Simplified Comorbidity Score and Eastern Cooperative Oncology Group Performance Score Predicts Survival in Patients Receiving Organ-preserving Treatment for Bladder Cancer

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Abstract. *Background/Aim: This study investigated three comorbidity scales and the Eastern Cooperative Oncology Group performance score (ECOG-PS) for survival in patients receiving local irradiation for bladder cancer. Patients and Methods: Sixty-four patients receiving organ-preserving radio-chemotherapy or radiotherapy for urinary bladder cancer were retrospectively evaluated. Charlson Comorbidity Index (CCI), Simplified Comorbidity Score (SCS), Age-Adjusted Charlson Comorbidity Index (AAC) and ECOG-PS were analyzed for associations with survival. Results: Patients with a SCS of 0-7 points had a significantly better survival than those with 8-18 points (p=0.018). Five-year survival rates were 64% and 32%, respectively. Patients with ECOG-PS of 0-1 had a significantly better 5-year survival than patients with ECOG-PS of 2-3 (64% vs. 0%, p<0.001). For CCI (p=0.16) and AAC (p=0.49), a significant association with survival was not observed. Conclusion: SCS and ECOG-PS were significantly associated with survival in patients irradiated for bladder cancer and can help estimate the prognoses of these patients.*

Radical cystectomy is considered standard treatment of carcinoma of the urinary bladder (1). However, since this approach is often associated with a considerable rate of surgery-related complication including perioperative death, many patients, particularly elderly patients and those with significant comorbidities are assigned to definitive radiotherapy or radio-chemotherapy with upfront

transurethral resection of the bladder (2-4). Moreover, with respect to their quality of life, a considerable number of patients refuse radical cystectomy and prefer an organ-preserving approach instead. In order to choose the optimal bladder-preserving approach for an individual patient, it would be helpful to have a precise idea of the patient's survival prognosis. Such estimation would likely be supported with the knowledge of prognostic factors including comorbidity scales. The predictive value of such scales to predict the survival of cancer patients had already been shown for lung cancer patients (5-7). The present study investigated the potential prognostic role of three comorbidity scales and the Eastern Cooperative Oncology Group performance score (ECOG-PS) in patients receiving organ-preserving local radiotherapy or radio-chemotherapy for invasive carcinoma of the urinary bladder (8-11).

Patients and Methods

Sixty-four patients who had received organ-preserving radio-chemotherapy or radiotherapy for urinary bladder cancer between 2000 and 2014 were retrospectively evaluated. Radiotherapy was performed with 6-18 MV photon beams from a linear accelerator after 3D-conformal treatment planning. The median dose was 59.4 Gy (range=50.4-63.0 Gy), which was delivered with conventional fractionation of 1.8 to 2.0 Gy on five consecutive days per week. Forty-six patients had received concurrent chemotherapy in addition to irradiation, which consisted of a platinum-based regimen in 28 patients, paclitaxel in 17 patients and vinflunine in 1 patient. Of these patients, 24 were female and 40 male. Median age was 76.5 years (range=50-89 years). Clinical tumor stage was T1 in 2 patients, T2 in 24 patients, >T2a in 17 patients T3 in 13 patients and T4 in 8 patients, respectively. Positive lymph nodes were diagnosed in 9 patients. All but 6 patients had received at least one transurethral resection of the bladder prior to radiotherapy.

In these 64 patients, three comorbidity scales and the Eastern Cooperative Oncology Group performance score (ECOG-PS) were investigated for a potential association with survival (8-11). The

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three comorbidity scales included the Charlson Comorbidity Index (CCI, Table I), the Simplified Comorbidity Score (SCS, Table II) and the Age-Adjusted Charlson Comorbidity Index (AAC, Table III).The survival analyses were performed with the Kaplan–Meier analysis and the log-rank test (12).

Results

Patients were followed-up until death or for a median 36 months following radiotherapy in survivors. The median survival time in the entire cohort was 66 months. The points of the CCI ranged from 0 to 7 points (median 2 points).The comparison of 0-2 *versus* 3-7 points did not reveal a significant difference with respect to an association with survival (p=0.16). The survival rates at 1 year, 3 years and 5 years of both CCI ranges are summarized in Table IV.

The range of points of the SCS was 0 to 18 with a median of 7 points. Patients achieving 0-7 points had a significantly better survival than patients with 8-18 points (p=0.018). The survival rates of both SCS ranges at 1, 3 and 5 years are shown in Table IV.

The points of AAC ranged from 2 to 10 points (median 5 points). The comparison of 2-5 *versus* 6-10 points did not show a significant difference in survival (p=0.49). The survival rates at 1, 3 and 5 years of both AAC ranges are given in Table IV.

In addition to the three comorbidity scales, the ECOG-PS was investigated. The median ECOG-PS was 1 (range=0-3). Patients with an ECOG-PS of 0-1 had a significantly better survival than those patients with an ECOG-PS of 2-3 (p<0.001). The corresponding survival rates at 1, 3 and 5 years are summarized in Table IV.

Discussion

Carcinoma of the urinary bladder is one of the less common solid tumors in adult cancer patients (13). Many patients cannot withstand radical cystectomy (14). Their prognoses can be improved with modern multi-disciplinary treatment regimens (15-21). Another important approach is the administration of personalized anticancer therapy taking into account many factors including the patient's remaining lifespan. In order to be able to have an idea of an individual patient's survival prognosis, a profound knowledge of predictive factors is mandatory. Comorbidity scales were reported to serve as indicators for survival of lung cancer patients (5-7). In the present study, three such scales plus the ECOG-PS were investigated for a potential association with the survival of patients with bladder cancer, who received bladder-preserving treatment in form of radiotherapy or radio-chemotherapy with or without upfront transurethral resection.

According to the results of this study, the SCS was significantly associated with survival in this group of patients. Patients with a SCS of 0-7 points had a significantly better

Table I. *Charlson Comorbidity Index (CCI) (7).*

Weight	Comorbidities
1 Point	Myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic obstructive pulmonary disease, connective tissue disease, ulcer disease, mild liver disease, diabetes mellitus
2 Points	Hemiplegia, moderate or severe renal disease, diabetes mellitus with end organ damage, any tumor, leukemia, lymphoma
3 Points	Moderate or severe liver disease
6 Points	Metastatic solid tumor, acquired immune deficiency syndrome (AIDS)

Table II. *Simplified Comorbidity Score (SCS) (7).*

Weight	Comorbidities
1 Point	Cardiovascular comorbidity, respiratory comorbidity, neoplastic comorbidity, alcoholism
4 Points	Renal insufficiency
5 Points	Diabetes mellitus
7 Points	Tobacco consumption

survival at 1, 3 and 5 years when compared to patients with a SCS of 8-18 points. This finding agrees well with the results of the study of Colinet *et al.* that included 735 patients with non-small cell lung cancer, who had received different types of treatment (10). In this study, the authors developed and validated the SCS and reported it to be more informative than the CCI. Following the study of Colinet *et al.*, other authors also investigated the value of the SCS with respect to estimating the survival of lung cancer patients (18-21). Singh *et al.* included 238 patients who received first-line chemotherapy for different histologic types of lung cancer (22). When comparing patients with a SCS ≤9 *versus* >9, the median survival did not significantly differ between both groups. Similar results were reported from a study of 73 patients with small-cell lung cancer, when comparing SCS ranges of 0-5 points, 6-11 points and 12-17 points (p=0.54) (23). In another prospective study form Australia that included 633 patients with non-small lung cancer, a SCS >9 was not associated with a worse survival prognosis than a SCS ≤9 (hazard ratio(HR)=1.0; p=0.8) (24). In contrast, on multivariate

Table III. *Age-Adjusted Charlson Comorbidity Index (AAC) (7).*

Weight	Comorbidities
1 Point	Myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic obstructive pulmonary disease, connective tissue disease, ulcer disease, mild liver disease, diabetes mellitus
2 Points	Hemiplegia, moderate or severe renal disease, diabetes mellitus with end organ damage, any tumor, leukemia, lymphoma
3 Points	Moderate or severe liver disease
6 Points	Metastatic solid tumor, acquired immune deficiency syndrome (AIDS)
1 Additional point	Each decade over the age of 40 years, up to 4 points

Table IV. *Comorbidity scales and the corresponding survival rates.*

	1 year (%)	3 years (%)	5 years (%)	*p*-Value
Charlson Comorbidity Index (CCI)				
0-2 Points (n=43)	86	68	60	
3-7 Points (n=21)	62	56	37	0.16
Simplified Comorbidity Score (SCS)				
0-7 Points (n=39)	87	78	64	
8-18 Points (n=25)	63	42	32	0.018
Age-Adjusted Charlson Comorbidity Index (AAC)				
2-5 Points (n=45)	82	65	67	
6-10 Points (n=19)	68	62	41	0.49
Eastern Cooperative Oncology Group performance score (ECOG-PS)				
0-1 (n=47)	87	72	64	
2-3 (n=17)	49	42	0	<0.001

analysis of a study with 172 patients with small cell lung cancer from Taiwan, patients with a SCS >9 had a significantly worse prognosis than patients with a SCS ≤9 (25). A significant difference was found in both patients with limited disease (hazard ratio(HR)=2.17; 95% confidence interval(CI)=1.12-4.21) and patients with extensive disease (hazard ratio 1.74; 95%-confidence interval 1.12-2.72). In addition, in patients with extensive disease, SCS >9 was associated with a worse response to anticancer treatment (60% *vs*. 82%, *p*=0.02). Considering the contradictory results from the studies reported in the literature, the predictive value of the SCS in lung cancer patients remains unclear.

However, our present study showed a significant association between SCS and survival in patients with bladder cancer, a tumor entity with a much different histology than lung cancer. In the present study, patients with a SCS of 0-7 points had a significantly better survival prognosis than patients with a SCS of 8-18 points. Thus, patients with 0-7 points may benefit from radiotherapy with higher total doses such as 59.4 Gy and the addition of radio-sensitizing chemotherapy to achieve a better long-term loco-regional control, since the risk of developing loco-regional recurrences increases with the patients' lifetime. Dose per fraction should be 1.8 Gy rather than ≥2.0 Gy to keep the risk of late radiation-related toxicities as low as possible. In addition to the SCS, our study demonstrated the ECOG-PS to be a significant predictor of survival. Patients with an ECOG-PS of 0-1 had a significantly better survival than patients with an ECOG-PS of 2-3. Similar to patients with a SCS of 0-7 points, patients with an ECOG-PS of 0-1 should receive radiotherapy with a total dose of 59.4 Gy supplemented with concurrent chemotherapy and doses per fraction of 1.8 Gy.

The significant prognostic role of the performance status for the survival of cancer patients has been extensively reported in the literature including patients with bladder cancer (26-28). This demonstrates some consistency of the data of our present study. One should bear in mind that retrospective studies always carry the risk of hidden selection biases. However, prospective trials are difficult to perform, because bladder cancer is an uncommon malignancy.

In conclusion, the SCS and the ECOG-PS were significantly associated with survival in patients receiving organ-preserving radiotherapy or radio-chemotherapy for bladder cancer. These scales can help physicians when aiming to estimate the survival prognoses of these patients.

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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