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1 **FULL TITLE**

2 Survival of patients undergoing surgery for metastatic spinal tumours and the impact of surgical site
3 infection

4

5 **RUNNING TITLE**

6 SSI and survival in spinal tumour patients

7

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25

26 **SUMMARY**

27 **Background**

28 Patients with metastatic spinal tumours have a limited prognosis. Surgical complications which may
29 result in prolonged hospitalisation or readmission are highly undesirable. Surgical site infection (SSI)
30 is one such complication which can, in extreme cases, lead to death.

31 **Aim**

32 To assess the impact of SSI on patient survival after surgery for spinal metastases.

33 **Methods**

34 Demographic, operative and survival data were collected on 152 patients undergoing surgery for
35 spinal metastasis at a large UK tertiary referral centre. American Society of Anesthesiologists (ASA)
36 grade and the Revised Tokuhashi Score (RTS) were determined as measures of health status and
37 prognosis, respectively, at baseline. A semi-parametric Cox proportional hazards survival analysis
38 was used to assess the relationships between covariates and survival.

39 **Findings**

40 Seventeen patients (11.2%) experienced SSI. Overall, median survival time from operation was 262
41 days (95% CI: 190-334 days) and 12 month survival was 42.1%. RTS ($p<0.001$; hazard ratio 0.82; 95%
42 confidence interval: 0.76-0.89) and ASA grade ($p=0.028$; hazard ratio 1.37; 95% confidence interval:
43 1.03-1.82) were significantly associated with survival, with better survival found in patients with
44 higher RTS and lower ASA scores. Infection status was of substantive importance, with better
45 survival in those without SSI ($p=0.075$).

46 **Conclusion**

47 Twelve month survival in patients undergoing surgery for spinal metastasis is approximately 42%.
48 RTS and ASA scores can be used as indicators of patient survival either in combination or
49 individually. While SSI has some negative impact on survival, a larger study sample would be needed
50 to confirm whether this is statistically significant.

51 **Key Words**

52 Metastasis; Spine; Surgical site infection; Survival.

53

54

55 INTRODUCTION

56 Surgical intervention for patients with metastatic spinal tumours is indicated in patients with pain,
57 instability, or neurological compromise who have a life expectancy exceeding 3 months, according to
58 the National Institute of Health and Care Excellence (NICE) Clinical Guideline 75¹. Surgery aims to
59 prevent or relieve pain, and symptoms associated with mechanical instability and neurological
60 compromise^{2,3}. Complications which jeopardise the success of the operation are therefore highly
61 undesirable. Surgical site infection (SSI) is one such complication, being the third most commonly
62 occurring healthcare-associated infection (HAI) in England (accounting for approximately 16%). SSI
63 has a significant impact on the management of patients undergoing spinal surgery, the length of
64 time they spend in hospital, and how much money is spent on additional treatment⁴.

65 Although there is little evidence available to demonstrate a direct link between SSI and mortality
66 specifically in spinal tumour patients, it has been suggested that those suffering SSI as a result of
67 several types of procedure are overall twice as likely to die and 60% more likely to spend time in the
68 intensive care unit⁵. Determining the risk of SSI and its potential impact on mortality in patients
69 undergoing specialist surgical treatment will further highlight the importance of this complication
70 and the need to implement preventative measures.

71 A significant proportion of patients presenting with spinal metastases are unaware that they have a
72 primary tumour, with symptoms of spinal cord compression being the first indication of the disease.
73 Others, however, are known to be suffering from cancer and receiving treatment. Baseline health
74 status for those undergoing surgery can vary substantially between patients. The Revised Tokuhashi
75 Score (RTS) is a published system recommended by NICE as a tool to determine eligibility for surgery,
76 as it is recognised as being able to accurately predict survival⁶. However, some healthcare
77 providers do not use the RTS to strictly determine which patients should be offered an operation
78 because not all have a bone scan or a staging computed tomography (CT) pre-operatively, and
79 because of the perceived palliative benefits of surgery even in those who might have a life
80 expectancy less than three months. Generally, the RTS suggests that those with a score of 8 or less
81 have a predicted survival of up to 6 months, meaning that conservative or palliative treatments are
82 indicated. Those with scores of 12 to 15 have a predicted survival of more than 12 months, meaning
83 that excisional surgery may be appropriate. Those with a RTS from 9 to 11 are more often suitable
84 for palliative surgery rather than excisional surgery. Given that RTS appears to be useful in
85 predicting outcomes for patients with spinal metastasis, this score could be used to standardise
86 patients at baseline (i.e. the time of their operation) when investigating whether there is an
87 association between SSI and mortality. Similarly, the American Society of Anesthesiologists (ASA)

88 grade is a recognised scoring system which can be used to determine patient fitness for surgery ⁷.
89 ASA grade is relatively more simple than the RTS to determine, and is routinely recorded prior to
90 surgery in the majority of cases. Its use is also recommended by NICE in determining the
91 appropriateness of surgery for patients with spinal tumours.

92 Therefore, the aim of this study was to assess the impact of SSI on patient survival following surgery
93 for spinal metastatic tumours, after controlling for baseline fitness using both RTS and ASA grades.

94

95

96 **METHODS**

97 This was a sub-study of an ethically approved case note review of all adult patients (aged ≥ 18 years)
98 who had undergone surgical treatment for spinal metastatic tumours at Salford Royal NHS
99 Foundation Trust (SRFT) between 1st January 2009 and 31st December 2012⁸. Demographic (age,
100 sex), operative (date of operation, type of procedure, presence or absence of SSI) and survival data
101 (date of death, if applicable) were collected. Final follow up assessment was conducted on 15th July
102 2014. In addition, the RTS was determined retrospectively using available medical records and ASA
103 grade was obtained from the surgical documentation. RTS and ASA were determined to give an
104 indication of health status at baseline (i.e. the time of surgery).

105 *Definition of SSI*

106 The presence or absence of a SSI (superficial or deep) was defined using the criteria set out by Public
107 Health England⁹, which is largely based on the definitions published by the Centers for Disease
108 Control and Prevention (CDC) and the work of Horan et al.¹⁰. SSIs were classified by the SSI
109 surveillance nurse for the neurosurgery department, as per standard routine for the reporting of SSIs
110 through the hospital SSI Surveillance Service.

111 *Data Collection*

112 Data were collected from existing patient case notes and associated medical records (e.g. medical
113 images) and were anonymised prior to analysis; no contact with patients or relatives was required
114 for additional data collection. RTS was calculated based on relevant clinically available data; ideally,
115 RTS would be determined pre-operatively in order that this score can be used to assist in assessing
116 patients' suitability for surgery. However, RTS is not formally recorded routinely at our institution
117 and so this score was determined retrospectively based on the method described by Tokuhashi et al.
118⁶ where possible, with the exception of instances where the number of extra-spinal bony metastases
119 was unavailable from bone scintigraphy or magnetic resonance imaging (MRI). In these cases,
120 staging CT was used. ASA grade was recorded directly from the surgical pathway documentation.
121 All patients were followed up at at least one year post-surgery. Data relating to infection status and
122 survival were collected at this time point.

123 *Statistical Analysis*

124 Overall survival was assessed using the Kaplan-Meier method. A semi-parametric Cox proportional
125 hazards survival (time-to-event) analysis was undertaken to assess the relationships between
126 covariates and survival.

127

128 **RESULTS**

129 A total of 152 patients (77 females and 75 males) underwent surgery for spinal metastasis over the
130 four year study period. Mean age at operation was 60.5 years (SD 12.9 years). Seventeen patients
131 (11.2%) experienced SSI (14 superficial and 3 deep). At the time of last follow up, 117 patients had
132 died. Median survival time from operation for the whole cohort was 262 days (95% CI: 190-334
133 days). This equates to 42.1% at 12 months, and 19.6% at five years. Median survival time for
134 patients experiencing SSI was 135 days (95% CI: 62-208 days), and for those without infection, 276
135 days (95% CI: 183-369 days).

136 The assumption of proportional hazards was found to be tenable, and measures of patient fitness
137 were not excessively correlated. The Cox analysis found both RTS and ASA score to be significantly
138 associated with survival (Table 1), with better survival found in patients with higher RTS and lower
139 ASA scores.

140 Direction of approach was not considered as a candidate factor due to only one patient with an SSI
141 experiencing an anterior approach, and less than 10% of patients in total experiencing an anterior
142 approach. Hence direction of approach does not adequately distinguish between either cases, or
143 between controls and was thus unsuitable as a candidate variable. All cases (infection and non-
144 infection) were instrumented and so this too was not included in the analysis.

145

146 [INSERT TABLE 1]

147

148 Survival curves for RTS and ASA are shown in Figures 1 and 2. Each additional point on the RTS scale
149 was associated with an 18% lowered hazard of death ($p < 0.001$). Each additional point on the ASA
150 scale is associated with a 37% raised hazard of death ($p = 0.028$).

151

152 [INSERT FIGURES 1 AND 2]

153

154 Infection status was found to be of substantive importance, with better survival shown by those
155 without SSI ($p = 0.075$) (Figure 3). Age at the time of surgery was not substantively related to survival
156 ($p = 0.299$).

157

158 [INSERT FIGURE 3]

159

160 **DISCUSSION**

161 The results of this study suggest that the median length of survival from the date of surgery for
162 spinal metastases is approximately 8.6 months. This is comparable to figures previously reported in
163 the literature ^{11,12}. Twelve month survival in the present cohort was 42.1% overall (29.4% in those
164 with SSI and 43.7%in those without SSI.

165 As expected, both ASA grade and RTS predicted survival effectively in patients in this study. When
166 using these scores to control for baseline health status, patients experiencing SSI survived on
167 average half as long as those without SSI (though the association between infection and survival was
168 substantive). The low number of cases represented in this study may be a limiting factor and a
169 reason why this association was not observed to be significant. Nevertheless, this study describes
170 the contemporary SSI rate in this patient group at a large UK specialist spinal centre, and is one of
171 the first to demonstrate a relationship between SSI and mortality in this type of patient.

172 It has been estimated that between 38 and 75% of deaths in patients with SSI are attributable to
173 infection itself ^{13,14}, with SSI being an independent predictor of mortality. Other studies have
174 suggested that the type of surgery, and whether SSIs are deep/organ space have some bearing on
175 the level of contribution of infection towards death ¹⁵. While this seems logical, it is impossible in
176 this study to indicate whether the type of infection (superficial or deep) had any effect on survival,
177 given that only three cases were documented as being deep. A larger case series would be needed
178 to determine whether additional factors such as this played an important role in affecting survival
179 outcome.

180 It is suggested that there are approximately 4,000 cases of metastatic spinal cord compression
181 diagnosed each year in England and Wales ¹, though this is likely to be an underestimate. Surgery is
182 generally undertaken as a palliative measure to relieve pain and stabilise the spine to prevent
183 further neurological damage. Estimating that only around 20% of these will undergo surgery
184 (Richards, personal communication), and based on the 11.2% infection rate demonstrated in this
185 study, 90 patients per year could be at risk of developing SSI. Given the differential in life expectancy
186 demonstrated in this study between patients with and without SSI (141 days shorter in SSI patients),
187 theoretically, this equates to approximately 12,600 days (34.5 years) of life lost which relates to the
188 onset of SSI for just those treated surgically over the period of one year. This, coupled with the
189 distressing consequences of infection (prolonged in-patient hospitalisation, isolation away from
190 home, additional treatments) and the inevitable economic costs associated with SSI ⁴, can be
191 exceedingly frustrating for a service under pressure to provide better care at a lower cost.
192 Scrupulous peri-operative practice and the standardisation of effective processes in the operating
193 theatre may go some way to improving outcomes in terms of SSI rates ¹⁶⁻¹⁸. In addition, effective

194 surgical work-up and the notion of ‘prehabilitation’ in the pre-operative period may better prepare
195 some elective spinal surgery patients physiologically to improve some outcomes¹⁹. However, there
196 is little evidence to support this approach in reducing post-operative complication rate.
197 Furthermore, in urgent cases – such as those needing surgery for spinal tumours – this window of
198 opportunity is generally not available to the care team, meaning that extra preventative measures
199 are highly desirable and clearly warranted. This is especially so in cancer patients given that they are
200 at increased risk of SSI, due largely to their immunosuppressed state^{20,21}.

201 The results provided by this study may be useful during the consenting process for spinal surgery.
202 The appropriateness and quality of information patients receive prior to their operation, about the
203 procedure and its associated risks are of utmost importance when ensuring their decisions are fully
204 informed and their expectations managed. Thus, patients have a right to know about the
205 implications of SSI. Despite this, it is evident from previous studies that many patients are poorly
206 informed about SSIs; some are unable to recognise the signs and symptoms of an infection or
207 unaware of the causes or the risk factors of SSI²². This low level of awareness about SSI, coupled
208 with the potential for such devastating effects on quality of life and clinical outcome indicates that
209 greater attention should be paid to this complication across the board. Statistics relating to
210 individual departments, such as those presented in this study, could go some way to educating both
211 staff and patients of the institution, in an effort to emphasise risk factors for SSI, what can be done
212 to combat them, and the importance of their consequences. It is hoped this would then translate
213 into the adoption of processes – on the part of both patient and care team – which drive down the
214 incidence of SSI.

215

216 **CONCLUSIONS**

217 One-year survival in patients undergoing surgery for spinal metastases is approximately 42%. Either
218 or both of RTS or ASA scores can be used as reliable indicators of survival in these patients. While SSI
219 has some negative impact on survival, a larger study sample would be needed to confirm that this is
220 a statistically significant association. The evidence provided by this study may raise awareness of the
221 importance of SSI as a complication of surgery for spinal metastasis.

222

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226

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