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# PRE AND POST RADIOTHERAPY PREDICTORS OF FUNCTIONAL OUTCOME AND SURVIVAL IN METASTATIC SPINAL CORD COMPRESSION

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## ABSTRACT

**Background:** Metastatic spinal cord compression (MSCC) patients have poor prognosis. Several predictors including, type of malignancy, duration of symptoms, performance status, other sites of bone and visceral metastases have been reported. We evaluated the pre and post radiotherapy predictors of motor dysfunction recovery and on survival in MSCC in patients with urologic malignancies. **Materials and methods:** From July 2006 to April 2009, forty seven patients were treated for MSCC. Descriptive statistics (type of malignancy, performance status, age, sex, duration of symptoms prior to radiotherapy (RT), different fractionation of RT, and other sites of metastases) were evaluated. Further multivariate analysis (Cox-proportional hazard model/Bonferroni method) was performed and Kaplan Meier survival curves were obtained using SPSS version 17.0. **Results:** The actuarial survival rate of study population was 55% at five months, 30 % at 10 months and 5% at 15 months. According to histology, overall survival rates seen were 13, 15, 16, and17 months for bladder, prostate, kidney and others (germ cell and ureteric) respectively. Complete responders were 100% in ambulatory patients as compared to non ambulatory (12% complete responders) p <0.0001. Complete responders were found to have better survival (8.5 months vs. 4 months in minimal/non-responders p < 0.001). However pretreatment ambulation, duration of symptoms, RT protocol, age, gender were not found as predictors of survival. **Conclusion:** Urologic malignancies are considered as aggressive. The ambulation and duration of symptoms at onset of RT are important prognostic factors like other malignancies at time of radiotherapy for predicting motor dysfunction recovery and survival benefit.

## INTRODUCTION

Metastatic spinal cord compression (MSCC) is a common oncologic emergency affecting approximately 5 % of all cancer patients; the early diagnosis and prompt treatment is must.[1] Magnetic resonance imaging (MRI) is the best tool for diagnosing MSCC.[2] When MSCC is diagnosed, radiotherapy (RT) with or without surgery is generally the treatment of choice.[3] Recently, a randomized clinical trial has shown conclusively that radiotherapy alone is significantly inferior to decompressive surgery plus radiotherapy for the treatment of MSCC[4]; further Thomas et al found it cost effective approach as compared to radiotherapy alone.[5] However optimal radiotherapy fractionation schedule is still matter of debate. Due to transport to radiation oncology department for these disabled patients and problems during treatment set up, the shorter treatment time is advised. Various protocols 3Gy × 10 fractions/2 weeks, 4 Gy × 5 fractions/1 week, 2.5 × 15/3 weeks and 8 Gy in single fraction have been demonstrated with similar efficacy.[6, 7]

The prognosis for MSCC is considered poor and is influenced by various clinical and neurological factors which have been described in various retrospective

and prospective studies.[8,9]

We aimed to see retrospectively, the impact of different clinical, neurological and treatment factors on motor dysfunction recovery and survival in patients with MSCC in urologic malignancies.

## METHODS

*Patients and treatment techniques:*

From July 2006 to April 2009, 47 consecutive MSCC patients with urological malignancies entered a protocol of early diagnosis and treatment. In these patients, with neurological symptoms and with bone scan positivity for vertebral involvement, Magnetic resonance imaging (MRI) was performed. After making the clinical/ radiological diagnosis of MSCC, steroids were given immediately (Loading dose 16mg dexamethasone intravenous followed by 4 mg q 6 hours). Radiotherapy alone was given without decompressive surgery. RT (6 MV photons) was delivered within 24 hours from diagnosis. All patients underwent virtual simulation using SOMATOM Emotion 6 CT scanner. After simulation all data was transferred through DICOM to COHERENCE V-Sim planning system. The Gross tumor volume (GTV), planning treatment volume (PTV) and normal organs at risk (OAR) in treated area (cervicothoracic spine: larynx, pharynx, esophagus; thoracolumbar spine: lungs, liver, and kidneys and small bowel) were marked. Treatment was given through either single posteroanterior PA, parallel opposed fields (anteroposterior AP and PA or right and left lateral for cervical spine) depending on the depth of spine and to OAR. Fractionation protocol 3Gy × 10 or 4Gy × 5 was left on the radiation oncologist's discretion and performance status of each patient.

*Motor dysfunction definition and post RT assessment:*

Motor dysfunction and ambulatory status were evaluated before RT and up to 24 months thereafter. Motor function was evaluated according to Tomita grading system (Grade 0 = normal strength, Grade 1 = ambulatory without aid, Grade 2 = ambulatory with aid, Grade3 = not ambulatory, Grade 4 = paraplegia) 10. Improvement of motor function was defined as a change of ≥1 point by clinical assessment at one month intervals after radiotherapy. Primary endpoint was motor dysfunction recovery. Complete responders were defined by patients achieving Tomita Grade 0 after RT. Rest were categorized as minimal responders. Non responders were defined as no change of ≥ 1 point after RT.

*Statistical analysis:*

Univariate analysis was performed using the Kaplan-Meier-method. The results were considered significant at $p < 0.05$. Further, a multivariate analysis (Cox proportional hazard model) was performed for clinical and neurological factors (age, gender, performance status, tumor type, other bone metastases, visceral metastases, extent of compression, ambulatory status before RT, and duration of motor symptoms at time of RT), effect of RT on motor dysfunction recovery and on survival. Further Bonferroni method was used for multiple factors. All data was analyzed using SPSS version 17.0

## RESULTS

The median follow-up for the study population was 20 months (range 3-36 months).

Table 1. *Patients characteristics*

| Variables | Number (%) |
|---|---|
| **Age** | |
| ≤ 65 years | 35 (74.5%) |
| ≥ 65 years | 12 (25.5%) |
| **Gender** | |
| Male | 39 (83%) |
| Female | 8 (17%) |
| **Functional Status before radiotherapy** | |
| Ambulatory (Tomita Grade 0-2) | 23 (48.9%) |
| Non-ambulatory (Tomita Grade3-4) | 24 (51.1%) |
| **Type of malignancy** | |
| Prostate | 21 (44.7%) |
| Bladder | 6 (12.8%) |
| Kidney | 12 (25.5%) |
| Others | 8 (17%) |
| Germ cell tumors | 7 |
| TCC pelvis/ureter | 1 |
| **Time of developing motor symptoms before radiotherapy** | |
| ≤ 7 days | 24 (51.1%) |
| 7-14 days | 15 (31.9%) |
| ≥14 days | 8 (17%) |
| **Other bone metastasis at time of radiotherapy** | |
| Yes | 40 (85%) |
| No | 7 (15%) |
| **Visceral metastasis at time of radiotherapy** | |
| Yes | 26 (55.3%) |
| No | 21 (44.7%) |
| **Palliative radiotherapy** | |
| Long course 30Gy in 10 fractions | 27 (57.5%) |
| Short course 20Gy in 5 fractions | 20 (42.5%) |
| **Follow up (months)** | 20 (3-36) |

*TCC= Transitional cell carcinoma*

The patient characteristics are given in Table 1. Comparing primary tumor type and site of spinal cord compression, Table 2 showed predominance of thoracic spine for MSCC (55.3%). The actuarial survival rate at 5, 10, 15 months was 55%, 30% and 5% respectively Figure 1.

**Table 2.** *Levels of spinal cord compression sites according to primary tumor.*

| Primary tumor | Cervical | Thoracic | Lumbar | Cervico-thoracic | Thoraco-lumbar | Total |
|---|---|---|---|---|---|---|
| Prostate | 2 | 11 | | 2 | 6 | 21 |
| Bladder | 1 | 3 | | | 2 | 6 |
| Kidney | | 7 | | 2 | 3 | 12 |
| Germ cell tumors | 1 | 5 | | 1 | | 7 |
| TCC Ureter/Pelvis | | | 1 | | | 1 |
| Total | 4(8.5%) | 26 (55.3%) | 1 (2.1%) | 5(10.6%) | 11(23.4%) | 47 |

**Figure 1.** *The actuarial survival rate*

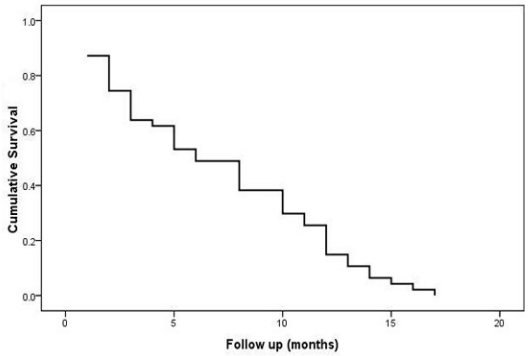


**Figure 2(a).** *Survival rates of complete responders and non/minimal responders.*

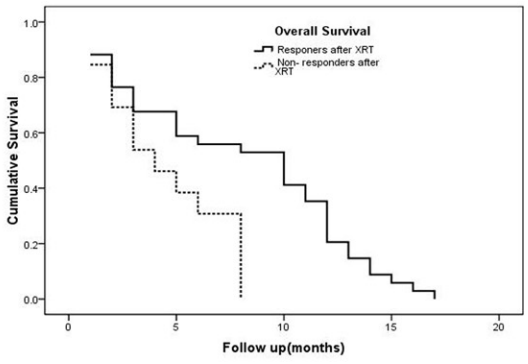


**Figure 2(b).** *Overall survival of patients with different RT fractionations.*

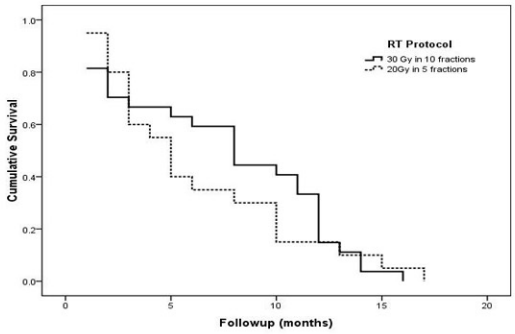


**Figure 3(a).** *Survival rates of patients according to duration of symptoms.*

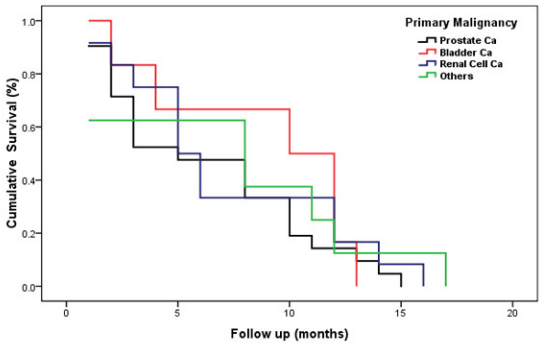


**Figure 3(b).** *Survival rates of patients according to RT fractionation.*

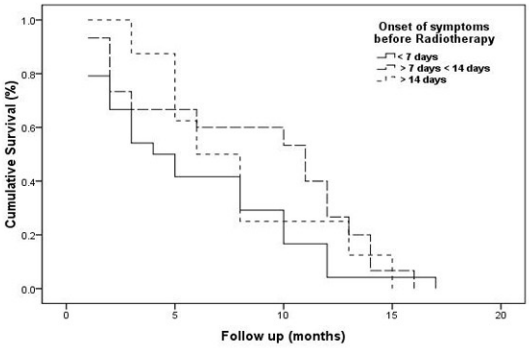


**Table 3.** *Post radiotherapy response in ambulatory and non-ambulatory patients.*

| Before Radiotherapy Motor function | Number of patients | Complete Recovery (%) | p- value |
|---|---|---|---|
| Ambulatory (walking with or without aid) | 23 (48.9%) | 23 (48.9%) | 0.0001 |
| Non-ambulatory (paraplegic) | 24 (51.1%) | 3 (12%) | |
| Additional urinary retention (catheterized) | 14 (29.8%) | 2 (14%) | |

## DISCUSSION

The life expectancy of most MSCC patients is relatively shorter, with reported median survival of a few months.[11] As we reported previously, in Asian countries the palliative RT burden for bone metastases in urologic malignancies is relatively higher (65.74%).[12] So a thorough understanding of different clinical and neurological prognostic factors in patients with MSCC would help in the RT decision making for the individual patient.

Thoracic spine was seen most common site of disease involvement, which could be understood by its high anatomic volume.

Overall survival in this small cohort was found low with radiotherapy alone as compared to other malignancies.[13, 14] The ambulation at time of RT was found important prognostic factor, as complete response was seen in all these patients. Ambulation has been widely described in literature as important prognostic factor.[15, 16]

Other factors including age, gender, and other sites of metastases were found insignificant. Probably, the natural history of urologic malignancies is more important than patient's age, gender, the extent of compression and other sites of metastases. We did not see any local relapse within the RT field. However post RT local relapse is very rare (3%), but associated with further poor survival.[17] The shorter protocols of RT were equally better in terms of motor dysfunction recovery and survival as longer RT protocols.

The most important post RT prognostic factor we found was the motor dysfunction recovery. The complete responders were found to have relatively better survival. Helweg-Larsen et al[18] investigated prognostic factors for gait function and survival in 153 MSCC patients. They also reported a dramatic difference in median survival between post-RT ambulatory and post-RT nonambulatory patients (7.9 vs. 1.2 months). The response to RT as a predictive factor for survival was also described for painful metastases of the spinal column not associated with neurological deficits. Van der Linden et al[19] reported median survival times of 8.1 months for responders vs. 3.4 months for non responders ($p < 0.001$).

Limitation in our study could any impact of hormonal, chemotherapy, biologic agents and bisphosphonates in motor and survival outcome in patients with MSCC.

## CONCLUSION

In conclusion, survival after irradiation of MSCC seems to be influenced by both pre-RT and post-RT factors. The ambulation and duration of motor symptoms at time of RT are important pre RT prognostic factors for motor dysfunction recovery and post-RT motor function recovery is an important predictor of survival. This information can help urologists and oncologists in making decisions regarding the administration of further therapies and the timing of follow-up.

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