 2.42; 95 % confidence interval [CI]: 1.23–5.05; $p = 0.011$), whereas visceral metastases (RR: 2.74; 95 %CI: 0.93–6.57; $p = 0.07$) were not significant. The significant impact of the radiation schedule was confirmed with the stratified model (RR: 2.46; 95 %CI: 1.22–4.96; $p = 0.012$).

The results of the univariate analysis of progression-free survival are summarized in Table 3. On univariate analysis, improved progression-free survival was associated with radiation dose greater than 30 Gy in 10 fractions ($p = 0.013$, Figure 1 middle) and slower development of motor deficits before radiotherapy ($p < 0.001$). On multivariate analysis, progression-free survival maintained significant associations with radiation schedule (RR: 2.12; 95 %CI: 1.19–3.88; $p = 0.010$) and time developing motor deficits (RR: 4.31; 95 %CI: 1.77–9.01; $p = 0.003$). The significant impact of the radiation schedule was confirmed with the stratified model (RR: 1.61; 95 %CI: 1.09–2.39; $p = 0.018$).

Table 5. Univariate analysis of posttreatment motor function.

Tabelle 5. Univariate Analyse für die motorische Funktion nach Therapie.

	Improvement n (%)	No change n (%)	Deterioration n (%)	p
Radiation schedule				
30 Gy/10 fractions (n = 191)	77 (40)	107 (56)	7 (4)	
Higher doses (n = 191)	78 (41)	107 (56)	6 (3)	0.98
Age				
≤ 63 years (n = 194)	86 (44)	101 (52)	7 (4)	
> 63 years (n = 188)	69 (37)	113 (60)	6 (3)	0.52
Gender				
Female (n = 200)	81 (41)	116 (58)	3 (2)	
Male (n = 182)	74 (41)	98 (54)	10 (5)	0.39
Tumor type				
Breast cancer (n = 158)	63 (40)	93 (59)	2 (1)	
Prostate cancer (n = 82)	26 (32)	51 (62)	5 (6)	
Myeloma/lymphoma (n = 56)	37 (66)	19 (34)	0 (0)	
Lung cancer (n = 22)	9 (41)	12 (55)	1 (5)	
Other tumors (n = 64)	20 (31)	39 (61)	5 (8)	0.017
ECOG Performance Score				
1–2 (n = 302)	115 (37)	174 (58)	11 (4)	
3–4 (n = 80)	40 (50)	38 (48)	2 (3)	0.22
Number of involved vertebrae				
1–2 (n = 196)	79 (40)	109 (56)	8 (4)	
≥ 3 (n = 186)	76 (41)	105 (56)	5 (3)	0.97
Visceral metastases				
No (n = 356)	146 (41)	197 (55)	13 (4)	
Yes (n = 26)	9 (35)	17 (65)	0 (0)	0.47
Other bone metastases				
No (n = 198)	78 (39)	111 (56)	9 (5)	
Yes (n = 184)	77 (42)	103 (56)	4 (2)	0.63
Interval from tumor diagnosis to radiotherapy				
≤ 15 months (n = 94)	41 (44)	46 (49)	7 (7)	
> 15 months (n = 288)	114 (40)	168 (58)	6 (2)	0.07
Ambulatory status				
No (n = 56)	32 (57)	23 (41)	1 (2)	
Yes (n = 326)	123 (38)	191 (59)	12 (4)	0.12
Time developing motor deficits				
1–7 days (n = 18)	1 (6)	12 (67)	5 (28)	
> 7 days (n = 364)	154 (42)	202 (55)	8 (2)	*<0.001*

The results of the univariate analysis of overall survival are summarized in Table 4. On univariate analysis, improved overall survival was associated with radiation doses greater than 30 Gy in 10 fractions (p = 0.032, Figure 1 bottom), female gender (p = 0.012), favorable tumor type (p = 0.001), better performance status (p < 0.001), lack of visceral metastases (p < 0.001), lack of other bone metastases (p = 0.049), and ambulatory status (p = 0.002). On multivariate analysis, overall survival remained associated with radiation schedule (RR: 1.64; 95 %CI: 1. 11–2.44; p = 0.014), tumor type (RR: 3.93; 95 %CI: 2.11–7.18; p < 0.001), performance status (RR: 2.37; 95 %CI: 1.48–3.73; p < 0.001), visceral metastases (RR: 5.40; 95 %CI: 2.83–9.88; p < 0.001), and ambulatory status (RR: 2.47; 95 %CI: 1.46–4.05; p = 0.001). A trend was observed for other bone metastases (RR: 1.50; 95 %CI: 0.97–2.32; p = 0.07). Gender was not significant (RR: 1.33; 95 %CI: 0.86–2.05; p = 0.20). The significant impact of the radiation schedule was confirmed with the stratified model (RR: 1.63; 95 %CI: 1.10–2.43; p = 0.015).

On univariate analysis, improved motor function was associated with favorable tumor type (p = 0.017) and slower development of motor deficits (p < 0.001) (Table 5). The radiation schedule had no significant impact on posttreatment motor function (p = 0.98). On multivariate analysis, time of developing motor deficits (estimate: + 1.53; 95 %CI: 0.11–2.95; p = 0.035) remained significant, whereas the tumor type showed a trend (estimate: –1.02; 95 %CI: –2.08 to + 0.46; p = 0.06).

Acute toxicity such as skin toxicity, nausea, and diarrhea was mild and did not exceed grade 1 according to the Common Toxicity Criteria (CTC 2.0) [18]. Late toxicity in terms of radiation induced myelopathy was not observed in the two treatment groups.

Discussion

The most commonly used fractionation regimen for MSCC is 30 Gy in 10 fractions which may be considered the standard regimen. It has been reported that longer-course radiotherapy with higher total doses resulted in better local control of MSCC than shorter radiotherapy programs with lower total doses [14, 15]. Local control is particularly important for patients with a favorable survival prognosis, as these patients may live long enough to experience a local recurrence of MSCC. Two retrospective studies did not show a significant difference in local control between 30 Gy in 10 fractions and higher doses [13, 15]. In contrast to those studies which included many patients with a poor expected survival, the present matched-pair analysis included only patients with a favorable survival prognosis. Because the risk of developing a local recurrence of MSCC increases with life expectancy, the proportion of events was expected to be higher in the present study than in the preceding retrospective study. And indeed, in

the present matched-pair study, 9.7 % (37/382) of patients experienced a local recurrence of MSCC, whereas in the preceding retrospective studies 4.4 % (34/764) of patients and 4.2 % (39/922) of patients treated with longer-course radiotherapy developed a local recurrence [13, 15]. Patients with a short life expectancy may confound the results of a study comparing 30 Gy to higher doses by masking the potential local control benefit from escalation of the radiation dose.

The present study demonstrated a significant improvement in local control with doses greater than 30 Gy. Furthermore, progression-free survival and overall survival were also better with doses greater than 30 Gy. In the present matched pair study, the matching of the patients followed strict criteria by taking into account ten potential prognostic factors. We felt that this approach provides highest quality outcome data possible short of a randomized trial. However, because this matched-pair study is based on retrospective data, a hidden selection bias cannot be completely excluded.

Local control and progression-free survival were only significantly associated with the radiation schedule. Overall survival was significantly associated with the radiation schedule and primary tumor type, ECOG performance status, visceral metastases, and ambulatory status prior to radiotherapy. The prognostic significance of these factors has been previously reported [11, 14]. Functional outcome was significantly associated with the time developing motor deficits prior to radiotherapy. This factor has already been demonstrated to be the strongest predictor for posttreatment motor function [11, 14, 15].

In patients with a favorable survival prognosis, more intensive treatment modalities such as decompressive surgery and high-precision radiotherapy (radiosurgery, fractionated stereotactic body radiotherapy, intensity modulated radiotherapy) may be considered to further improve the results. However, decompressive surgery is generally indicated only in a limited proportion of MSCC patients [8]. Furthermore, a recent matched-pair analysis did not reveal a significant benefit for decompressive surgery preceding radiotherapy when compared to radiotherapy alone with respect to local control, overall survival, and functional outcome [12]. The role of decompressive surgery for MSCC needs to be re-defined in a large randomized trial. High-precision radiotherapy is very effective in achieving pain relief [2, 5]. In case of MSCC when the spinal cord is involved, adequate sparing of the spinal cord is not always possible. However, in selected patients with neurologic deficits due to MSCC, response rates up to 84 % can be achieved [2, 5]. Therefore, high-precision radiotherapy techniques can be considered for MSCC patients with good survival prognosis. If high-precision radiotherapy is not available, administration of doses greater than 30 Gy appears reasonable in favorable patients.

Conclusion

In MSCC patients with favorable survival prognoses, escalation of the radiation dose beyond 30 Gy in 10 fractions resulted in significantly better local control, progression-free survival, and overall survival rates. This matched-pair study is a prerequisite for a randomized trial.

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