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En Bloc Resection of Tumors of the Lumbar Spine: A Systematic Review of Outcomes and Complications

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ABSTRACT

Background: The literature on total en bloc spondylectomy (TES) of bone tumors of the lumbar spine is sparse and heterogeneous. Therefore, the aim was to systematically pool the data from the published studies to quantitatively summarize the morbidity and mortality and to identify factors associated with favorable outcomes and complications.

Method: A systematic literature search for studies with individual patient-level data was conducted using specific medical subject heading (MeSH) terms. The outcome measures assessed included complications, tumor recurrence, survival, and function. Individual patient data were pooled from all the studies and quantitatively analyzed to assess the association of different factors with outcomes and complications.

Results: Twelve studies were included in this review with a total of 145 TES cases. Of all patients, 50% had at least 1 reported complication post surgery and this was associated with advancing age (OR 1.04, \( P < 0.001 \)), metastatic disease (OR 5.61, \( P < 0.001 \)), and adjuvant chemo and/or radiotherapy (OR 20.3, \( P = 0.001 \)). Intralesional excision (OR 5.2, \( P = 0.01 \)) and primary malignant tumors (OR 3.3, \( P = 0.02 \)) were associated with a high recurrence rate. However, the surgical approach was not associated with differences in survival (\( P = 0.874 \)) or recurrence (\( P = 0.525 \)) rates. L5 tumor resection was associated with excessive bleeding. Postoperatively, there was an overall improvement in the Frankel grades in most patients.

Conclusion: TES is associated with high rates of complications especially in association with primary malignant and metastatic diseases. However, the number of publications on this topic remain scarce and heterogeneous. Hence, there is a need for standardization in the reporting of the outcomes and complications to help with decision-making and consenting for this procedure.

Tumor Keywords: lumbar, thoracolumbar, spine, en bloc, spondylectomy, tumor, malignant, primary en bloc resection, complications, outcome

INTRODUCTION

Total en bloc spondylectomy (TES) is an extensive surgical technique often carried out for primary malignant bone tumors, aggressive benign tumors, and, infrequently, solitary metastatic spinal lesions.\(^1\) While TES is widely accepted as a definitive surgical treatment, its complexity and the relative infrequency of the type of tumors amenable for this procedure limit the amount of currently available data to fully inform surgical practice.\(^2\)

The rate of complications reported in the literature following TES has varied between 34% and 77%.\(^3\)\(-\)\(6\) Survivorship is also varied and largely determined by the nature and extent of the original pathology. Tomita et al has reported an overall 5-year survival rate of 67% for primary malignant spinal tumors and 100% for aggressive benign tumors following TES.\(^1\) However, the para-lumbar anatomy makes TES in the lumbar spine more challenging and potentially increases the rate of complications which may impact the survival rate following surgery.

The currently available data on lumbar TES informing practice are largely based on heterogeneous case series of variable quality, utilizing different techniques across multiple spinal levels for a range of pathologies.\(^2\)\(-\)\(4\),\(^7\)\(-\)\(10\) This makes objective description of the risk and benefits of the surgery specific to an individual patient during preoperative counseling difficult. Hence, there is a need to pool and summarize the overall outcome results of TES in the lumbar regions in order to facilitate a clear understanding of the benefits, risks and complications of this procedure.

The aim of this study was to undertake a systematic review of the literature on en bloc resection of tumors in the lumbar and thoracolumbar region and pool the results to identify predictors of favorable outcomes and complications.
MATERIALS AND METHODS

Literature Search Strategy

A systematic literature search was conducted for articles reporting individual patient-level data on 4 databases: PubMed, OVID Midline, EMBASE, and Cochrane from the date of their inception till the end of November 2019. The searched terms were used in the following way in combination with the Boolean operators “AND,” and “OR”: (lumbar OR thoraco-lumbar OR spine) AND (en bloc OR spondylectomy) AND (tumor OR tumour OR malignant OR primary).

The databases, EMBASE, and OVID Medline were searched simultaneously using the OVID search platform. Case reports, abstracts, non-English language articles, and animal studies were excluded during the initial search. The review of the literature was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2009) chart (Figure 1). The selection of appropriate articles was conducted independently by 4 authors (M.J., Z.A., O.U., and M.C.), and any disagreement was resolved by consensus.

Figure 1. Flow chart of systematic search and review process conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement criteria.
Eligibility Criteria

The search strategy was to identify articles reporting individual patient-level data and describing the outcome of patients with lumbar spinal tumors (benign primary, malignant primary, and metastasis) who underwent TES. The outcome measures considered were the following: complications, tumor recurrence, survival, and quality of life indicators. Only articles in the English language were considered. Level 1 to 4 evidence studies as defined by the Centre for Evidence Based Medicine (CEBM) were eligible for inclusion, and there were no restrictions on publication date. Level 5 evidence, case reports, case series with fewer than 3 patients, biomechanical studies, technical reports, cadaveric studies, animal studies, epidemiological studies, review articles, editorials, expert opinion, abstract-only publications, dedicated articles on cervical, thoracic or sacral pathology, and those not reporting outcomes or individual patient-level data were not included.

Assessment of Methodological Quality

A standardized critical appraisal form was utilized to extract data and assess the risk of bias (Table 1). Two reviewers (Z.A. and O.U.) independently assessed the risk of intrastudy bias using the 12-point Methodological Items for NonRandomized Studies (MINORS) scale.

Data Extraction

The following variables were included in the analysis: age, sex, resection level, Weinstein-Boriani-Biagini (WBB) staging, surgical approach, operation time, blood loss, adjuvant treatment, Frankel score, complications (cerebrospinal fluid [CSF]) leak, failure of metal works, weakness; including temporary weakness and nerve root sacrifice, surgical site infection [SSI]), follow-up, functional assessment, recurrence and mortality.

Statistical Analysis

Continuous data were expressed as mean and standard deviations, while categorical data were expressed by numbers and percentages. Contingency tables were used to present the results in association with each outcome and complication. Univariate logistic regression model was used to assess the association between specific variables and the risk of developing recurrence and complications. Survival analyzes of the primary and metastatic cases were performed, and the log rank test was used to compare the differences. Analysis of variance and the Student t test were used to evaluate the differences in operative time and blood loss. A P value of ≤0.05 indicated statistical significance.

All statistical analysis was performed using IBM SPSS Statistics (IBM Corp., Armonk, NY, USA).

RESULTS

Studies Included

Initially, 62 papers were considered for inclusion, but only 12 studies fulfilled the eligibility criteria; these were included in the final analysis (Figure 1).

Risk of Bias

Table 1 summarizes the risk of bias according to the MINORS grading system. The overall methodological quality was poor for all the studies, with an average score of 11 (range 9–13). All the studies were retrospective case series, which is a major limitation for this study. Overall, there was a marked heterogeneity particularly in tumor types (both primary and metastases), adjuvant treatment, baseline characteristics, and the type of data.
reported (Table 2). Despite the inherent bias across the studies, well-defined primary end points were presented (mortality and recurrence) and most papers provided some details of postoperative complications.

Patient and Tumor Characteristics

Out of a total of 225 available patients across the 12 studies, only 145 had lumbar (or T12, n = 10) en bloc spondylectomies with a mean age of 40 years (Table 2). Based on the reported data for 129 patients, there was equal proportion of males and females. The most common primary tumor was giant cell tumor (52.8%), and the most common metastatic tumors were breast and thyroid (Table 2).

Surgical Characteristics

The commonest levels resected were L2 and L3 with the same proportion (26%). The excision margin was reported in 82 cases, and the surgical approach was reported in 72 cases. However, the surgical approach along with the excision margin was reported in only 9 cases; therefore, it was not possible to correlate the approach to the clearance of the tumor. WBB staging system was reported in 67 cases but was reported along with a surgical approach in only 28 cases.

The operative time and amount of blood loss were reported in 84 patients. Three of the studies reported excessive blood loss in some cases. The combined approach was associated with high blood loss and longer operative time (relative to the posterior-only approach) P = 0.024 and P < 0.001, respectively (Table 3). The amount of blood loss in the 2-staged combined approach (mean 4867 [SD 5438] mL) was higher than single-staged combined approach (mean 2976 [SD 3536] mL), P < 0.001. The mean duration of surgery was also higher in the 2-staged combined approach (mean 1195 [SD 220] min) than single-staged combined approach (mean 720 [SD 207] min), P < 0.001. The amount of blood loss also varied with the pathology and the level resected (Figures 2 and 3). L5 TES was associated with the highest blood loss and operative time compared to other levels (Figure 3).

Outcomes

The median length of follow-up was 70 months ranging between 2 and 295 months, (Table 2). All papers provided data on recurrence, follow-up periods, and survival. Univariate analysis revealed that the overall survival was dependent on tumor histology and excisional margins (Figures 4 and 5). Patients with metastatic disease and primary malignant tumors had the worst survival rates relative to benign primary tumors (P < 0.0001 and P < 0.001, log rank test, respectively). Five-year survival was 63.6% and 59.8% in the primary
Table 3. The outcome of each approach based on a total of 72 cases.

<table>
<thead>
<tr>
<th>Approach</th>
<th>Compartment, Extra:Intra n = 28</th>
<th>Total Blood Loss in mL</th>
<th>Total Operation Time in Minutes</th>
<th>SSI N/Total N</th>
<th>Weakness N/Total N</th>
<th>Any Form of Complication N/Total N</th>
<th>Recurrence N/Total N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total, n = 72</td>
<td>19:9</td>
<td>2934 (150–19225)</td>
<td>680 (245–1516)</td>
<td>6/58</td>
<td>33/58</td>
<td>72/72</td>
<td>9/72</td>
</tr>
<tr>
<td>Posterior</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total, 35 (49%)</td>
<td>14:9</td>
<td>2024 (150–5500)</td>
<td>421 (245–675)</td>
<td>0/21</td>
<td>9/21</td>
<td>35/35</td>
<td>3/25</td>
</tr>
<tr>
<td>Primary</td>
<td>malignant, 6 (17%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary benign (aggressive), 10 (29%)</td>
<td>1:2</td>
<td>1462 (180–2688)</td>
<td>476 (290–655)</td>
<td>0/5</td>
<td>2/5</td>
<td>6/6</td>
<td>0/6</td>
</tr>
<tr>
<td>Metastasis, 19 (54%)</td>
<td>11:4</td>
<td>2372 (1000–4000)</td>
<td>388 (245–630)</td>
<td>0/6</td>
<td>3/6</td>
<td>19/10</td>
<td>3/19</td>
</tr>
<tr>
<td>Total, 37 (51%)</td>
<td>5:0</td>
<td>3794 (160–19225)</td>
<td>926 (475–1516)</td>
<td>6/37</td>
<td>24/37</td>
<td>37/37</td>
<td>4/37</td>
</tr>
<tr>
<td>Primary</td>
<td>malignant, 9 (24%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary benign (aggressive), 18 (49%)</td>
<td>1:0</td>
<td>3853 (160–12370)</td>
<td>1083 (475–1516)</td>
<td>3/18</td>
<td>12/18</td>
<td>18/18</td>
<td>1/18</td>
</tr>
<tr>
<td>Metastasis, 10 (27%)</td>
<td>3:0</td>
<td>3257 (900–13460)</td>
<td>704 (540–990)</td>
<td>0/10</td>
<td>4/10</td>
<td>10/10</td>
<td>0/10</td>
</tr>
</tbody>
</table>

Abbreviations: N, number of cases; SSI, surgical site infection.

*SSI and weakness data were available for only 58 cases. Extra:Intracompartment ratio data were available for only 28 cases.

Malignant and metastatic groups, respectively. Clear margins were achieved in 43% of cases (35 out of 82) (see Tables 2 and 3).

Primary malignant tumors, intralesional excision, and extracompartimental tumors were also associated with high risk of recurrence on univariate analysis (Table 4).
The Frankel grading of the 82 cases was reported, and this showed an overall improvement postoperatively as most patients ended up with grade E (Figure 6).

Complications

Complications (CSF leak, SSI, metal work failure, postop weakness, and/or nerve compromise) were reported in a total of 72 (50%) cases. CSF leak occurred in 10 out of 51 cases, weakness (including transient or permanent as a result of nerve resection) occurred in 33 out of 58 cases, SSI occurred in 8 out of 58 cases, and metalwork failure occurred in 8 out of 58 cases. On univariate analysis, age, metastases, and adjuvant treatment (chemotherapy and/or radiotherapy) were associated with high rates of complications (Table 4).

DISCUSSION

To our knowledge, this is the largest review of the available literature on outcomes and complications of lumbar spondylectomy for primary bone and metastatic tumors. As predicted, there was better survival in patients presenting with primary benign tumors and those with wide excision margins in primary malignant and metastatic tumors.

It’s well known that margin clearance influences local recurrence rate and survival. A previous systematic review that did not focus on lumbar en bloc resections quoted a rate of 88% in attaining a wide or marginal excision margins in TES. In the papers included in our current review, there was limited description of the resected margins in relation to the preoperative surgical staging or to the type of surgical approach used. Resection margin was reported in 82 cases and a clear margin was achieved in only 35. The high rates of failure to achieve clear surgical margins can be interpreted in a number of ways. Either it could be a reflection of the difficulty of this surgical procedure coupled with the challenging nature of the local anatomy, or the difficulty in selecting appropriate cases where clear margins were achievable. The data suggest that despite carefully considered selection of cases for TES, those with apparently isolated metastatic disease were still associated with poor survival, similar to those cases with primary bone tumors.
Due to the complexity of the procedure, complication rates were high (50%). Patients with extracompartmental tumors, primary malignancies, and intralesional excision were at significant risk of increased complications. This may be a reflection of more aggressive tumors combined with a greater likelihood of multi-level resection, increased operative time, blood loss, and implant failure rates associated with such surgery. We were unable to demonstrate significant association with any of the other variables although this is likely to be in part due to the low number of cases available for analysis.

There is limited reporting of neurological complications, although in the studies reviewed neurological status appeared to be well maintained or improved following lumbar TES. Abe et al\textsuperscript{13} suggested that removing a lumbar vertebra en bloc without sacrificing nerve roots puts the lumbar plexus or nerve roots at risk of injury. However, other authors warned of serious neurological deficit following the sacrifice of L3, L4, or L5 nerve roots. In 4 of the studies\textsuperscript{13,14,17,24} the authors described performing nerve root sacrifice as part of their surgical techniques. It appears from the reported data that this can be well tolerated by patients from a functional point of view. There was an overall improvement in the Frankel grade postoperatively and also acceptable Oswestry Disability Index and Short Form (SF) 36 scores reported by Melcher et al\textsuperscript{20} and Liljenqvists et al\textsuperscript{18} studies. Melcher et al\textsuperscript{20} reported a decrease in SF-36 scores compared to the German national population, but higher than chronic back-pain patients. Liljenqvist et al\textsuperscript{18} SF-36 analysis reported normal mental component scores and only slight decrease in the physical component in patients without disease recurrence.

The amount of blood loss (when reported) featured prominently in some cases especially with the combined approach. None of the papers discussed the use of cell salvage even when reporting excessive estimated blood loss. Kawahara et al\textsuperscript{17} stated that in 4 cases there was excessive bleeding of >3000 mL, requiring embolization prior to the second stage. In the remaining cases, the feeding as well as the segmental arteries was embolized before surgery to reduce the risk of excessive bleeding. Our results demonstrate that the resection of L5 was associated with the highest mean blood loss even when compared to multilevel resection (at other levels). This calls for further scrutiny of the vasculature.

Figure 4. Survival Kaplan-Meier graphs from the 3 types of tumors. Malignant primary and metastasis had the worst survival.
in the vicinity of the L5 during preoperative planning and embolization of vessels if needed.

The surgical approaches for TES have varied, and there is still an ongoing debate as to the preferred approach (posterior-only or combined posterior and anterior). In this review, the posterior-only approach (reported in 35 cases) was used by several authors, utilizing the technique described by Tomita or a similar description. The surgical strategy employed, however, has largely depended on the nature of the local anatomy, extent of the disease, range of patient factors, and surgeon’s experience. Isolated posterior approaches may be effectively used when adequate anterior soft tissue release can be achieved posteriorly and the tumor is isolated to the posterior elements or the vertebral body. However, an important consideration here is the origin of the psoas and iliacus that may present a particular challenge. Furthermore, a single posterior approach may not be viable in the presence of tumor invasion of anterior structures, adhesions from previous surgery, inability to mobilize or deliver a large tumor through a posterior incision, and involvement of

<table>
<thead>
<tr>
<th>Variable</th>
<th>Recurrence Odd Ratio (95% CI)</th>
<th>P</th>
<th>Complications Odds Ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.99 (0.96–1.02)</td>
<td>0.407</td>
<td>1.04 (1.02–1.06)</td>
<td>0.001</td>
</tr>
<tr>
<td>Gender (female vs male)</td>
<td>1.75 (0.67–1.56)</td>
<td>0.252</td>
<td>0.85 (0.43–1.70)</td>
<td>0.650</td>
</tr>
<tr>
<td>Metastatic disease (vs benign primary)</td>
<td>0.66 (0.16–2.70)</td>
<td>0.560</td>
<td>5.61 (2.17–14.52)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Primary malignancy (vs benign primary)</td>
<td>3.30 (1.19–9.13)</td>
<td>0.022</td>
<td>0.63 (0.28–1.40)</td>
<td>0.254</td>
</tr>
<tr>
<td>Primary malignancy (vs metastatic disease)</td>
<td>5.03 (1.31–19.30)</td>
<td>0.018</td>
<td>0.78 (0.07–0.46)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Extra compartmental tumor (vs intra-compartmental tumor)</td>
<td>7.5 (0.9–61.8)</td>
<td>0.060</td>
<td>0.50 (0.16–1.52)</td>
<td>0.223</td>
</tr>
<tr>
<td>Combined approach (vs single approach)</td>
<td>1.29 (0.27–6.24)</td>
<td>0.749</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Adjuvant chemo and/or radiotherapy (vs no adjuvant treatment)</td>
<td>0.97 (0.32–2.93)</td>
<td>0.95</td>
<td>20.31 (5.21–79.21)</td>
<td>0.001</td>
</tr>
<tr>
<td>Intra-lesional margins (vs complete resection)</td>
<td>5.17 (1.45–18.4)</td>
<td>0.011</td>
<td>1.0 (0.00–E)</td>
<td>1</td>
</tr>
<tr>
<td>Marginal (vs complete resection)</td>
<td>1.03 (0.17–6.29)</td>
<td>0.97</td>
<td>1.0</td>
<td>1</td>
</tr>
</tbody>
</table>
the neural arch.\textsuperscript{34} Another anatomical landmark to consider is the iliac wing that obstructs access to the L5 (and possibly the L4) vertebra, and therefore, Stener\textsuperscript{35} suggests a combined approach at these levels. Abe et al\textsuperscript{13} recommended posterior TES for L1 or L2 lesions (though this would necessitate ligating nerve roots and requiring longer fusion constructs), and combined anterior and posterior approaches for L3 to L5 lesions or for extravertebral extension. Similarly, Tomita highlighted the need for posterior laminectomy and stabilization followed by anterior en bloc corpectomy for spinal tumors at the level of L5 (or L4) due to the anatomy of the iliac wings and lumbosacral plexus.\textsuperscript{1} Liljenqvist et al\textsuperscript{18} used a single-stage combining posterior-anterior approach, with the initial excision of the posterior elements, mobilization of dura, ligation of the nerve roots involved within tumor, and corpectomy through a lateral extraperitoneal approach. This helps to fuse the simultaneous control of the neural elements posteriorly and the viscera anteriorly. Kawahara et al\textsuperscript{17} used a combined approach where the nerve roots were initially dissected out to the conjunction of the adjacent lumbar nerves, thereby facilitating mobilization of the dural tube. If the tumor did not have paravertebral extension, then an anterolateral extraperitoneal approach was used. However, if a paravertebral mass compressed major vessels anteriorly, then they performed a midline transperitoneal or bilateral extraperitoneal approach. The former was used to gain access to the L4/L5 level. A second posterior approach was done if using titanium mesh cage (to compress the rods) and an AP-connecting device was inserted if more than 2 levels were resected.

A range of stabilization techniques have been reported—from single-level instrumentation above and below resections in children\textsuperscript{18} to 360-degree instrumented reconstructions with vascularized autograft and cages.\textsuperscript{20} It is worth noting that a 40\% incidence of spinal instrumentation failure following TES has been reported in a series of 15 patients.\textsuperscript{36} However, due to the limited reporting of the techniques, it is difficult to predict which cases are likely to lead to pseudoarthrosis/failure. In a biomechanical study using a vertebrectomy model, Oda et al\textsuperscript{37} found that a combination of posterior and anterior instrumentation (using anterior cage) provided the best stability. Given that patients may survive for a long time as a result of curative TES, metalwork failure can be an issue\textsuperscript{36,38} and every effort should be made to reduce the risk of nonunion and subsequent reconstructive failure.

**Limitations**

This review is limited by a range of inconsistencies in the reported data, the retrospective nature, and the low quality of all the studies included. These problems have previously been highlighted in the literature.\textsuperscript{2}
description and reporting of surgical techniques, extent of resection, reconstruction techniques used, and complications were not clearly stated in many cases. The lack of standardized reporting represents a potential opportunity for the limited number of centers undertaking this type of surgery to reach a consensus on data reporting and defining the indications for TES. Therefore, standardization through a registry approach may help on improving the reporting of surgical approaches and outcome, including complications and survival. Until there is a systematic and standardized pooling of data from surgeons engaged in this challenging surgery, it will remain difficult to determine which factors contribute most to complications or failures of treatment. This is important because a more complete understanding of morbidity, survivorship, and outcomes associated with TES in the lumbar spine will allow us to better manage and counsel this hugely heterogeneous group of patients.

CONCLUSION

TES is a complex procedure associated with high rates of complications. The factors associated with recurrence and complications are largely nonmodifiable factors, such as malignant primary and metastatic diseases. The L5 vertebra was associated with the highest amount of blood loss. However, the publications on this topic remain heterogeneous, and there is inconsistency in the reporting of outcomes and complications in the literature. This calls for standardization in the reporting of these complex procedures and their associated outcome to allow for a better understanding of factors associated with better survival and outcome.

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