En Bloc Resections in the Spine: The Experience of 220 Patients During 25 Years

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■ BACKGROUND AND OBJECTIVE: **En bloc resections aim at surgically removing a tumor in a single, intact piece. Approach must be planned for the complete removal of the tumor without violation of its margins. The shared knowledge of the morbidity, mortality, risk assessment for local disease recurrence, complications, and death, related to spine tumors excised en bloc could improve the treating physician's apprehension of the diseases and decision making process before, during, and after surgical treatment. The purpose of this study was to review and report the experience gained during 25 years in one of the world's biggest spine oncologic centers.**

■ METHODS: **A retrospective study of prospective collected data of 1681 patients affected by spine tumors, of whom 220 had en bloc resections performed.**

■ RESULTS: **Most tumors were primary—165 cases (43 benign and 122 malignant); metastases occurred in 55 patients. A total of 60 patients died from the disease and 33 local recurrences were recorded. A total of 153 complications were observed in 100 of 216 patients (46.2%); 64 of these patients (30%) suffered 1 complication, whereas the rest had 2 or more. All complications were categorized according to temporal distribution and severity. These were further divided into 7 groups according to the type of complication. There were 105 major and 48 minor complications. Seven patients (4.6%) died as a result of complications. There were 33 local recurrences (15.28%) recorded. Contaminated cases, surgical margins of the resected tumor—intralesional, marginal, and malignant tumors—were statistically significant independent risk factors for local recurrence of the tumor. Contamination, local recurrence, neoadjuvant radiotherapy, number of levels resected, and metastatic tumors compared with primary malignant tumor were shown to be independent risk factors for a patient's death.**

■ CONCLUSIONS: **Treatment of spinal aggressive benign and malignant bone tumors with en bloc resection is beneficial in terms of better local control and prognosis, although it is a highly demanding and risky procedure. Margins are the key point of this procedure, thus a careful preoperative oncologic and surgical staging is necessary to define the optimal surgical approach. The adverse event profile of these surgeries is high. Therefore, it should be performed by experienced and multidisciplinary teams in specialized high volume centers.**

Key words
- En bloc resection
- Morbidity
- Spine tumors
- Surgical planning

Abbreviations and Acronyms
CC: Contaminated cases
CH: Chordoma
CHS: Chondrosarcoma
NCC: Noncontaminated cases
OGS: Osteogenic sarcoma
OR: Odds ratio
PE: Pulmonary embolism
WBB: Weinstein, Boriani, Biagini

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INTRODUCTION

Unlike appendicular skeletal primary bone tumors, primary bone tumors of the spine are very rare,[1] comprising only 10% or less of all bone tumors. In the United States, 7500 new cases are estimated per year.[1] The estimated overall world occurrence is between 2.5 to 8.5 cases per million inhabitants per year.[1] Spinal metastatic tumors, most common skeletal region for secondary tumors, are estimated to be 30–50 times more frequent compared with primary bone tumors of the spine.

Due to their low relative prevalence, primary spinal tumors can be misdiagnosed and consequently managed incorrectly.

En bloc resections[2] are the procedures aimed at surgically removing a tumor in a single, intact piece, fully encased by a continuous shell of healthy tissue, which is defined as the margin. In the spine, these procedures are surgically demanding,[3-9] mostly due to the proximity of neural elements and anatomic limitations. The limitation in mobilizing the spinal cord, neural roots, or the dural sac mandates either combined multiple surgical approaches or an enlarged single posterior approach. Achieving tumor-free margins of the resected specimen requires, at times, the sacrifice of adjacent anatomic structures (e.g., pleura, dura, muscles, nerve roots, nerves, vessels).[10-15] An intentional violation of oncologic principles[2,5,16] is considered for reduced morbidity and better functional results, but this is weighed against the higher risk of recurrence.

Successful en bloc resection has shown to result in fewer local recurrences and improved prognosis in both primary[7,16-19] and isolated spinal metastases such as renal cell carcinoma and thyroid cancer.[20-22] Previous studies that compared true en bloc to intralesional resections reported improved local control, where the recurrence was 92.3% versus 72.2% for giant cell tumors,[22,23] 78% versus 22% for chordoma (CH),[17] and 82% versus 0 in chondrosarcoma (CHS).[18] In an earlier study[16] reporting our previous experience of a series of 103 patients, marginal and intralesional resections were shown to be an independent risk factor for local recurrence, with hazard ratios of 9.45 and 38.62, respectively.

It is reported that major spine surgery can be associated with high morbidity.[24-33] To that extent, spinal en bloc resection, due to multiple surgical approaches, tumor surgery, and lengthy surgical procedures,[34] can be expected to involve intraoperative, early postoperative, and long-term adverse events. At present, few reports focusing on complications and outcomes of en bloc resections in the spine have been published.[16,35-37] Some focusing on specific area of resection such as the cervical spine,[38] sacrum,[39,40] whereas others addressing complications related to surgical treatments of various pathologies such as CH[38,39] and metastatic thyroid carcinoma.[20] In a recent study published by our group,[36] focusing on the morbidity of 220 en bloc resection conducted between 1990 and 2015, a 45.45% complication rate was observed. This high rate requires continuous attention and effort to understand and reduce the morbidity of this operation.

Because these operations are not performed frequently in the world, it is imperative that the experience gained in large centers specialized in treating these pathologies be reviewed and shared. This shared knowledge of the morbidity, mortality, risk assessment for local disease recurrence, complications, and death, related to spine tumors excised en bloc could improve the treating physician's understanding of the diseases and the decision-making process before, during, and after the surgical treatment. This report includes a summary of the previously reported morbidity,[36] as well as local recurrence and mortality, and a thorough review of the gained experience approaching the surgical management of these tumors.

The purpose of this study is to review and report the experience gained in one of the world's largest spine oncologic centers conducting these surgeries during 25 years.

METHODS

From January 1990 to July 2015, 1681 consecutive patients with spine tumors were diagnosed and treated in one referral center. A total of 220 en bloc resections were performed on 216 patients by Stefano Boriani and his team. For all patients, clinical radiographic and histologic studies were completed and classifications according to the Enneking,[2] Frankel[41], and the Weinstein, Boriani, Biagini (WBB)[42] staging systems were determined before the surgical intervention.

Data were prospectively collected to build a database for clinical and research use.

Patients who were diagnosed and treated at the Department of Oncologic and Degenerative Spine Surgery, Unit of Oncologic Spine Surgery, Rizzoli Institute, Bologna, Italy, were classified as noncontaminated cases (NCC). Conversely, patients who were referred for treatment after either open biopsies or an initial surgical attempt of resecting the tumor at another institution were categorized as contaminated cases (CC).

Patient outcome factors including local recurrence, mortality from the disease, morbidity (intraoperative, early and late postoperative complications), and change in neurological status were reviewed in the present study.

The morbidity is summarized in this report in concordance with our recent article describing the complications of en bloc resection.[36] Major complications were considered as "any complication that appeared to substantially alter an otherwise full and expected course of recovery," as described by McDonnell et al.[26] Other complications were regarded as minor.

Complications were studied and stratified based on temporal distribution (intraoperative, early postoperative [within the first 30 days after surgery], and late postoperative [>30 days after surgery]), type of resection, and the approach adopted (single posterior approach or combined anterior and posterior approaches in the same surgical session). All complications were categorized into 7 groups (vascular failure and bleeding, hardware failure, injury to adjacent structures during and after surgery, injury to the dural sac and neurological unplanned deficit, infections of soft tissue and wound problems, systemic morbidity [including cardiac, renal, respiratory, and immunologic systems], and hypercoagulable problems [including pulmonary embolism, PE, and deep vein thrombosis]).

Terminology for Resections

1. Intralesional excision: piecemeal removal of the tumor, further subcategorized into:
   a. Intracapsular—incomplete tumor removal where gross or histologic remnants inside the tumor capsule could be expected.
   b. Extracapsular—complete resection of the entire tumor's mass together with the peripheral tissue (3–5 mm of healthy peripheral tissue).
2. En bloc resection: removal of the entire tumor's mass, including a cuff of healthy tissue encasing the tumor. After histopathologic evaluation of the resected specimen, further subclassification as:

a. Intralesional—if the tumor was violated, thereby causing tumor spillage.

b. Marginal—if a thin shell of normal tissue covered the tumor without breach of tumor tissue through the shell.

c. Wide—if a thick layer of peripheral healthy tissue, a dense fibrous cover (e.g., fascia), or an anatomic barrier not yet infiltrated (e.g., pleura), fully covered the tumor.[2,42]

Statistical Analyses

Continuous variables were expressed as mean ± standard deviation, if Gaussian, or as median and 25th–75th percentile, if skewed. Normality of distribution was assessed by means of the Kolmogorov-Smirnov test. Categorical data were shown as absolute and relative frequencies.

A logistic regression analysis was applied to find predictors of local recurrence, complications, effect of contamination, and death, considering gender, age, staging, contamination, surgical approach, and neoadjuvant and adjuvant therapy (chemical and radiation) as covariates. The multivariate model included only covariates with a $P < 0.05$ in univariate analysis and was adjusted for location and number of resected levels. Calibration and discrimination of the multivariable model were evaluated by means of the Hosmer-Lemeshow test and the c-statistic, respectively.

A 2-sided P value <0.05 was considered to be significant.

For all analyses, SPSS 23.0 statistical software was used (SPSS Inc., Chicago, Illinois, USA).

RESULTS

From January 1990 to July 2015, 1681 consecutive patients with spine tumors were diagnosed and treated in one referral center. A total of 220 en bloc resections were performed on 216 patients by Stefano Boriani and his team.

A total of 113 male and 103 female patients with an average age of 44.1 ± 18 years (range, 3–82 years) were surgically treated. Median follow-up was 45 months (0–371 months). Follow-up visits were performed routinely for all patients. Additional visits were conducted based on specific need—disease progression or complication. Patients were followed by physical examination and imaging (roentgenogram, computed tomography, positron emission tomography, and magnetic resonance imaging) as required. Follow-up was available for at least 24 months in 139 patients (63.2%); 25 of the remaining 81 died <2 years after surgery (7 from complications and 18 from the disease). Overall, a total of 60 patients died from the disease. Considering the 220 procedures, 165 cases involved resection of primary tumors (43 benign and 122 malignant), and 55 involved resection of spinal isolated metastases. A total of 114 tumors were located in the lumbar spine, 95 in the thoracic, and 11 were located in the cervical spine. A single posterior approach was performed in 81 procedures, whereas in 139 cases, a combined anterior and posterior approach was used during the same anesthesia. No resection was staged in more than 1 operation.

Postoperative histopathologic analysis of the resected specimens determined 128 cases as wide margins, 61 as marginal, and 31 cases as intralesional resection of the tumor.

Neurological deficits that followed planned sacrifice of nerve roots or other neural elements, for oncologic purpose, were not considered a complication.

Complete resection of neural elements occurred in 6 patients. In 4 patients, spinal cord resections (CHS at T8, osteogenic sarcoma [OGS] at T11, OGS at L1, and CH at L2—where the conus medularis had to be resected below T12) and in 2 patients, resections at the level of the cauda equina (OGS at L3 and CH at L3) were performed. Nerve root resections were performed frequently as required.

In all cases where an unplanned neurological deficits occurred, such as accidental dural tears or transient paraplegia after the manipulation of the spinal cord and neural Cauda elements during tumor resection, were considered as complications for analysis.

No spinal cord ischemia was documented after segmental artery ligation, including the sacrifice of the Adamkewicz artery, where a new artery was demonstrated by postoperative angiogram. This finding corresponds to the experimental work published by Kawahara et al,[43] demonstrating that the risk of spinal cord ischemia primarily relates to the number of nerve roots ligated, as well as a recent study by Salame et al,[44] where preoperative occlusion of segmental arteries including the Adamkewicz artery did not cause cord ischemia.

Of the 216 patients reviewed for this study, 168 (77.8%) underwent 170 en bloc resections were solely treated in the attributing authors Institute and were defined NCC and 48 (22.2%) who underwent 50 en bloc resections were previously treated elsewhere and were defined as CC. Comparison of these 2 groups with regard to demographic and baseline pathologic parameters (gender, malignancy of tumor [primary benign, malignant, or metastatic], and age), had no statistically significant difference when performing the χ^2 and the *t*-tests. The distribution and staging of the pathologies in the 2 groups were similar with regard to common pathologies (e.g., CH, CHS, OGS, giant cell tumor, metastatic renal cell carcinoma, osteoblastoma). Patients with other pathologies (e.g., metastatic thyroid carcinoma, angiosarcoma, metastatic liposarcoma) were not referred from other institutions. Overall, CCs included 6 of 43 cases with primary benign tumors, 35 of 122 with malignant tumors, and 9 of 55 with metastases. Follow-up was available for at least 24 months in 111 patients (66%), and 26 patients (54%) in the NCC and CC groups, respectively. The distribution of follow-up times appeared to be without significant difference (**Figure 1**).

Morbidity

A total of 153 adverse events after en bloc excision were observed in 100 of 220 procedures (45.45%). Almost half involved 1 event (64 cases [41%]), and 5 events occurred in 2 patients (1.3%).

Of the 48 patients in the CC group, 28 (58.33%) had at least 1 complication, whereas in the NCC group, of the 168 patients, 72 (42.86%) suffered from ≥1 complication. A total of 48 complication occurred in these 28 patients of the CC group—39 major and 9 minor. This is compared to 105 complications occurring in the 72 patients in the NCC group (66 major and 39 minor). The neurological status was preoperatively intact in 177 patients and postoperatively in 175 patients. The neurological status before and after the operation was followed for all patients (**Table 1**). The neurological status was assessed using the Frankel score—18

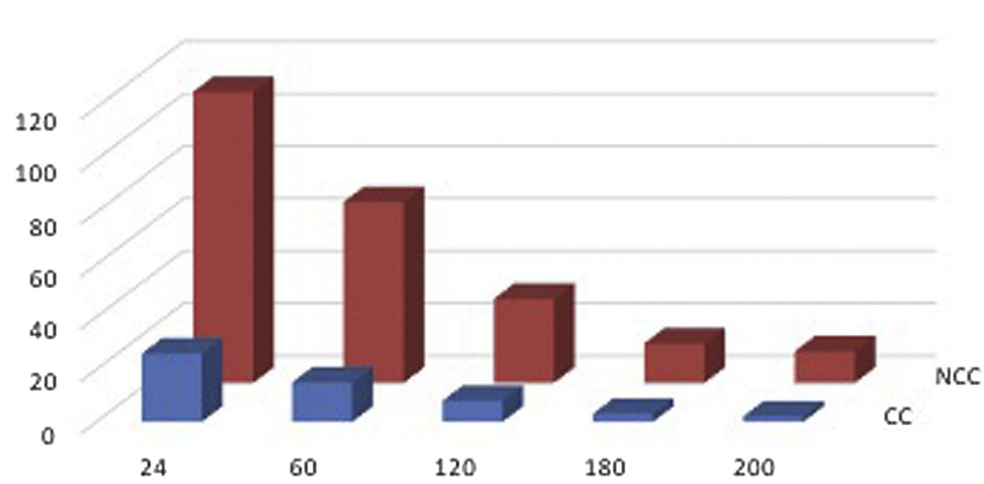

Figure 1. Follow-up in months. CC, contaminated cases; NCC, noncontaminated cases.

patients had improved neurological status and 27 deteriorated postoperatively. No statistically significant predictive factor was found related to a neurological status change.

As described in the Methods section, complications were categorized as major and minor according to the McDonnell classification[26] and were further divided by temporal distribution into 7 categories (Figures 2 and 3). A comprehensive review of all complications was recently reported.[36]

Severity

A total of 105 major complications occurred in 71 patients, and 48 minor complications were observed in 36 patients. The worst major complications were 1 intraoperative death due to injury of the vena cava, 3 late dissections of the aortic wall (2 of which were fatal), and 1 case of early postoperative fatalPE. Overall, of the 216 patients operated on, 7 patients (3.2%) died as a result of complications.

Hardware failure was the most common minor complication occurring in the late postoperative period in 22 patients, which did not require further treatment during the entire follow-up period.

Temporal Distribution

Most major complications occurred in the early postoperative period, whereas most minor complications were recorded in the late postoperative period.

Intraoperative Complications

Major (30) and minor (13) intraoperative complications were recorded. Major events included vena cava lesion leading to death, aortic wall damage, massive hemorrhage, and a dural tear that could not be repaired. Minor events included malposition of the anterior cage, and dural and vascular injuries that were immediately repaired successfully.

Early Postoperative Complications

Major (54) and minor (6) complications were observed. Major events included a fatal massivePE and a postoperative paraplegia due to a massive hematoma and hemothorax. Deep vein thrombosis, pneumothorax, and tracheal lesions during intubation were reported as minor events.

Late Postoperative Complications

Major (21) and minor (29) complications were recorded. The most severe cases were 2 aortic dissections, which occurred 3 and 8 months after surgery, 1 was fatal, whereas the other was successfully surgically treated.

Most major complications occurred in the early postoperative period, whereas most minor complications occurred in the late postoperative period (Figures 2 and 3).

Surgical Approach

Combined, simultaneous anterior and posterior approaches were performed in 139 cases, and of them adverse events occurred in 74 patients (53.24%). En bloc resection was achieved by means of an extended single posterior approach in 81 cases, and of them adverse events occurred in 26 patients (32.1%).

Predictors of Complications

Age, gender, oncologic stage as described by Enneking,[2] type of tumor (benign, malignant, metastatic), contamination, surgical approach (single or combined), number of levels resected, and type of treatment, neoadjuvant and adjuvant therapy (chemotherapy and radiotherapy) were included in the multivariate model used to predict complications. The model's calibration was Hosmer-Lemeshow test = 0.526; $\chi^2 = 7.096$; the Omnibus test of models coefficients, $\chi^2 = 35.352$; $P = 0$.

The combined approach (odds ratio [OR], 3.28, $P = 0.002$), neoadjuvant chemotherapy (OR, 4.25, $P = 0.01$), and neoadjuvant radiotherapy (OR, 3.2, $P = 0.038$) were statistically significant independent risk factors for complication occurrence. Although age was also a statistically significant risk factor, the ORs were clinically irrelevant in this study group (OR, 1.021, $P = 0.05$). All other variables tested in the model were not statistically significant risk factors for complications to occur.

Table 1. Neurological Status Change

Frankel Grade	Preoperative	Postoperative
E	177	175
D	27	24
C	10	6
B	4	7
A	2	8

For the prediction of a major event to occur, multivariate analysis was performed. In this analysis, the combined approach (OR, 3, $P = 0.01$), neoadjuvant chemotherapy (OR, 5.5, $P = 0.006$), and neoadjuvant radiotherapy (OR, 4.2, $P = 0.022$) were still statistically significant risk factors, but also adjuvant radiotherapy (OR, 3.01, $P = 0.042$) was shown to be a statistically significant independent risk factor for the occurrence of a major complication. Using this model, age was a statistically significant risk factor, but with a clinically irrelevant OR (OR, 1.024, $P = 0.038$).

Local Recurrence

A total of 33 local recurrences (15.28%) were recorded after a median follow-up of 45 months (range, 0–371 months). In the CC group 14 patients (29.17%) and in the NCC group 19 patients (11.31%) suffered from local recurrence of the tumor.

Age, gender, oncologic stage as described by Enneking,[2] type of tumor (benign, malignant, metastatic), contamination, surgical approach (single or combined), surgical margins (intralesional, marginal and wide), number of levels resected, and adjuvant and neoadjuvant chemotherapy and radiotherapy treatment were included in the multivariate model used to predict local recurrence. The model's calibration was Hosmer-Lemeshow test $= 0.694$; $\chi^2 = 5.58$; the Omnibus test of models coefficients, $\chi^2 = 34.9$; $P = 0$.

Contaminated cases (OR, 4.43, $P = 0.005$) and surgical margins of the resected tumor—intralesional (OR, 7.28, $P = 0.002$), marginal (OR, 2.69, $P = 0.031$), and malignant tumors (OR, 7.09, $P = 0.022$)—were statistically significant independent risk factors for local recurrence of the tumor. Metastatic tumors were not shown to be statistically significant risk factor for local recurrence.

As the distinction between marginal and wide excision is difficult and requires a postoperative pathologic examination, it is, in the surgeon's point of view, irrelevant to the intraoperative decision-making process. These 2 groups, marginal and wide margins, were therefore combined for statistical analysis. When doing so, in this multivariate model, intralesional resection showed a statistically significant increased risk for local recurrence (OR, 4.54, $P = 0.008$).

Mortality

As a result of the disease 60 patients died during the entire follow up period. In the CC group 21 patients (43.75%) and in the NCC group 39 patients (23.21%) died.

The multivariate model used to predict death from the disease included adjustment for age, gender, oncologic stage as described by Enneking,[2] type of tumor (benign, malignant, metastatic), contamination, surgical approach (single or combined), number of levels resected, whether complete vertebrectomy was performed, and neoadjuvant and adjuvant chemotherapy and radiotherapy treatment. The model's calibration was Hosmer-Lemeshow test $= 0.155$; $\chi^2 = 11.91$; the Omnibus test of models coefficients, $\chi^2 = 53.56$; $P = 0$.

When applying the multivariate model to predict death from the disease, contamination (OR, 2.56, $P = 0.022$), local recurrence (OR, 7.4, $P = 0.001$), neoadjuvant radiotherapy (OR, 5.91, $P = 0.01$), the number of levels resected (OR, 1.87, $P = 0.018$), and metastatic tumors compared with primary malignant tumor (OR, 2.67, $P = 0.042$) were shown to be independent risk factors for patient's death.

All other variables were not shown to be statistically significant risk factors for patient's death.

DISCUSSION

A review of a series of 220 consecutive cases treated with en bloc resection was analyzed of the related morbidity, mortality, risk assessment for local disease recurrence, complications, and death. All surgical procedures were performed in the same institution by the same team, after full staging and oncologic planning.

Although there are few reports on large series of spinal tumors resected en-bloc, these surgical procedures seem to dramatically improve local control in aggressive benign and low-grade malignant bone tumors.[2-9,11,16-19,21-23,34,35,42,45]

The ultimate goal of locally controlling the disease to improve quality of life as well as patient mortality is the basis of performing such an extensive and major surgical procedure. Thus these outcome measures should always be evaluated when assessing en bloc resection of spine tumors.

Surgical treatment has changed and evolved throughout the years of this report, as the experience gained by our group as well as reports from other groups around the world, new surgical techniques, and innovative surgical devices developed. Furthermore, advancement in radiation technology, stereotactic radiotherapy, carbon ion therapy, and novel medical therapies[46-53] have dramatically changed the indications and surgical timing of these procedures. Yet surgical en bloc resections remain an important and major part of the management of spinal tumors.

Planning En Bloc Resection

Seven different surgical strategies based on 4 combinations of surgical approaches (anterior, posterior, anterior followed by posterior, posterior followed by simultaneous anterior and posterior) are proposed to perform en bloc resection (Figures 4–10). Preoperative planning is based on the WBB surgical staging and is designed to achieve the required oncologic margin with the least possible morbidity. The techniques of en bloc resections have evolved throughout the years based on both local and international experience and reports.

Surgical parameters that need to be considered are:

- Visual control is mandatory to achieve the required margin.
- Important anatomic structures must be released or resected under visual control.

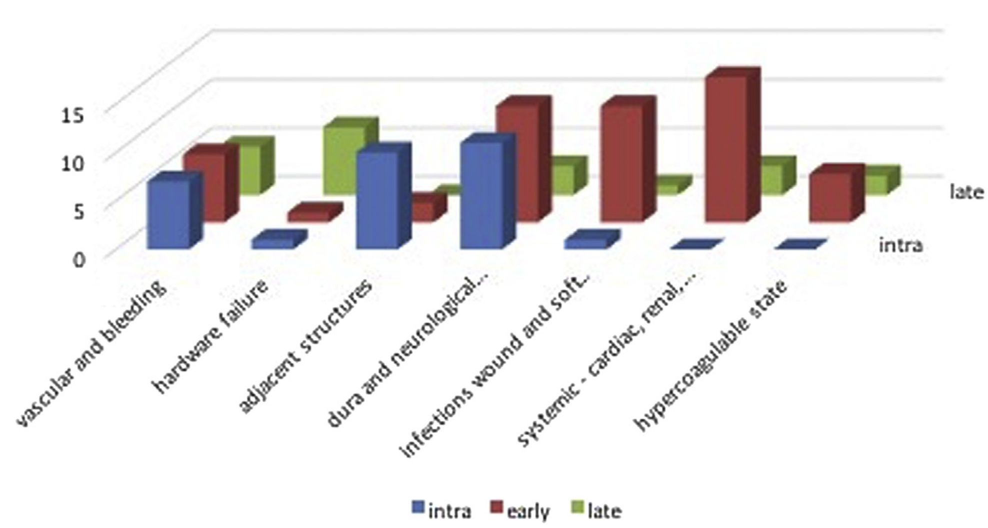

Figure 2. Temporal distribution, major.

- Combined simultaneous approaches are associated with higher morbidity and should be performed only when mandatory.
- Cord vascularity must be considered in multisegmental resections.
- Epidural bleeding can become a serious problem if underestimated.
- Removal of the specimen must be planned by the best approach to avoid tractions or torsions of the cord.

The proposed steps for surgical planning are:

- Oncologic staging and defining the suggested margins.
- Defining the functional implications of the margins regarding anatomic features.
- Review of tumor extension.

Oncologic Staging

Diagnosis and staging relate to the tumor's aggressiveness. The Enneking staging system[2] suggests the required surgical margin. If tumor is growing in the epidural space (layer E), resecting the dura together with the tumor can be considered.[11] In planning such a step, the surgeon must consider that the epidural space is extracompartmental, and dura covering the tumor would be expected only if the epidural space is occupied by scar, as commonly occurs in cases of tumor recurrence. With a tumor

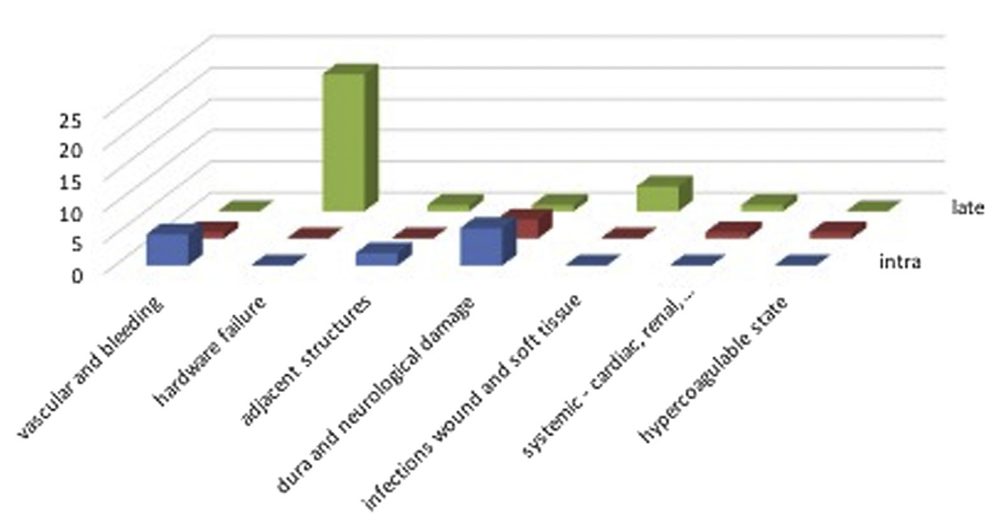

Figure 3. Temporal distribution, minor.

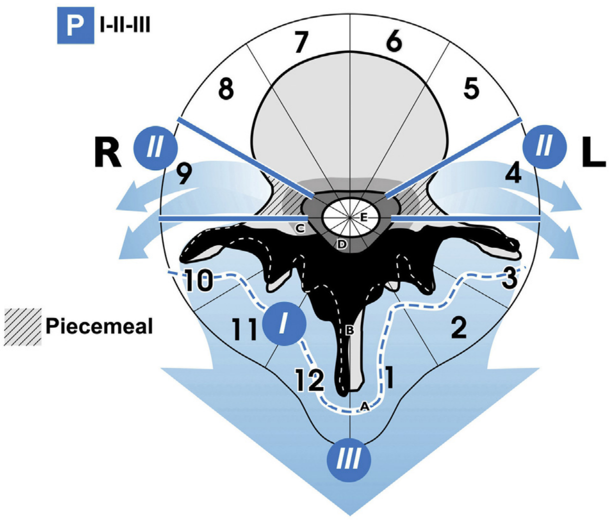

Figure 4. Using the single posterior (P) approach for an en bloc resection is the obvious strategy to remove a tumor arising in the posterior arch. Criteria to achieve an appropriate margin include freeing sectors 9 and 4 from the tumor. If the tumor grows in layer D, the margin will be intralesional during the release from the dura. The tumor is removed in 3 steps. First, provide the appropriate margin over the tumor posteriorly by resecting inside the posterior muscles covering the tumor mass if it is expanding in layer A (I). Second, piecemeal excision of sectors 9 and 4 or osteotomy by wire saw, chisel, high speed burr, or ultrasound osteotome (II). Third, once a transverse laminotomy above and below is performed, the tumor is released from the dura and the specimen is resected en bloc (III).

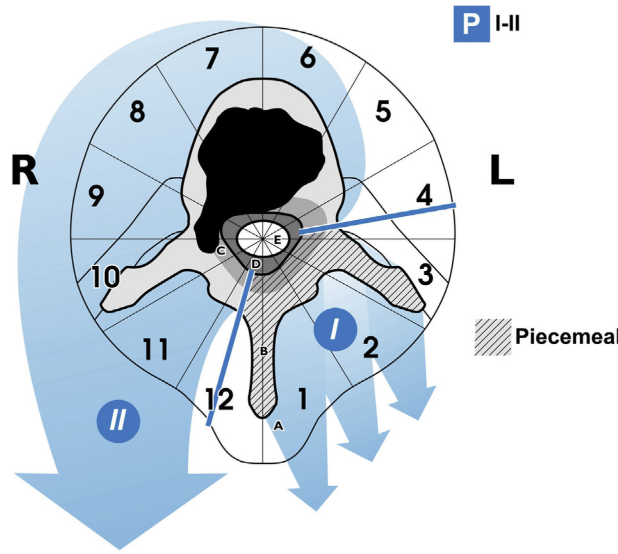

Figure 5. Single posterior (P) approach. A tumor arising in the vertebral body of a thoracic vertebra can be removed by en bloc resection. Criteria to achieve an appropriate margin include freeing sector 9 or 4 from the tumor. If the tumor grows in layer D, the margin will be intralesional during the release from the dura. If the tumor grows in layer A, the margin will be intralesional during the release from the anterior structures. The tumor is removed in 2 steps. First, piecemeal excision of the posterior arch not involved by the tumor. At least 4 sectors are required, starting from sector 4 or from sector 9 (I). Release from the dura and section of the nerve root(s) involved by the tumor. Second, blunt dissection of the anterior part of the vertebral body from the mediastinum, osteotomy or discectomy above and below the tumor, full release from the dura, and finalize the resection (II).

that has never before been operated on, extension into the epidural space can presumably be considered as contamination of all the space from the skull to the sacrum. Surgery leading to further morbidity should not be recommended in this situation, as there is no evidence suggesting that even en bloc resection could prevent recurrence.

Functional Relevance of the Margins

If a marginal/wide margin is required due to tumor histology but the margin involves a structure of some functional relevance that would be sacrificed, the decision-making process must include a cost/benefit discussion. If the tumor is growing around a nerve root, the sacrifice of such a root must be considered. If the patient refuses such a surgical step, intentional violation of the surgical margin should be considered. The patient should be fully informed of the risk of this strategy with reference to local control and final outcome, and adjuvant therapy is indicated. This careful planning obviously becomes more important when an increasing number of extraspinal structures, such as major vessels, lung, and ureter, are involved. The concept guiding the planning will always be the relationship between the appropriate surgery (based on oncologic criteria) and the related morbidity. If surgery is appropriate based on evidence that local control can be achieved with a higher probability of a better outcome, then the option of functional sacrifice or a higher risk of surgical morbidity should be discussed with the patient.

Tumor violation can occur during surgery if the surgeon unintentionally enters the tumor. Even after the most careful planning, this can occur unexpectedly as tumor visualization in preoperative imaging cannot be complete.

Tumor Extension

Tumor extension necessarily dictates surgical planning. If the tumor is growing anteriorly into the mediastinum (layer A in WBB staging, extracompartmental), an anterior approach will be required to visualize the tumor and leave a shell of healthy tissue around it as a margin. The pleura is considered an appropriate margin and can be resected over the tumor only by the anterior approach, even thoracoscopically. A posterior-only approach, according to the Roy-Camille et al[6] and Tomita et al[9] technique, cannot provide such margin, as digital dissection will necessarily violate the tumor's anterior aspect. Only the visual control provided by the anterior approach can provide resection with a safe margin.

Local Recurrence

The main aim of en bloc resection is local control and eradication of the disease. In an isolated disease after successful wide resection of the tumor, this allows the possibility of cure. This justifies the high level of morbidity reported to be related to this

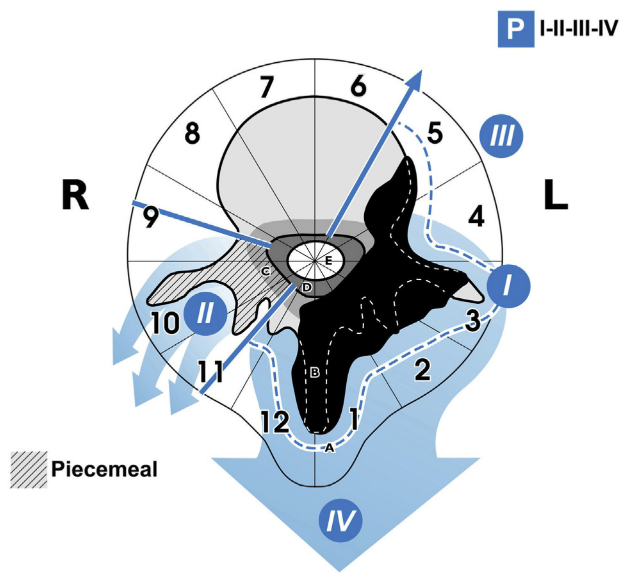

Figure 6. Single posterior (P) approach with sagittal osteotomy. A tumor excentrically growing in thoracic or lumbar spine can be removed en bloc by a single posterior approach provided that the body is not involved over sector 5 on the left and over sector 8 on the right. At least 3 sectors posteriorly must be not involved by the tumor (4 to 1–2 or 12–11 to 9). The tumor is removed in 4 steps. First, provide the appropriate margin over the tumor posteriorly by resecting inside the posterior muscles covering the tumor mass if it is expanding in layer A (I). The release will proceed laterally until the lateral side of the vertebral body. In the thoracic spine, the pleura can be left on the tumor; in the lumbar spine, the posterior part of the psoas must be dissected, but the segmental vessels must be found and ligated. Second, piecemeal excision of the posterior arch not involved by the tumor (II). Approach to the canal, release of the dura from the tumor. If the tumor grows in layer D, the margin will be intralesional and the nerve root(s) involved by the tumor need to be sectioned. Third, displace carefully the dura and perform osteotomy from posterior to anterior in sector 8 or 5 (III). Fourth, the specimen is finally removed (IV).

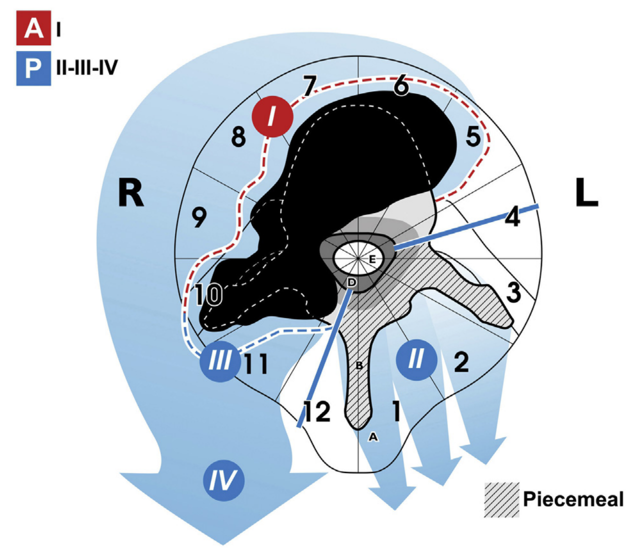

Figure 7. When the tumor is growing anteriorly (layer A), an anterior (A) approach must be performed as the first step to provide a wide/marginal margin under visual control. In case of tumors mostly occupying the vertebral body, the anterior approach can be the first step to release it from the mediastinum or retroperitoneal, eventually leaving the involved structures as margin (I). A sheet of silastic or similar can be left as protection. In the second stage, the posterior (P) approach is used. Piecemeal excision of the posterior arch not involved by the tumor (II). Starting from sector 4 or from sector 9, 3–4 sectors are required. Third, release of the dura from the tumor, section of the nerve root(s) involved by the tumor, and provide the appropriate margin over the tumor posteriorly growing by resecting inside the posterior muscles covering the tumor mass, if it is expanding in layer A (III). Fourth, finally the specimen is removed by rotating around the dural sac (IV).

procedure. The risk of local recurrence is directly related to the margin of resection.[2,54] Epidural extension of the tumor increases the risk of local recurrence.[5,9,11,19] Therefore, even major neurological sacrifices must be considered in the preoperative planning given that a local recurrence jeopardizes neurological function and worsens the prognosis. The survival and quality of life of patients with recurrences are very poor. In the series, 33 patients suffered from local recurrence of the disease.

As is well reported in the literature, clear margins have a direct relation to the local recurrence of tumors.[16,54] In the present study when applying the multivariate model, independent risk factors for local recurrence of the tumor were contamination, inadequate resection of the tumor (i.e., intralesional or marginal), and malignant type tumors. Interestingly, there was no higher risk of local recurrence in metastatic tumors. This finding is probably biased as the indications for en bloc resection for metastatic tumors are very limited to a single lesion of specific pathology. To that extent, in primary and indicated cases of metastatic tumors, the complete resection of the tumor with clear margins is of paramount importance in terms of local recurrence and disease control. The high OR for intralesional resection compared with wide margins (OR, 7.28) suggests that extreme care and measures should be taken to prevent tumor margin violation. As it is almost impossible for the surgeon to differentiate between wide and marginal margins during surgery, a more clinically relevant distinction between intralesional and either marginal or wide resection was performed in this study. This distinction represents better the surgical parameters on which the surgeon should base his or her intraoperative decision and planes of resection. When analyzing the data based on this distinction, the increased risk for local recurrence remained when an intralesional (violated margins) resection was performed compared with clear (wide or marginal) margins (OR, 4.54).

A higher rate of local recurrence was observed in the CC group compared with the NCC group (29.1% vs. 11.3%). This higher rate was maintained and was shown to be a statistically significant independent risk factor when performing a multivariate analysis that addressed all the possible confounding factors, where the OR for local recurrence was 3.97 ($P = 0.006$).

It appears that the prognosis is mainly related to the first treatment (more specifically, the experience and expertise of the team performing the initial assessment and treatment). As

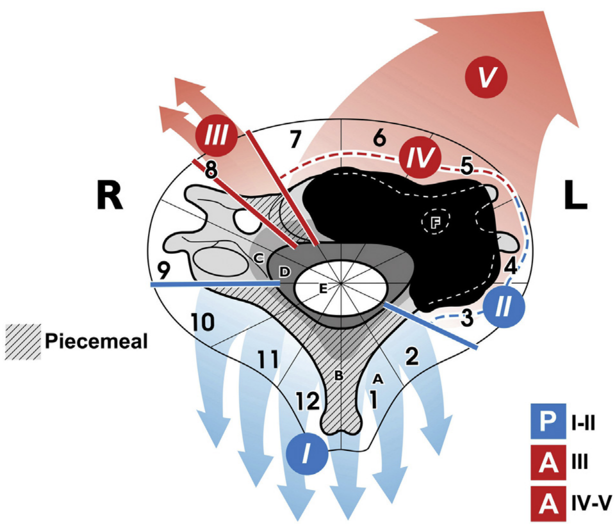

Figure 8. In the cervical spine, 3 approaches can be required: first posterior (P), second anterior (A) contralateral to the tumor side, third anterior (A) on the tumor side. The combined simultaneous second and third approaches are required if the tumor is particularly huge, extending over the midline. First, in the prone position: piecemeal excision of the posterior arch not involved by the tumor. At least 3 sectors are required, starting from sector 4 or from sector 9 (I). Second, in case the tumor is growing posteriorly and invading layer A, an appropriate margin must be provided by resecting the inside of the posterior muscles covering the tumor mass (II). Third, release the dura from the tumor. If the tumor grows in layer D, the margin will be intralesional and the nerve root(s) crossing the tumor must be sectioned. The second and third steps are in the supine position. A sagittal groove is performed in the vertebral body not occupied by the tumor (III), until the vertebral artery, which must be spared as the other vertebral artery is involved by the tumor on the other side must be sacrificed. Fourth, the anterior margin is provided by leaving healthy soft tissue over the tumor mass (IV). Diskectomies or transveral grooves in vertebral bodies are performed to define the upper and lower margins. Fifth, the tumor is finally removed by the third approach (V), once finalized the upper and lower diskectomies or osteotomies, including ligation of the vertebral artery.

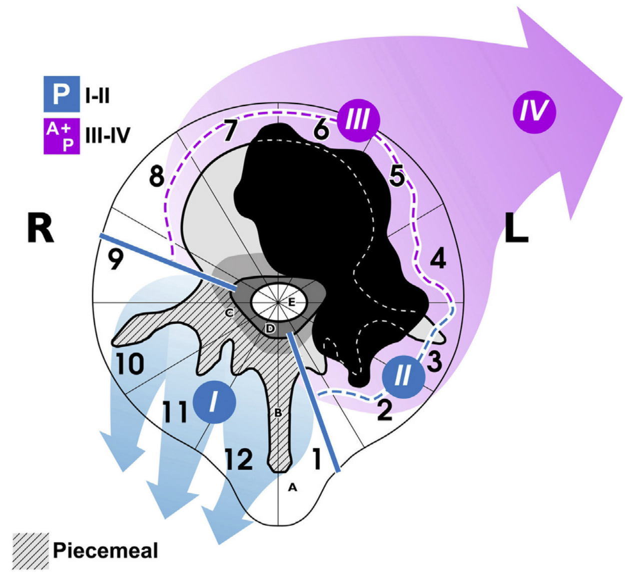

Figure 9. For most lumbar tumors the en bloc resection is best performed, in our experience, with, first, the posterior (P) approach and, second, a combination of the anterior (A) and posterior approaches. This allows the best margin control but is associated with the highest rate of morbidity and complications. First, in the prone position: piecemeal excision of the posterior arch not involved by the tumor. At least 3 sectors are required, starting from sector 4 or from sector 9 (I). Second, in case the tumor is growing posteriorly and invading layer A, an appropriate margin must be provided by resecting inside the posterior muscles covering the tumor mass (II). Third, the dura is released from the tumor. If the tumor grows in layer D, the margin will be intralesional and the nerve root(s) crossing the tumor must be sectioned. Diskectomies or transveral grooves in vertebral bodies are performed to define the upper and lower margins. The second stage is in the lateral position. Anterolateral approach (thoracotomy, thoracoabdominal, retroperitoneal) and reopening of the posterior approach. Third, provide an appropriate margin over the tumor; it must remain covered by pleura or by psoas (III). Spiral wires are used to embolize the segmental arteries to make it easier to release the aorta on the contralateral side. Fourth, once finalized with the upper and lower diskectomies or osteotomies. With these combined maneuvers the specimen is removed (IV).

violation of oncologic principles may be followed by very serious consequences, where tumor recurrence is increasingly more difficult to control. Intentionally violating oncologic principles to improve the functional outcome means performing intralesional surgery, which reduces the possibility of local control.[3-9,11,16-19,21-23,35]

Morbidity

It is commonly accepted that the morbidity as a result of surgical procedures for spine tumors is related to the altered anatomy secondary to the tumor growth and the fibrosis caused by preoperative radiotherapy or previous surgery. To that extent, a revision surgery and procedures conducted after oncologic contamination of the surgical field mandates a more aggressive approach and, at times, the necessity of sacrifice of important adjacent anatomic structures.

As the need to achieve clear margins requires a more aggressive surgical approach involving the resection of anatomic structures, as well as the manipulation or sacrifice of neural and vascular structures, it is expected to involve a higher rate of complications.

In 110 of the 220 cases, at least 1 unplanned adverse event occurred. This rate is very high and reflects the complexity of resecting spinal tumors in an intact piece. This rate was similar throughout the study's period; no improvement in this rate was demonstrated when comparing the earlier and late cases. In a previous report published by our group[35] a similar rate of complications was demonstrated. As the incidence of complications is considered to be mainly related to the complexity of the procedure and the experience of the surgeon, it would be expected to improve with the years of experience. However, more elaborate and complex procedures were performed, expanding the indications and surgical ability to remove complex tumors en bloc, in concordance with the team's experience and developed expertise.

Most intraoperative complications were associated with manipulation of major structures such as neural and vascular elements. Therefore, in the preoperative planning, addressing

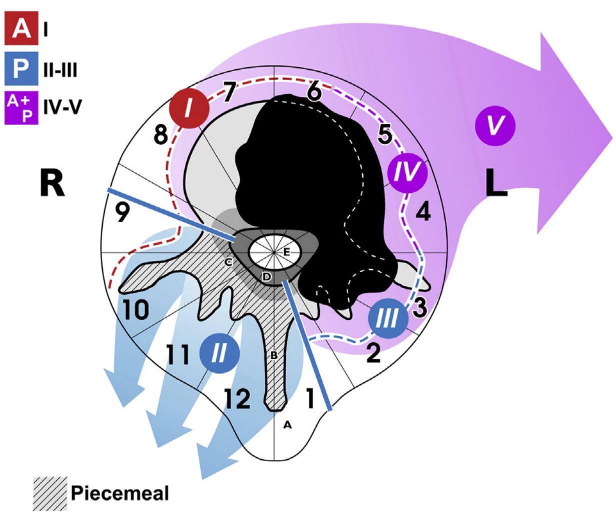

Figure 10. To perform en bloc resection of a tumor of L5 a double anterior (A) approach is required to fully release the aorta/cava bifurcation. Our technique includes: first, an anterior approach on the contralateral side of the tumor, second, a posterior (P) approach, third, a combination of the anterior and posterior approaches. First, in the supine position: release the aorta/cava bifurcation and do partial diskectomies or osteotomies to define upper and lower margins (I). Second, in the prone position: piecemeal excision of the posterior arch not involved by the tumor. At least 3 sectors are required, starting from sector 4 or from sector 9 (II). Third, in case of tumor is growing posteriorly and invading layer A, an appropriate margin must be provided by resecting inside the posterior muscles covering the tumor mass (III). Then release the dura from the tumor. If the tumor grows in layer D, the margin will be intralesional and the nerve root(s) crossing the tumor must be sectioned. Diskectomies or transveral grooves in vertebral bodies are performed. The third stage is in the lateral position. Retroperitoneal approach and reopening of the posterior approach. Provide appropriate margin over the tumor by leaving it covered by psoas (IV). Then finalize the diskectomies or transveral grooves in vertebral bodies to remove the specimen by the anterior approach (V).

elements at risk, such as the spinal cord, major blood vessels, and other vital structures, is required. This is even more important in revision surgery and after radiotherapy where scar tissue is present and tissue fragility might be encountered. In cases where tumor is expected to be attached to vital structures such as the aorta or the dural sac, and detachment might be difficult or impossible without jeopardizing the integrity of this vital structure, it is advisable to include an aortic bypass or dural reconstruction in the preoperative planning. Immediate suturing of dural tears with either muscular graft coverage or other nonorganic grafts generally leads to prompt and satisfactory healing. However, when waterproof suturing cannot be performed, cerebrospinal fluid depletion may lead to complications requiring, at times, further revisions and a longer hospital stay. When surgical limitations might prevent the successful achievement of the oncologic treatment planned, a joint decision (patient and treating physician) should be performed acknowledging the risks and outcomes of limited surgical treatment versus a dangerous complete resection.

Thoracic root transection causes minimal postoperative problems yet allows an easier approach to the tumor's mass by reducing traction and manipulation of the cord. As manipulation of the spinal cord, especially in the thoracic spine, increases the risk of neurological injury (transient or permanent), it is, based on our experience, advised to extend the root resection, thus limiting the need for cord manipulation.

In a recent article reporting on the morbidity of en bloc resection by our group,[36] a 45.5% rate of complication occurred. Only 4.6% of the patients died as result of these complications, most other cases benefited from a low recurrence rate when true en bloc resection was achieved. The high risk of complications should, therefore, not discourage surgeons from performing en bloc resection when needed, provided that it is technically possible. Conversely, local recurrences negatively affect prognosis and may be associated with a higher risk of complications during subsequent revision surgery.

Surgical Approach

A higher risk of complications occurring in the combined approach remained statistically significant in the multivariate analysis model, after adjustment to confounding factors that were shown as risk factors in an univariate analysis. This suggests that a combined approach has an increased risk of complications irrelevant of the complexity of the procedure performed. However, the benefit of conveniently approaching a tumor without manipulation to neural or vascular elements outweighs the added risk of complications from a combined approach.

Adjuvant Therapy

Adjuvant radiotherapy was shown to be a statistically significant independent risk factor for the occurrence of a major complication. These data support the notion that although this treatment does not affect the rate of complications, once occurring after adjuvant radiotherapy, there will be a major effect on the patient as described by McDonnell et al.[26] As for adjuvant chemotherapy, data collected with regard to en bloc resection did not demonstrate an effect on morbidity, local recurrence, and mortality. This is contrary to what was expected. Because most patients in this study received adjuvant treatment, it is expected that the effect of such treatment on morbidity and mortality could not be demonstrated with a statistically significance in our cohort.

Hardware Failures

As the ultimate purpose of performing this complex and morbid surgical procedure is to improve local control of the disease, thus improving survival, one must plan preoperatively for structural stability after the resection where complex circumferential reconstruction is required.[4,55-57] Implants, autogenous grafts and/or bone substitutes, and various induction materials should be used to achieve spinal fusion at the resected level. Chemotherapy and radiotherapy may negatively affect the possibility of achieving this fusion, and timing is critical. The reconstructive technique that was used in most patients included posterior pedicle screws and rods and an anterior column reconstruction construct filled with allogenous graft or bone substitutes.[55] Failure of the fusion occurred in 31 patients (14%). However, only in 9 cases (4.09%) this failure was clinically significant and required revision surgery. No revision surgery was required for anterior column failure. It is of note that most hardware failures occurred at the late postoperative period. The success of the surgical resection and the local control is usually known then, and a better revision surgery can be tailored to the specific purpose of spinal stability and fusion.

A higher rate of complications was observed in the group of patients who underwent en bloc resection after open biopsy or previous treatment followed by recurrence. Twenty-eight of 48 patients (58.33%) in this latter group had at least 1 complication, compared with 72 of 168 patients (42.8%) treated from the beginning in the same center. In particular, a higher rate of major complications was observed—39 major complications of 48 events (81.2%) in the CC group, compared with 66 major complications of 105 events (62%) in the NCC group. Nevertheless, in the multivariate model, contamination was not shown to be a statistically independent risk factor for complications to occur. To that extent, the relatively small number of events combined with the established contributing factors that are known as risk factors for complications, such as previous chemotherapy and radiotherapy, combined surgical approach,[35] might have caused this difference to be statistically insignificant as an independent factor.

Patient's Death From the Disease

A total of 60 patients died from the disease. A previous invasive attempt at treating the tumor in an institution that was not specialized in this procedure was shown to be an independent risk factor for patient's increase mortality, as the OR for patient's death from the disease was 2.55 ($P = 0.022$). Independent risk factors of death from disease were shown to be patients that began their treatment in a less experienced institution, local recurrence, the number of levels resected, and previous radiotherapy. This suggests that the initial management of the patient, diagnostic (invasive) and therapeutic (neoadjuvant radiotherapy), has a direct effect on the patient's mortality. To that extent, the surgical and oncologic limitations subjected by an inappropriate open biopsy or an inadequate initial surgical treatment mandates a more aggressive surgical resection and at times even prevents a complete oncologic removal of the tumor, affecting the patient's quality of life as well as mortality. It is, therefore, reasonable to perform the entire management, from the initial invasive diagnostic procedures through the preoperative assessment and surgical attempt at complete tumor removal in a high volume specialized center.

Limitations

In this study, all cases of spinal tumors treated by en bloc resection at the attributing author's institution are reported. Adjuvant radiation and chemical treatment is not reported in this article. During the years, surgical and adjuvant treatment of spinal tumors has evolved greatly. The introduction and advancement of radiation-induced therapy, stereotactic surgery, and novel chemical therapy has altered the management of some of these tumors. These less invasive techniques changed the indications for performing this aggressive and demanding surgical procedure; however, its role in treating spinal tumors with the aim of local control still remains. As the surgical experience as well as the use of these modalities improve, management of spinal tumors mandates a multidisciplinary approach.

Referral for further treatment to a more experienced center holds a potential bias. It is assumed that the more difficult or recurrent cases were referred to a more experienced center, having a worse prognosis and a higher likelihood of recurrence. In this report, both groups of CC and NCC where similar in terms of patient demographics, disease diagnosis, and staging. Because differences exist in the number of patients in these 2 groups as well as the lack of presentation of some of the less frequent pathologies in the CC group, it is reasonable to assume that a bias still exist.

In the spine, different tumors have different behaviors, tendency for local recurrence, metastasis, and prognosis. The value of summing these pathologies in a single report is not in the specific surgical treatment for a specific disease, rather it allows a better understanding of this surgical tool of en bloc resection. Knowing the preoperative planning, intraoperative and postoperative complications, and outcome might improve the use of this important, yet demanding, surgical modality.

This study describes the outcomes recorded in a large single-center series of en bloc resections, and stratifies the risk factors for failures in terms of both disease control and patient morbidity.

Because some risk factors are uncontrollable, it is imperative to understand the risk factors that the treating physician does have control of. These factors are the successful removal of the tumor with clear margins and the performance of the invasive procedures by an experienced team.

CONCLUSIONS

The data support the conclusion that local recurrence is the worst complication, as this negatively affects quality of life and prognosis. The results in terms of better prognosis and better local control[3-9,11,16-19,21-23,35,39] justify performing such highly demanding and risky procedures in aggressive benign and in low-grade malignant bone tumors.

The surgeon who treats the patient has a great responsibility, as it is the first treatment that most affects prognosis. To reduce the chance of local recurrence, morbidity, and mortality, this should be performed by an experienced team as the consequences are dramatic.

Margins are the key point of this surgical procedure. Wide or marginal margins are necessary to improve outcomes in term of lower risk of local recurrence and tumor-related mortality. In addition, a careful preoperative oncologic and surgical staging is necessary to define the optimal surgical approach. The adverse event profile of these surgeries is high; therefore, it should be performed by experienced and multidisciplinary teams in specialized high volume centers.

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