Prognostic factors for survival and ambulatory status at 8 weeks with metastatic spinal cord compression in the SCORAD randomised trial

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Abstract

Background

Metastatic spinal cord compression (MSCC) carries a poor prognosis and management is based on the likelihood of maintaining mobility and predicted survival.

Patients and Method

SCORAD is a randomised trial of 686 patients comparing a single dose of 8Gy radiotherapy with 20Gy in 5 fractions. Data was split into a training set (412, 60%) and a validation set (274, 40%). A multivariable Cox regression for overall survival (OS) and a logistic regression for ambulatory status at 8 weeks were performed in the training set using baseline factors and a backward selection regression to identify a parsimonious model with $p \leq 0.10$. Receiver Operating Characteristic (ROC) analysis evaluated model prognostic performance in the validation set. Validation of the final survival model was performed in a separate registry dataset (n=348).

Results

The survival Cox model identified male gender, lung, gastrointestinal, and other types of cancer, compression at C1-T12, presence of non-skeletal metastases and poor ambulatory status all significantly associated with worse OS (all $p<0.05$). The ROC AUC for the selected model was 75% (95%CI: 69 to 81) in the SCORAD validation set and 68% (95%CI: 62 to 74) in the external validation registry data.

The logistic model for ambulatory outcome identified primary tumour breast or prostate, ambulatory status grade 1 or 2, bladder function normal and prior chemotherapy all

significantly associated with increased odds of ambulation at 8 weeks (all $p<0.05$). The ROC AUC for the selected model was 72.3% (95% CI 62.6-82.0) in the validation set.

Conclusions

Primary breast or prostate cancer, and good ambulatory status at presentation, are favourable prognostic factors for both survival and ambulation after treatment.

Key words

Spinal cord compression, metastatic, radiotherapy, prognostic index, nomogram

Introduction

Metastatic spinal cord compression (MSCC) carries a poor prognosis for most patients. Typical primary sites are lung, breast and prostate. Whilst localised MSCC in patients with low volume metastatic disease and a controlled primary site may benefit from surgical treatment [1], the majority have advanced disease and are treated with radiotherapy [2]. Identifying prognostic factors for survival in this population has been of growing interest to better inform clinical decisions and patient management, as well as defining areas for future clinical research. Several studies have attempted to evaluate prognostic factors for survival in MSCC [3-13]. The majority of studies were derived from relatively small surgical cohorts, with only three from radiotherapy cohorts and one with mixed surgery and radiotherapy. Only one [10] used data from a prospective randomised trial, the others reflecting retrospective analyses with recognised inherent limitations. There is therefore a need for a prognostic index specific for patients treated by radiotherapy based on a large contemporary prospective series, in which patient factors have been collected systematically and rigorously.

Methods

This analysis makes use of data from the SCORAD trial [14], which is the largest randomised trial in patients with MSCC. The primary aim of the trial was to compare a single dose of 8Gy with 20Gy in 5 fractions in terms of ambulatory status at 8 weeks. The detailed results of SCORAD have been published previously [14]. There were no clinically important differences in ambulatory status, overall survival (OS), recovery or pain control between the dose groups, such that patients can be treated with the single dose.

Here, we aim to develop a model for overall survival and ambulatory status status at 8 weeks. Using key variables (radiotherapy dose, ambulatory status, primary tumour and extent of metastases), the SCORAD dataset was randomly divided into two groups: a training set to develop the model, and a validation set to test the model in an internal independent dataset and produce measures of prognostic performance. The training set included 412 patients (60%) with 205 deaths by 13 weeks and 198 patients assessed for ambulatory status at 8 weeks (136 with ambulation grade 1-2 and 62 with grade 3-4); where grade 1 is defined as ambulatory without the use of walking aids and complete muscle power in all muscle groups, and grade 4 as absence (0/5 muscle power) or flicker (1/5 muscle power) of motor power in any muscle group. Although the validation set had 274 patients (40%), only 240 patients with survival status information available at 13 weeks and 141 with ambulatory status at 8 weeks were included in the survival and ambulatory status analyses, respectively. In the validation set, there were 128 deaths and 112 alive patients by 13 weeks, and at 8 weeks 104 patients presented a grade 1-2 and 37 a grade 3-4 ambulatory status. We had more patients (and events) in the training dataset (60:40 split) to produce a more reliable model (decided before the analysis).

The following baseline factors were considered: radiotherapy dose, sex, age, extent of metastases, number of MSSC sites, baseline bowel function, baseline bladder function, prior

chemotherapy, prior radiotherapy, prior hormonal therapy, baseline ambulatory status, primary tumour and location of MSCC site.

In the training set, a multivariable regression was performed; first using all of the baseline factors (model 1), and then a backward selection regression was applied to identify a subset of all factors that together are expected to have the best prognostic performance (model 2) using a significance level of ≤0.10 for inclusion of a factor [15]. A Cox regression was used for predicting OS, and a logistic regression for predicting ambulatory status at 8 weeks.

The regression coefficients from models 1 and 2 were then applied to each patient in the validation dataset to produce a prognostic score. The prognostic performance for each model and each outcome measure was then assessed using Receiver Operating Characteristic (ROC) curve analysis [16]. ROC curves were used to estimate sensitivity (percentage of patients who died by 13 weeks who had a prognostic score above a certain threshold [OS], or percentage who had ambulatory grade 1-2 with scores exceeding a threshold), and false-positive rate (percentage of patients who were alive at 13 weeks who had a prognostic score above a certain threshold [OS], or percentage who had ambulatory grade 3-4 with scores exceeding a threshold).

To make the chosen model easy to use in clinical practice, we developed nomograms [17] using the regression coefficients estimated in the training dataset. The nomogram converts each specific baseline characteristic of a patient into a score, then the sum of scores is used to predict their expected survival rate at 8, 13, 26 and 52 weeks or their probability of ambulatory status at 8 weeks.

In addition to the SCORAD trial, we also used a real-world registry database of 348 consecutive patients in routine practice who presented with MSCC and were treated between 2016 and 2020 at the Christie Hospital, Manchester, UK as an external independent dataset.

This dataset had survival data (195 deaths by 13 weeks) but not ambulatory status data at follow-up. Therefore, it could only be used to externally validate our prognostic model for survival.

The association between the predicted OS using the prognostic model and observed OS was evaluated using Harrell's C-statistic and Cox regression, in the external Christie data. This was done by categorising the prognostic score into tertiles, and examining the Kaplan Meier plots in each tertile.

Results

SCORAD included 686 patients of whom 341 were randomised to 20Gy/5f and 345 to 8Gy/1f. There was no difference in OS between the two arms (HR=1.02, 95%CI: 0.86 to 1.21), and the Kaplan-Meier curves almost completely overlaid each other. Among all patients, the 8, 13, 26- and 52-weeks OS rates were 63%, 50%, 36% and 19%, respectively. These are consistent with other published series of patients with MSCC in the literature. A total of 342 patients were assessable at 8 weeks for ambulatory status of whom 243 (71%) had grade 1-2.

The training and validation datasets were well balanced for patient characteristics (Table 1). OS was similar between these two datasets. The median OS in training dataset was: 12.6 weeks (95%CI: 10.1 months to 14.4 months) and in the validation dataset: 14.7 weeks (95%CI: 11.3 months to 18.6 months).

There were 136/198 (69%) who achieved positive ambulatory status in the training set and 104/141 (74%) in the validation set (p=0.31). Appendix Table 2 shows the characteristics of patients from the external registry dataset (348 patients, 280 deaths).

Using the training dataset, the multivariable analyses are shown in Table 2. Using either model 1 or 2, the same factors were found to significantly increase the risk of death: being male, having lung, gastrointestinal, and other types of cancer, compression at C1-T12, presence of non-skeletal metastases and poor baseline ambulatory status (grade 3-4) (all $p<0.05$). Figure 1 (upper) shows the ROC curves for models 1 and 2 in predicting OS at 13 weeks among patients in the validation dataset and model 2 in the external registry set. There was no difference in prognostic performance between the two models (AUC 74% vs 75%, $p=0.21$), confirming that the subset of factors (model 2) is an appropriate choice, and including additional factors does not improve prognostic performance. The AUC in the Christie dataset was 68% (95%CI: 62 to 74). From Figure 2, model 2 had high sensitivities but also moderately high false-positive rates, in both the validation and external Christie datasets. For example, at a score cut-off of ≥12 (corresponding to a predicted risk of dying at 13 weeks of 46.5%), the sensitivities are 69% (SCORAD) and 69% (Christie), with corresponding false-positive rates of 35% and 41%.

Figure 3(a) shows the nomogram, with a worked example. Appendix table 3(a) shows the numerical scores associated with each factor produced by the model. The estimated Harrell's C-statistic for the association between the nomogram prognostic score and survival time was 0.67 (95%CI: 0.63 to 0.71) in the SCORAD validation data.

In the external Christie dataset, the prognostic score using our nomogram was strongly associated with OS (Figure 4) with a Harrell's C-statistic of 0.62 (95%CI: 0.58 to 0.65); HRs were 1.33 ($p=0.05$) for medium score and 2.16 ($p<0.001$) for high score, each compared to the low score group.

Table 2 shows the results from the logistic regression for ambulatory status in the SCORAD training dataset. Only four factors were selected by the backward selection regression, so model 2 contained: primary tumour, ambulatory status, bladder function and prior

chemotherapy. In the SCORAD validation set, the ROC AUC for models 1 was 70% (95% CI 59-81) and for model 2 it was 72% (95% CI 63-82) (Figure 1, lower). The prognostic score model was associated with high sensitivities and relatively high false-positive rates (Figure 2). For example, based on the SCORAD validation set, using a threshold of ≥0.65 for the chance of having ambulatory status grade 1-2, the sensitivities are 74% with corresponding false-positive rates of 49%.

The nomogram with a worked example is shown in Figure 3 (b) and Appendix table 3(b) shows the numerical scores associated with each factor produced by the model.

Discussion

SCORAD is, to date, the largest prospective dataset of patients with metastatic spinal cord compression receiving radiotherapy. This analysis has identified clinically relevant factors to guide clinical practice using both an internal validation dataset for ambulatory status and OS and an external validation set for OS. Primary tumour, baseline (pre-treatment) ambulatory status, bladder function and prior chemotherapy were significantly associated with ambulatory status at 8 weeks; while gender, primary tumour, location of MSCC site, presence of non-skeletal metastases and baseline ambulatory status were associated with OS.

This study identified that patients with breast or prostate primary tumours with preserved mobility and normal bladder function who have received no prior chemotherapy have the best outcome for ambulatory status. Female patients with breast cancer and MSCC below T12 presenting with preserved mobility and having no extra-skeletal metastases have the best outcome for survival. These findings are both plausible and consistent with other published data and clinical observations [3,4,5, 6,7,8,9,10,11,12,13,18 The ROC AUC for the survival analysis was 0.68 (95%CI: 0.62 to 0.74) which compares to 0.71 (95% CI not given) from the updated Tokuhashi dataset [19] and 0.72 (95% CI, 0.68–0.77) from the Barthels index [9], the only two which report an ROC analysis in their publications.

The strengths of this study are that the prognostic model development represents a large modern series of patients treated in a consistent way with rigorous follow-up and high-quality recording of patient characteristics, in a randomised trial setting. This has enabled a model to be developed for ambulatory status measured objectively using a four-point scale whereas other models focus on OS except for one retrospective analysis in breast cancer patients [18]. Another key strength is that we had two independent validation datasets for OS: internal (SCORAD) and external (Christie Hospital) in which patient and tumour characteristics represent real world observations. Although these generally differed from SCORAD, the prognostic performance of our model was close. This model has a moderately high false-positive rate which is acceptable as it helps to identify most of the patients who will die early. External validation is an important criterion when evaluating a prognostic model [20], but none of the previously proposed models (Appendix Table 1) were applied to external datasets.

The most widely used model prior to our study is the Tokuhashi score with over 200 citations predominantly in the surgical literature [3,4,5]. Common themes emerge in these previous models, with most showing that better performance status, absence of extra-skeletal metastases and solitary rather than multiple bone metastases are associated with better survival. Consistent patterns in primary tumour type are seen, with lung cancer having universally the worse prognosis, while patients with breast cancer, myeloma and lymphoma tended to have the best prognoses. A large validation study in 1,469 patients in the Global Spine Tumour Study Group database evaluated the prognostic indices in Appendix Table 1 [21] calculating Harrell's C-statistic which measures the utility of a prognostic model for each. The range of C-statistic was 0.54 to 0.66 with the highest being for the Bollen index [13]. However, the Bollen evaluation was based on patients treated with a mixture of surgery and radiotherapy and therefore has limited relevance to the SCORAD population in which all patients received radiotherapy. The model presented here performs slightly better with a C-

statistic of 0.67 and it is of greater relevance to current practice because it reflects a contemporary series receiving supportive and systemic treatment, which has changed considerably since the publication of the studies dating from 1990 to 2014.

The main limitations of our study were that the SCORAD patients predominantly had advanced disease (median OS 13 weeks) and therefore there was a considerable loss of evaluable patients by the 8 week time point.Many had prostate cancer (44%) and patients with a better prognosis, those with breast primary and limited disease, were not well represented; patients with myeloma and lymphoma were ineligible for the trial but they do only account for <5% of all cases of MSCC [20]. However, in the external validation dataset, where only 24% had prostate cancer, the prognostic model had a ROC AUC of 68%, sufficiently close to 75% from SCORAD (p=0.10). When external cohorts are not too similar to the internal cohorts, in this case, a lower median survival, this represents one of the main reasons for having an external cohort, ie to see if the model works similarly in variable patient groups as would be expected in routine practice. However, despite the difference in survival the performance of the model was consistent (AUC 0.67: 95% CI 0.62-0.74), compared to ~0.74 for the validation dataset. External validation of the prognostic model for ambulatory status would be useful although this is often poorly recorded in routine practice. The generalisability of both models would benefit from further external validations, including among patients with better survival. Given the size of the training dataset we were unable to reliably examine interactions between some of the factors, which may potentially influence the model specification and estimates. Finally, some variables such as site of MSCC Group 3 (T6-L5) had small numbers.

When faced with a patient presenting with spinal cord compression, two important factors which direct management are the likelihood of restoring or retaining mobility and the predicted survival of the patient. Using the largest prospective randomised dataset in metastatic spinal cord compression, we have identified a set of patient and tumour factors that

most influence mobility and survival. In practice clinical decisions will take into account a number of factors not included here including the likely response of the tumour to further treatment, patient frailty, comorbidity and the views of the patient with regard to active treatment. When discussing with a patient the value of treatment the two prognostic indices and nomograms presented here should be used in conjunction with each other. Clearly in a patient with a predicted short survival and little likelihood of recovering ambulation it may be reasonable to withhold radiotherapy. More difficult cases will be those with contrary predictions, either short survival with high likelihood of recovery or long survival with low likelihood of recovery. In the former case, given the substantial morbidity of paraplegia treatment should be considered, and the advantage of a single dose of radiotherapy is particularly strong in this group with short survival. However where there is little chance of recovery despite a longer predicted survival the case for radiotherapy may be less compelling. Alongside this the role of single dose radiotherapy for local pain should never be forgotten. In conclusion the prognostic indices for survival and recovery of ambulation reported here may be used to individualise management considering the likelihood of these important outcomes. It is however important to realise that any model has limitations and ultimately a comprehensive clinical assessment of each patient is required to deliver optimal patient care.

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Figure captions

Figure 1: ROC curves for predictive performance for overall survival at 13 weeks for Model 1 and Model 2 in the SCORAD validation dataset

Figure 2(a): Prognostic performance in terms of sensitivity and false positive rate derived from overall survival model 2 applied to the SCORAD validation set and to the Christie Hospital set

Figure 2(b): Sensitivity and false positive rate from multivariable model 1 and model 2 for positive ambulatory response in the SCORAD validation dataset (N=141)

Figure 3 (a): Nomogram for prognostic factors for overall survival in patients MSCC derived from model 2 (for more information use Supplementary 3). An example calculation is shown of a male (2.94) with GI cancer (7.81), no non-skeletal mets (0), with cord compression at C1-T12 (2.54) and ambulatory status 2 (3.92). This gives a total score of 17.21 reflecting a ≈45% probability of surviving beyond 8 weeks or ≈27% probability of surviving beyond 13

weeks or ≈14% probability of surviving beyond 26 weeks or ≈3% probability of surviving past 52 weeks.

Figure 3 (b): Nomogram for prognostic factors for ambulatory status at 8 weeks in patients MSCC derived from model 2 (for more information use Supplementary 4). An example calculation is shown of a patient with breast cancer (7.83), ambulatory status 2 (8.04) who received prior chemotherapy (0) and has normal bladder function (5.06). This gives a total score of 20.93 reflecting a ≈60% probability of being ambulant at 8 weeks after treatment.

Figure 4: Association between survival and the model prognostic score from nomogram in the registry dataset (N=348). The HR for score as continuous was 1.07 (95%CI: 1.05 to 1.10), p<0.001. The HR for medium score (≥9.78 to <15.16) vs low score (<9.78) was 1.33 (95%CI: 1.00 to 1.78), p=0.05 and HR for high score (≥15.16) vs low score (<9.78) was 2.16 (95%CI: 1.61 to 2.91), p<0.001.

Table 1: Demographics of training and validation sets from XXXXXX trial

Variables	Training	Validation
	N=412	N=274
Treatment		
20Gy/5f	204 (50%)	137 (50%)
8Gy/1f	208 (50%)	137 (50%)
Sex		
Male	301 (73%)	202 (74%)
Female	111 (27%)	72 (26%)
Age (years)		
<65 years	117 (28%)	87 (32%)
≥65 years to <75 years	164 (40%)	93 (34%)
≥75 years	131 (32%)	94 (34%)
Primary tumour		
Prostate	183 (44%)	121 (44%)
Lung	81 (20%)	51 (19%)
Breast	46 (11%)	33 (12%)
GI	43 (10%)	30 (11%)
Other	59 (14%)	39 (14%)
Renal	12 (20%)	11 (28%)
Gynaecological	3 (5%)	3 (8%)
Skin	8 (14%)	7 (18%)
Bladder	7 (12%)	4 (10%)
Head & neck	5 (8%)	1 (3%)
Sarcoma	7 (12%)	1 (3%)
Other/Unknown	17 (29%)	12 (31%)
Location of SCC site		
Group 1 (C1- T12)	296 (72%)	196 (72%)
Group 2 (L1-S2)	92 (22%)	67 (24%)
Group 3 (T6-L5)	22 (5%)	11 (4%)
Not reported	2 (0%)	0%
Extent of Metastases		
Nonskeletal mets absent	223 (54%)	148 (54%)
Nonskeletal mets present	189 (46%)	126 (46%)
No of SCC Sites		
Single Site of Compression	368 (89%)	246 (90%)
Multiple Sites of Compression	44 (11%)	28 (10%)
Baseline ambulatory status		
1	90 (22%)	63 (23%)
2	180 (44%)	118 (43%)
3	108 (26%)	73 (27%)
4	34 (8%)	20 (7%)
Baseline bladder function		
Normal	316 (77%)	189 (69%)
Abnormal	94 (23%)	84 (31%)
Not reported	2 (0%)	1 (0%)
Baseline bowel function		
Normal	206 (50%)	134 (49%)
Abnormal	204 (50%)	139 (51%)

Not reported	2 (0%)	1 (0%)
Prior chemotherapy		
No	366 (89%)	243 (89%)
Yes	46 (11%)	31 (11%)
Prior hormone therapy		
No	270 (66%)	172 (63%)
Yes	142 (34%)	102 (37%)
Prior radiotherapy		
No	329 (80%)	220 (80%)
Yes	83 (20%)	54 (20%)
Overall Survival		
Median in weeks (95%CI)	12.6 (10.1 to 14.4)	14.7 (11.3 to 18.6)
Rate at 13 weeks	49% (44% to 54%)	53% (46% to 58%)
Survival status at 13 weeks from randomisation		
Died ≤13 weeks	205 (50%)	128 (47%)
Alive >13 weeks	166 (40%)	112 (41%)
Censored ≤13 weeks	41 (10%)	34 (12%)
Ambulatory status at 8 weeks*		
Assessed at 8 weeks	198 (48%)	141 (51%)
Grade 1 or 2	136 (69%)	104 (74%)
Grade 3 or 4	62 (31%)	37 (26%)

* Three patients with positive ambulatory status in the training dataset were excluded from the table because they had missing data in at least one of the prognostic factors considered

Table 2: Multivariate regression model 1 and model 2 estimates for overall survival (Cox regression) and for positive ambulatory status at 8 weeks (logistic regression). Model 1 includes all baseline factors and Model 2 is the subset identified from backward selection.

Prognostic factors	Overall survival					Logistic regression: positive ambulatory status at 8 weeks*			
	Cox Model 1 (N=408) (all factors)		Cox Model 2 (N=410) (subset of factors)			Model 1 (N=198) (all factors)		Model 2 (N=198) (subset of factors)	
	HR (95CI)	p	HR (95CI)	p		OR (95CI)	p	OR (95CI)	p
Primary tumour									
Prostate	1.00 (reference)	P<0.001	1.00 (reference)	P<0.001		1.00 (reference)	0.02	1.00 (reference)	0.0001
Lung	4.28 (2.86 to 6.4)		3.94 (2.83 to 5.49)			0.18(0.04 to 0.76)		0.13 (0.04 to 0.42)	
Breast	1.11 (0.66 to 1.88)		1.10 (0.65 to 1.85)			1.3(0.22 to 7.58)		1.00 (0.31 to 3.2)	
GI	3.12 (2.01 to 4.85)		2.95 (2.00 to 4.33)			0.15(0.03 to 0.75)		0.13 (0.03 to 0.49)	
Other	2.53 (1.67 to 3.83)		2.39 (1.66 to 3.44)			0.39(0.09 to 1.69)		0.22 (0.08 to 0.63)	
Ambulatory status									
1	1.00 (reference)	0.0001	1.00 (reference)	P<0.001		1.00 (reference)	0.0001	1.00 (reference)	0.0007
2	1.64 (1.2 to 2.24)		1.72 (1.26 to 2.34)			0.52(0.19 to 1.43)		0.59 (0.23 to 1.53)	
3	2.31 (1.62 to 3.29)		2.49 (1.79 to 3.47)			0.10(0.03 to 0.36)		0.16 (0.05 to 0.5)	
4	1.88 (1.14 to 3.11)		2.00 (1.28 to 3.14)			0.03(0.003 to 0.24)		0.07 (0.01 to 0.39)	
Sex									
Male	1.00 (reference)		1.00 (reference)			1.00 (reference)		-	-

Female	0.67 (0.48 to 0.94)	0.02	0.66 (0.47 to 0.92)	0.02		0.87(0.26 to 2.95)	0.825	-	-
Location of SCC site									
Group 1 (C1-T12)	1.00 (reference)	0.02	1.00 (reference)	0.02		1.00 (reference)	0.02	-	-
Group 2 (L1-S2)	0.71 (0.54 to 0.95)		0.70 (0.53 to 0.93)			1.43(0.52 to 3.89)		-	
Group 3 (T6-L5)	0.69 (0.42 to 1.13)		0.71 (0.44 to 1.16)			3.73(0.81 to 17.13)		-	
Nonskeletal mets									
Absent	1.00 (reference)		1.00 (reference)			1.00 (reference)		-	-
Present	1.29 (1.02 to 1.63)	0.03	1.32 (1.05 to 1.65)	0.02		1.00 (0.44 to 2.27)	0.03	-	-
Baseline bladder function									
Normal	1.00 (reference)		-	-		1.00 (reference)		1.00 (reference)	
Abnormal	1 (0.74 to 1.35)	0.99	-	-		0.26(0.1 to 0.73)	0.01	0.27 (0.1 to 0.69)	0.007
Prior chemotherapy									
No	1.00 (reference)		-	-		1.00 (reference)		1.00 (reference)	
Yes	1.11 (0.78 to 1.57)	0.57	-	-		0.30(0.09 to 1.02)	0.05	0.31 (0.11 to 0.93)	0.04
Treatment									
20Gy/5f	1.00 (reference)		-	-		1.00 (reference)		-	
8Gy/1f	1.1 (0.88 to 1.38)	0.4	-	-		0.52(0.23 to 1.19)	0.12	-	-
Age									
<65 years	1.00 (reference)	0.4	-	-		1.00 (reference)	0.18	-	-
≥65 years to <75 years	1.2 (0.91 to 1.59)		-	-		1.22(0.48 to 3.11)		-	-
≥75 years	1.17 (0.87 to 1.59)		-	-		2.54(0.88 to 7.36)		-	-
Number of SCC sites									
Single Site	1.00 (reference)		-	-		1.00 (reference)		-	-

Multiple Sites	1.17 (0.81 to 1.68)	0.41	-	-		0.43(0.12 to 1.64)	0.218	-	-
Baseline bowel function									
Normal	1.00 (reference)		-	-		1.00 (reference)		-	-
Abnormal	1.09 (0.86 to 1.39)	0.47	-	-		1.13(0.5 to 2.53)	0.77	-	-
Prior hormonal therapy									
No	1.00 (reference)		-	-		1.00 (reference)		-	-
Yes	1.08 (0.78 to 1.48)	0.65	-	-		1.55(0.55 to 4.34)	0.409	-	-
Prior radiotherapy									
No	1.00 (reference)		-	-		1.00 (reference)		-	-
Yes	1.12 (0.84 to 1.48)	0.45	-	-		0.76(0.29 to 2.02)	0.585	-	-
Baseline odds	-	-	-	-		12.28 (2.92 to 51.54)	-	15.34 (5.66 to 41.59)	-

Figure 1: ROC curves for predictive performance for overall survival at 13 weeks for Model 1 and Model 2 in the SCORAD validation dataset

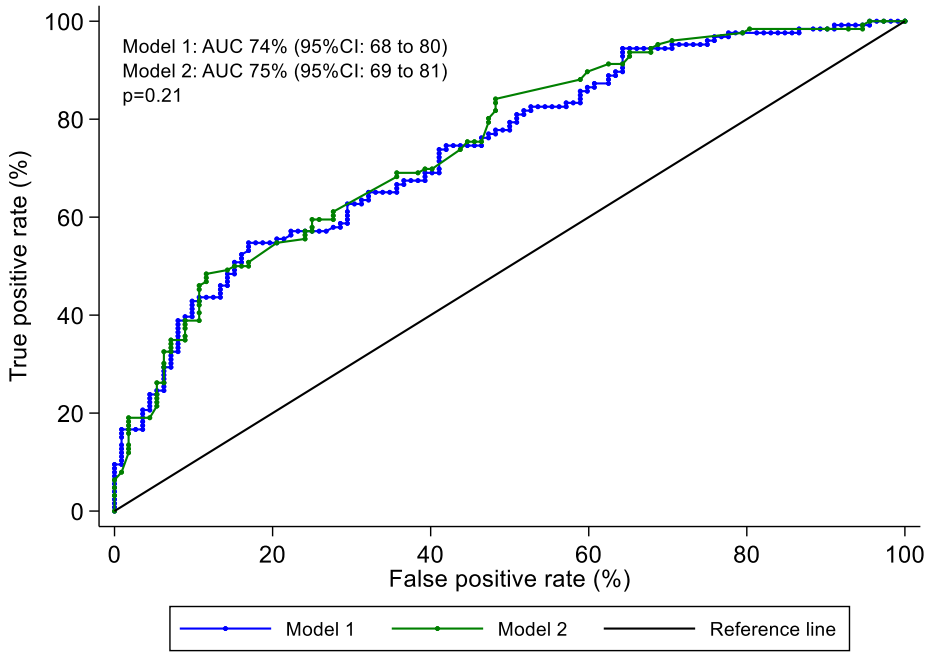


Figure 2(a): Prognostic performance in terms of sensitivity and false positive rate derived from overall survival model 2 applied to the SCORAD validation set and to the Christie Hospital set

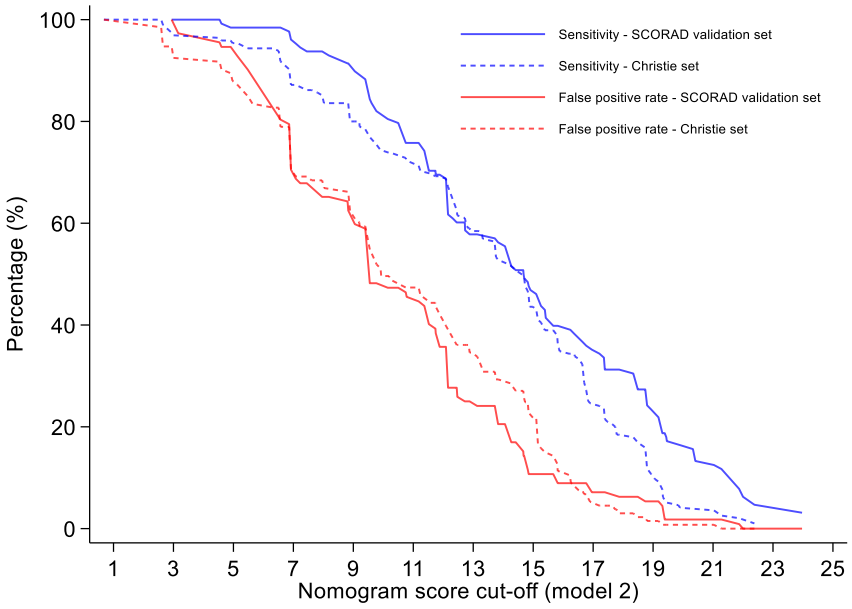


Figure 2(b): Sensitivity and false positive rate from multivariable model 1 and model 2 for positive ambulatory response in the SCORAD validation dataset (N=141)

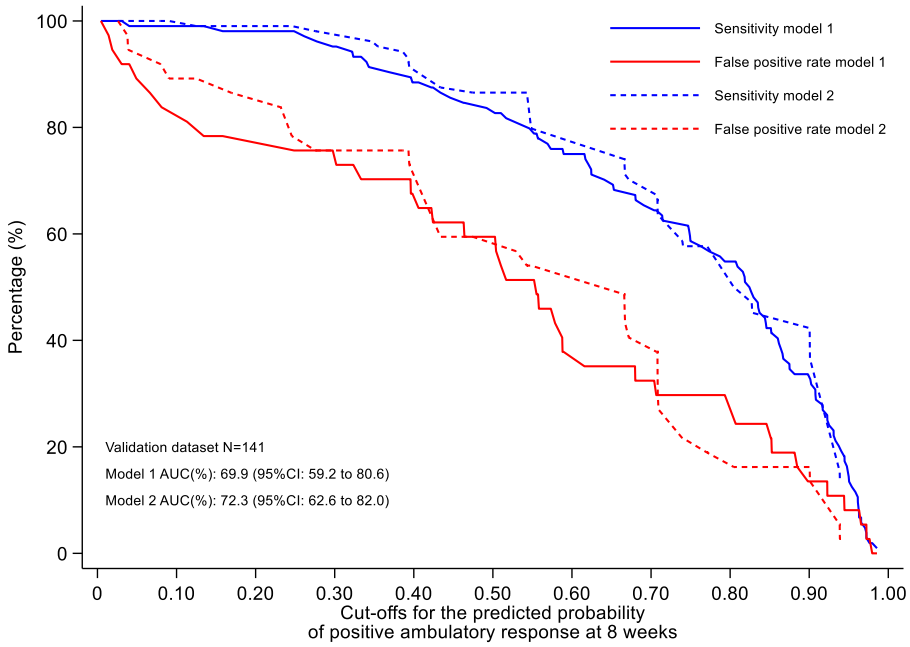


Figure 3 (a): Nomogram for prognostic factors for overall survival in patients MSCC derived from model 2 *(for more information use Supplementary 3). An example calculation is shown of a male (2.94) with GI cancer (7.81), no non-skeletal mets (0), with cord compression at C1-T12 (2.54) and ambulatory status 2 (3.92). This gives a total score of 17.21 reflecting a ≈45% probability of surviving beyond 8 weeks or ≈27% probability of surviving beyond 13 weeks or ≈14% probability of surviving beyond 26 weeks or ≈3% probability of surviving past 52 weeks.*

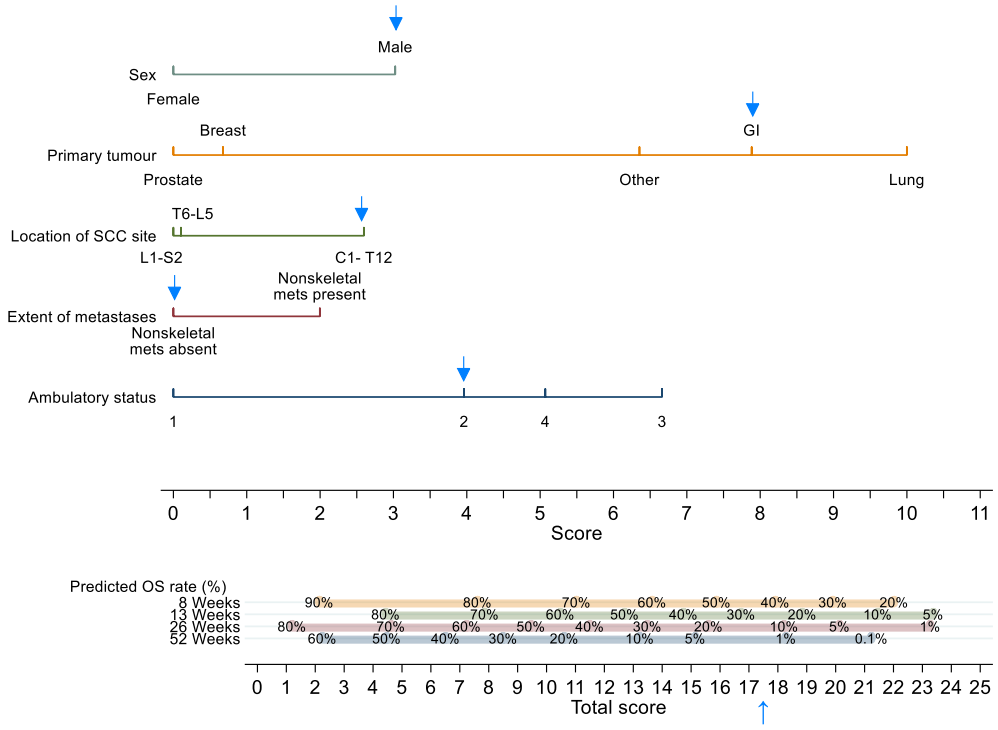
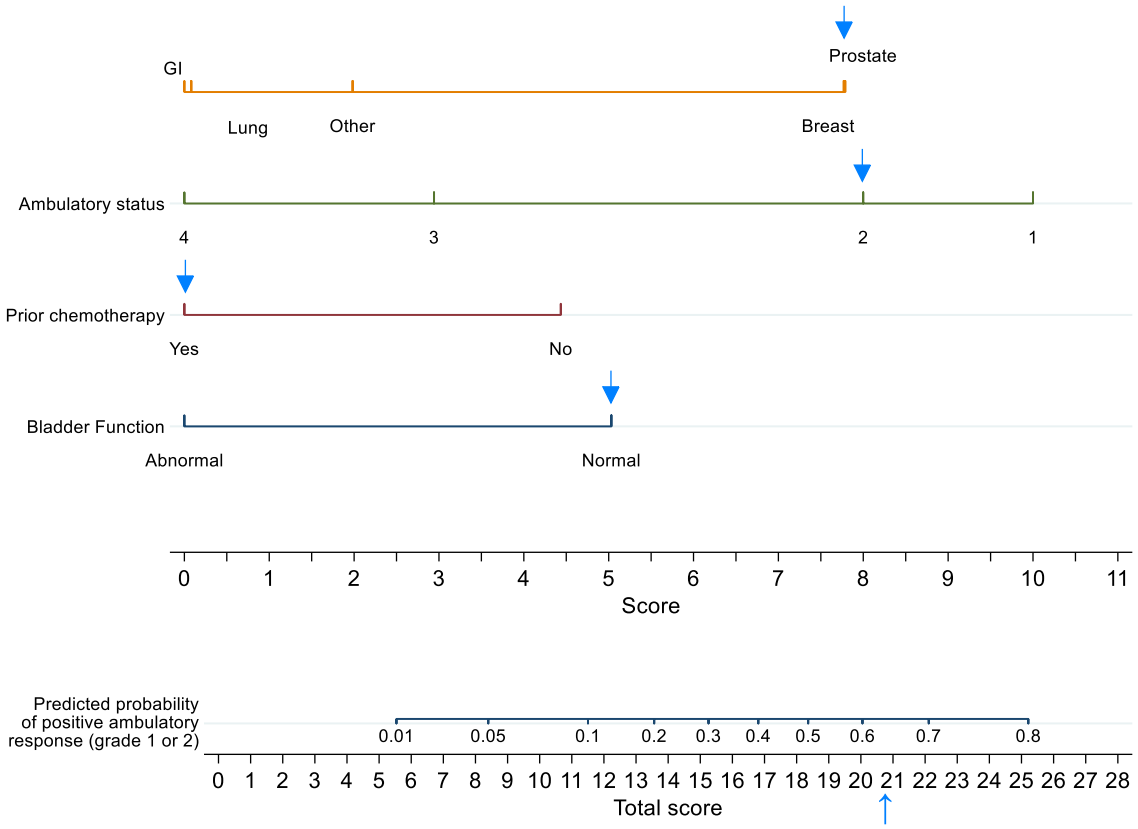


Figure 3 (b): Nomogram for prognostic factors for ambulatory status at 8 weeks in patients MSCC derived from model 2 (for more information use Supplementary 4). *An example calculation is shown of a patient with breast cancer (7.83), ambulatory status 2 (8.04) who received prior chemotherapy (0) and has normal bladder function (5.06). This gives a total score of 20.93 reflecting a ≈60% probability of being ambulant at 8 weeks after treatment.*



Positive response = SCORAD grade 1 or 2 ie ambulatory without the use of walking aids and grade 5 of 5 muscle power in all muscle groups or ambulatory with assistance of walking aids or grade 4 of 5 muscle power inany muscle group.

Figure 4: Association between survival and the model prognostic score from nomogram in the registry dataset (N=348). The HR for score as continuous was 1.07 (95%CI: 1.05 to 1.10), p<0.001. The HR for medium score (≥9.78 to <15.16) vs low score (<9.78) was 1.33 (95%CI: 1.00 to 1.78), p=0.05 and HR for high score (≥15.16) vs low score (<9.78) was 2.16 (95%CI: 1.61 to 2.91), p<0.001.