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A Case-Matched Study Comparing Surgery to No Surgery in Patients with Metastatic Spinal Cord Compression

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Abstract

Background: Patients with MSCC present with pain and/or neurological loss. NICE guidance recommends surgery to prevent paralysis or manage pain in paralysed patients. There is only one RCT comparing surgery with no surgery, which strongly recommends surgery, however, there have been advances in radiotherapy with better local control and lower normal tissue toxicity.

Objectives: To compare surgery with no surgery for neurological change, survival, length of stay and re-admissions.

Methods: A case-matched cohort study. To overcome the ethical difficulty of not offering surgery to MSCC patients; patients declining offered surgery were matched with patients proceeding with surgery. Twenty-seven patients declining surgery were matched to 54 receiving surgeries. Match criteria were in order by the primary tumour, presentation neurological grade (ambulatory, weight-bearing, bed-bound and paralysed), co-morbidities (ASA grade), age and gender. Data collected from the MSCC database, clinical letters and clinical coding. Statistical analysis used GraphPad Prism version 8.2.

Results: Matching accuracy was confirmed with no significant difference shown between the groups, $p>0.6$. Of those declining surgery, 3 improved and 3 deteriorated by 1 grade. Of those proceeding with surgery, improvement occurred in 1 by 2 grades and 5 by 1 grade; deterioration occurred in 3 by 2 grades and 9 by 1 grade. The net neurological grade change with no surgery was 0 whereas with surgery there was a loss of 8 grades ($p=0.047$).

At 3 months, survival rates were 83% in the surgery group and 61% in the no surgery group ($p=0.05$). The average initial length of stay in the surgery group was 21 vs. 10 days in the no surgery group ($p<0.001$). Readmission rates were similar between the groups.

Conclusion: Surgery resulted in a higher proportion of patients deteriorating neurologically and a longer length of stay but patients lived longer.

Keywords: Case-matched; Metastases; MSCC; Spinal metastases; Neurological outcomes

Background

The latest Cancer Research UK (United Kingdom) figures estimate a lifetime cancer risk of 1 in 2 for those born after 1960 [1]. UK incidence is ranked higher than 90% of the world and two-thirds of Europe [1]. The incidence of metastatic spinal cord compression (MSCC) is 5-10% of all cancers with a lifetime risk of 2.5 to 5% [2]. MSCC can be the first presentation of cancer and usually presents with pain and/or neurological loss.

Patchell et al. conducted the only RCT comparing surgery and radiotherapy to radiotherapy alone in 2005 [3]. The RCT was stopped early as there was a clear benefit seen in the surgery group. Subsequently, running other RCTs have been hampered by ethics.

In the UK, in 2008, the National Institute for Clinical Excellence (NICE) guidelines (CG75) on MSCC recommended urgent decompression with or without stabilisation for patients with spinal metastases and spinal instability to prevent paralysis. NICE also recommended surgery in patients with spinal metastases and mechanical pain resistant to conventional analgesia, even if completely paralysed [4]. Despite the NICE guidelines there remains a wide variation in the threshold for surgical intervention for MSCC patients.

Objectives

To compare surgery with no surgery for short-term neurological function, length of hospital stay, re-admissions and 1-year survival.

Methods

Regional database, clinical letters and clinical coding, and Hospital Episode Statistic (HES) data were used. The project was registered as an audit at the University Hospital of Leicester (10551). A regional database was started in 2014 and has been regularly upgraded to the current scannable admission booklet completed on the initial presentation. Data collected included demographics, type of treatment given, the primary tumour, neurological function on presentation and discharge, co-morbidities, the initial length of stay, re-admission and survival. Survival was collected for a minimum of 1 year.

Neurological function was divided into 4 grades:

1. Ambulatory: ability to independently walk to the desired destination with or without walking aids and an MRC grade 4 or 5.
2. Weight-bearing or transferring: ability to stand or transfer from bed to chair and an MRC grade of 3 or more.
3. Bedbound: ability to move freely in bed but the inability to weight-bear and an MRC grade of 2 more.
4. Paralysed: the inability to move in bed and an MRC grade of 0 or 1.

Twenty-seven patients were identified to have declined surgery when offered, case matching was performed at a ratio of 1:2. Matching criteria were by order of primary tumour, neurological function on presentation, comorbidities, age and gender. Comorbidities were graded using the American Society of Anesthesiologists (ASA) grades as well as individual conditions and diseases.

A posthoc analysis was performed on the surgical target segment to confirm the location of metastases was also similar between the groups.

Statistics

Categorical variables are presented in number and percentage (%). Continuous variables are presented as mean ± standard deviation or median ± range. The normality of data was tested by the Kolmogorov-Smirnov test when normality was rejected, a non-parametric test was used.

Comparisons used Chi-Squared and Fisher's Exact tests. Student t-test for normally distributed quantitative data and Mann-Whitney U test for non-parametric quantitative data between two groups. Survival analysis was performed using the Log-rank (Mantel-Cox) test and the Cox proportional hazard model. A p-value of <0.05 was considered statistically significant.

Results

The regional MSCC database provided 469 patients with MSCC; 171 had surgery and 271 did not and 27 declined surgery when offered (Figure 1). To overcome the ethical difficulty of not offering surgery to MSCC patients; patients declining offered surgery were matched with patients proceeding with surgery. Twenty-seven patients declining surgery were matched to 54 of the 171 patients that received surgery. Matching accuracy was confirmed with no significant difference shown between the groups, p>0.6. (Figures 2 and 3) (Table 1). Solid tumours – prostate, breast, renal cell carcinoma, lung and Multiple Myeloma were the commonest occurring tumours (Figure 2). The commonest neurological function on presentation was weight-bearing, representing just over 50% (Figure 3).

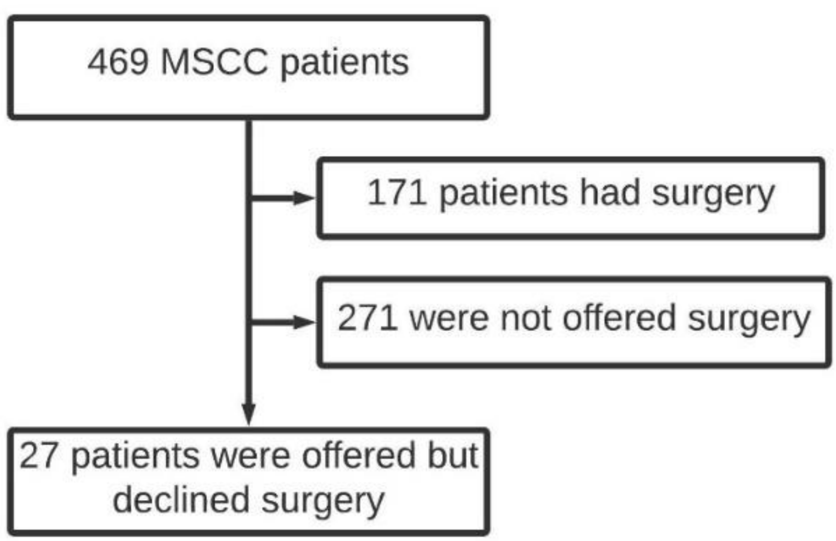

Figure 1: Flowchart of patients in the regional database.

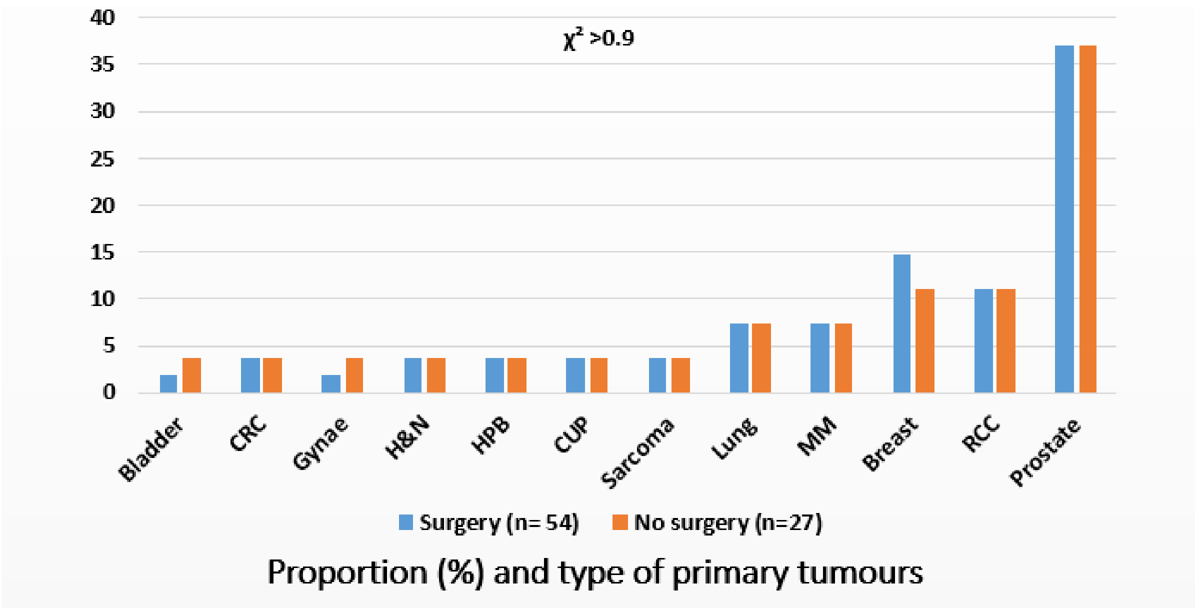

Figure 2: Matching accuracy of primary tumours.

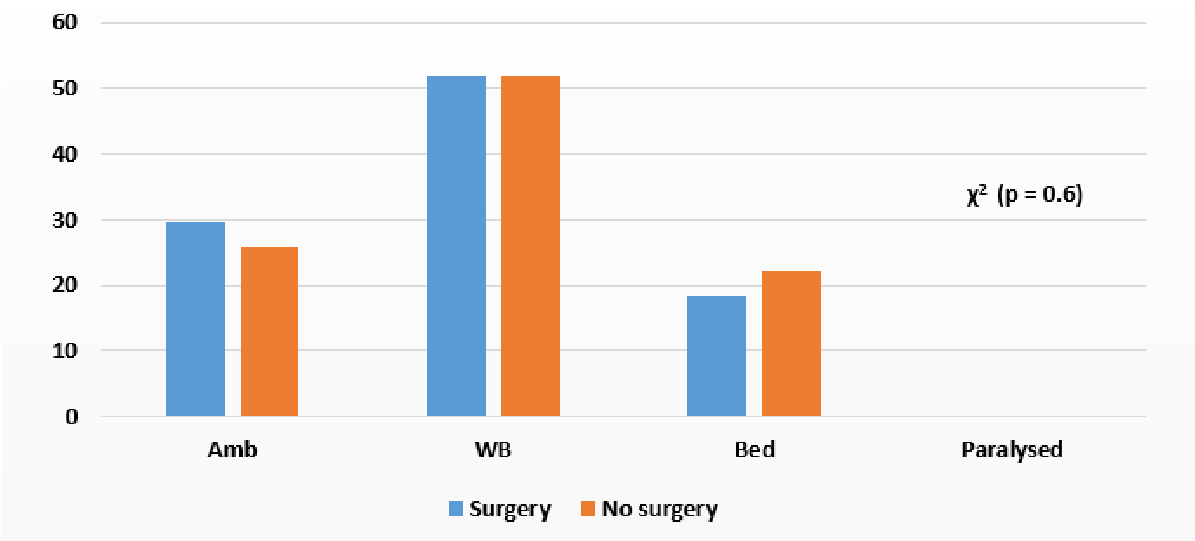

Figure 3: Matching accuracy of neurological function at presentation.

Table 1: Matching accuracy of ASA grade, age and gender.

	Surgery (54)	No Surgery (27)	p value
ASA l: ll: lll	24:41:35	33:26:41	0.8
Age (mean)	68	68	0.9
F: M	2.8:7.2	3:7	0.9

More patients deteriorated, by at least one neurologic grade, with surgery 13% (n= 7/54) vs. 4% (n=1/27) with no surgery. More patients improved with no surgery 11% (n=3/27) vs. 9% (n=5/54) with surgery, Chi-squared p=0.4 (Figure 4).

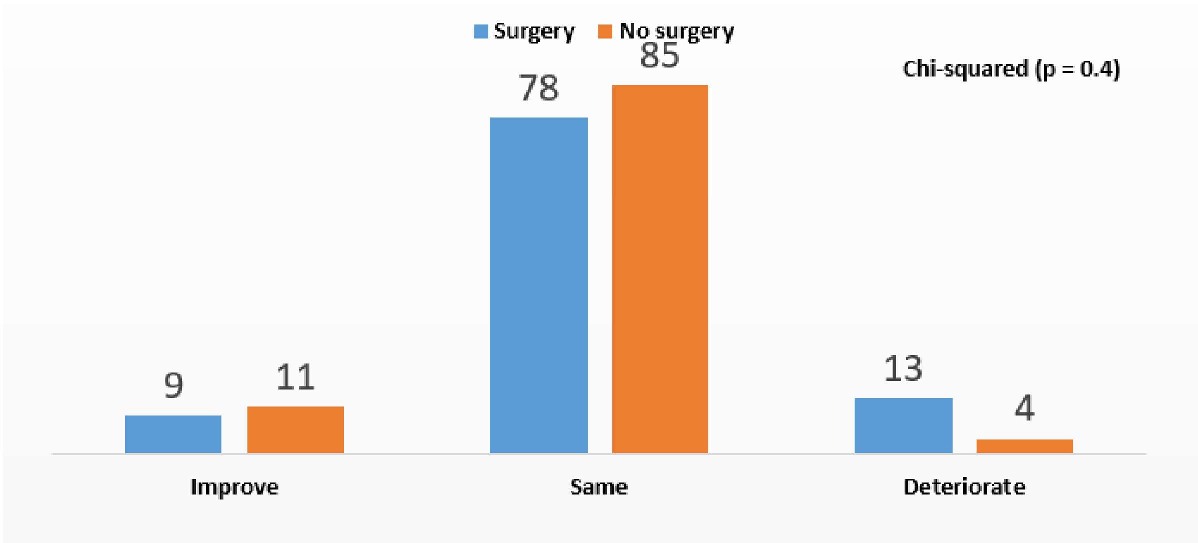

Figure 4: Barchart showing changes in neurological function from presentation to discharge.

In the 27 patients declining surgery, 3 improved by 1 grade compared to 5 improving by 1 grade and 2 improving by 2 grade in the 54 patients receiving surgery.

In the 27 patients declining surgery, 3 deteriorated by 1 grade, but 9 deteriorated by 1 grade and 6 deteriorated by 2 grades in the 54 patients receiving surgery.

The net change in neurological grade in the 27 patients declining surgery was zero, but the net change in neurological grade in the 54 patients receiving surgery was negative 8, (Fisher's exact p=0.047) (Table 2).

Table 2: Showing net change in neurological function.

Change in neurologic grade	**Surgery**	**No surgery**
Improved 2 grades	+2	0
Improved 1 grade	+5	+3
No change	0	0
Deteriorated 1 grade	-9	-3
Deteriorated 2 grade	-6	0
Net difference	-8	0
Fisher's exact p= 0.047		

The location of the surgical target segment was similar between the groups. Those declining surgery had a surgical target above the conus in 74% (n=20/27) vs. 76% (n=41/54) in those receiving surgery, below the conus in 19% (n=5/27) vs. 11% (n=6/54) and both above and below the conus in 7% (n=2/27) vs. 13% (n=7/54) respectively, (Chi-squared p=0.5).

The median length of stay was 7.5 days in those declining surgery compared to 15.5 days in those receiving surgery (Mann Whitney U p=<0.001). Also, 15% of those receiving surgery required intensive care admission (Table 3). Readmission rates were similar between the groups (Chi-squared p=0.46) (Figure 5). The median survival of 382 days in the surgery group compared to 185 days in the no surgery group, Log-rank (Mantel-Cox) p=0.05, Hazard Ratio 1.69 (95% CI 0.95 – 2.9) (Figure 6).

Table 3: Showing median length of stay and ITU admission.

Surgery	No Surgery	P value
15.5 (15% ITU)	7.5	Mann Whitney U <0.001

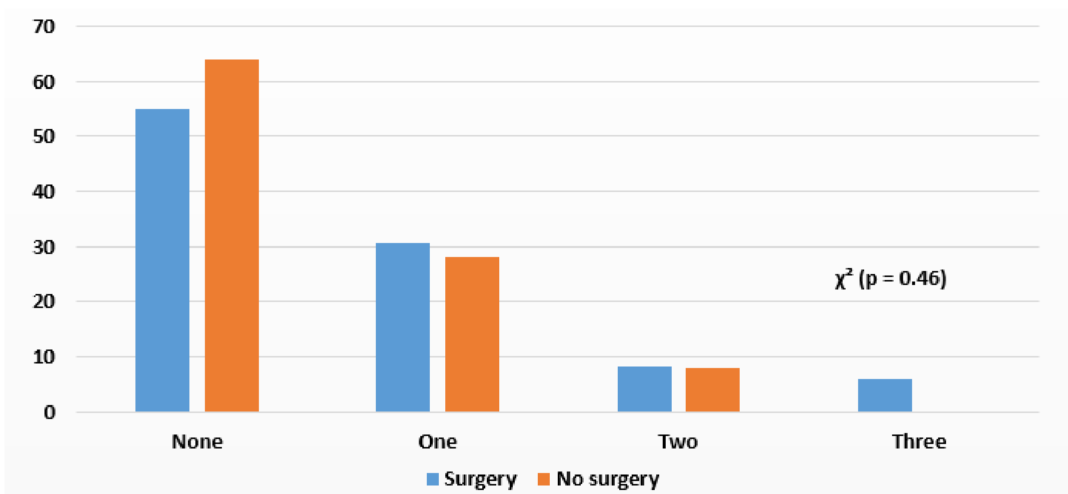

Figure 5: Bar chart showing readmission rates.

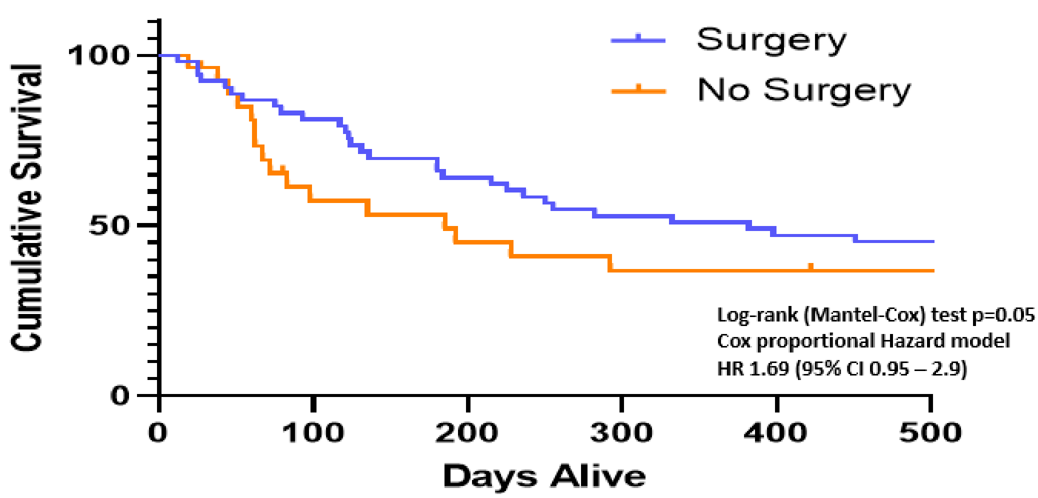

Figure 6: Kaplan Meir graph showing survival rates for surgery versus no surgery, red line depicts median survival.

There was no difference in survival between patients receiving decompression alone (n=17), decompression and stabilisation (n=27) or vertebral body augmentation (n=6) (Figure 7).

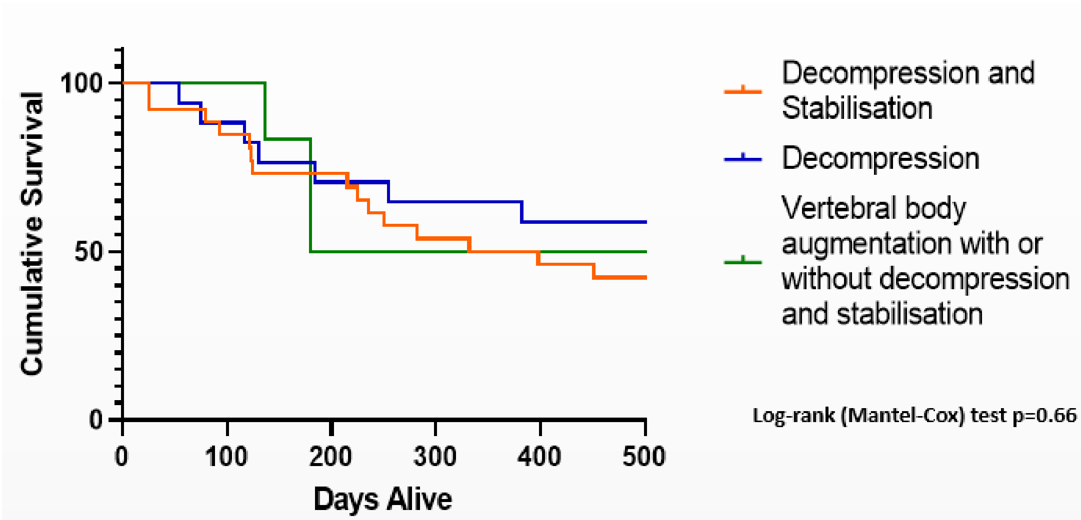

Figure 7: Kaplan Meir graph showing survival rates by operation type.

Discussion

In an attempt to make a comparison to the only RCT available in the literature, Patchell et al, we consolidated our neurological groups from 4 to 2. This enabled us to join the groups of patients able to walk or transfer and those bedbound or paralysed. Patchell had 68% of patients able to walk at presentation compared to 32% unable to walk, n=101. We had 80% of patients able to walk and 20% unable to walk at presentation, n=81. The patients in our study had a better starting neurology and thus more to lose. In the surgery group, Patchell had a 6% (2/34) deterioration in those able to walk at presentation compared to 16% (7/44) in our study group.

However, in the no surgery group, Patchell reported a 26% (9/35) lost their ability to walk compared to 5% (1/21) in our group. This could be explained by a longer follow-up by Patchell of 4 months compared to ours on discharge. Also, in the no surgery group, there were 19% (3/16) in the Patchell group that improved compared to 50% (3/6) in our group.

While these were not statistically significant, they showed a reverse trend between surgery and no surgery. In those 4 months from initial presentation, neurological injury from surgery could have improved, deterioration from metastases could progress and adjuvant treatments in the surgery group have been given.

In our study, no paralysed patients were offered surgery; this can be explained by the reluctance of most spinal surgeons to offer surgery to paralysed patients that present beyond 24 hours because of little to no chance of neurologic recovery, despite NICE guidelines.

Another observed difference between Patchell and our study is the difference in radiotherapy regime. While all patients received radiotherapy, the dose and number of fractions differed. Our patient cohort received 25Gy in 5 divided doses compared to Patchell with 30Gy divided into 10 doses.

Patients receiving surgery lived longer, 50% lived to 382 days vs. 185 days in those declining surgery. Although the groups had very similar survival in the first 6 weeks, which coincides with the start of Radiotherapy following surgery, there was a sharp decline in survivorship in the group declining surgery. An explanation for this could be that patients receiving surgery were mobilised with physiotherapy sooner thus reducing risks associated with prolonged immobility. Another possibility could be that patients declining surgery may have declined other treatments, although we did not find any evidence of this when looking at outpatient and ward and day care attendances for Oncological treatment.

Limitations

Our study aimed to match patients as closely as possible; we were limited by the small number of patients declining surgery. Our length of follow-up was short, from presentation to discharge. There were no pain scores available.

Conclusion

This is the first matched patient cohort study comparing short-term outcomes of surgery to no surgery. We have demonstrated that in the short-term patients undergoing surgical intervention are more likely to deteriorate neurologically. Surgical patients have a longer hospital stay and are more likely to be readmitted to the hospital post-discharge. Surgical patients do, however, live longer. Further work is required to look at longer follow-up, pain scores and outcome measures.

Author’s Contributions

- Sheweidin Aziz: Project idea, data collection, analysis, presentation, write up, review and submission.
- Omar A. Gabbar: Critique of methods and results and review of paper.
- Grahame J.S. Taylor: Project idea, supervision of project, statistical support, write up and review of paper.

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