Clinical features and surgical outcomes of patients with skull base chordoma: a retrospective analysis of 238 patients

*Liang Wang, MD,1,2 Zhen Wu, MD,1,2 Kaibing Tian, MD,1 Ke Wang, MD,1,2 Da Li, MD,1,2 Junpeng Ma, MD,1 Guijun Jia, MD,1,2 Liwei Zhang, MD,1,2 and Junting Zhang, MD1,2

1Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University; and 2China National Clinical Research Center for Neurological Diseases, Beijing, People’s Republic of China

OBJECTIVE  Skull base chordoma is relatively rare, and a limited number of reports have been published regarding its clinical features. Moreover, the factors associated with extent of resection, as well as the value of marginal resection for long-term survival, are still in question for this disease. The objective of this study was to investigate these factors by evaluating their clinical features and surgical outcomes.

METHODS  A retrospective analysis of 238 patients with skull base chordomas, who met the inclusion criteria, was performed. This study summarized the clinical features, selection of approaches, degree of resection, and postoperative complications by statistical description analyses; proposed modified classifications of tumor location and bone invasion; studied the contributions of the clinical and radiological factors to the extent of resection by Pearson χ², ANOVA, rank test, and binary logistic regression analysis; and estimated the differences in overall survival and progression-free survival rates with respect to therapeutic history, classification of tumor location, extent of bone invasion, and extent of tumor resection by the Kaplan-Meier method. A p value < 0.05 was considered statistically significant.

RESULTS  The study included 140 male and 98 female patients with a mean age of 38.1 years. Headache and neck pain (33.2%) and diplopia (29%) were the most common initial symptoms. Sphenoclival type accounted for the largest proportion of tumor location (59.2%); endophytic chordoma was the more common type of bone invasion (81.5%). Lateral open approaches were performed in two-thirds of the study population (78.6%). The rate of marginal resection was 66%, composed of gross-total resection (11.8%) and near-total resection (54.2%). Meningitis (8%) and CSF leakage (3.8%) were the most frequent complications. The mean follow-up period was 43.7 months. The overall survival and progression-free survival rates at 5 years were 76% and 45%, respectively. Recurrent tumor and larger tumor volume (≥ 40 cm³) were identified as risk factors of marginal resection. Patients who presented with recurrent tumor and underwent intralesional resection had a worse long-term outcome.

CONCLUSIONS  The classifications of both tumor location and bone invasion demonstrated clinical value. Marginal resection was more likely to be achieved for primary lesions with smaller volumes (< 40 cm³). The rate of CSF leakage declined due to improved dura mater repair with free fat grafts. Marginal resection, or gross-total resection when possible, should be performed in patients with primary chordomas to achieve better long-term survival.

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KEY WORDS  chordoma; skull base; surgery; classification; extent of resection; outcome

CHORDOMAS are relatively rare malignant tumors that are believed to originate from remnants of the notochordal elements. Skull base chordomas account for approximately one-third of chordoma cases and constitute < 1% of all intracranial neoplasms.27,29 A combination of maximally safe cytoreductive surgery and advanced external-beam radiation therapy has been viewed as the gold-standard treatment for this locally aggressive and destructive tumor, although new clinical trials using targeted molecular therapies are also in progress.3,25–27 Nevertheless, tumor resection still has a major role in treatment.1,5,9,21,23

Various skull base clinical centers have published the clinical outcomes of patients with skull base chordomas...
for the last 2 decades. Although the overall treatment effects, such as the rate of gross-total resection (GTR) and long-term survival, are stable, controversies remain regarding optimal surgical approaches, factors associated with the extent of resection, and corresponding complications. However, because the reported surgical series usually have small sample sizes due to the rarity of the disease, and because the meta-analyses based on public-use databases did not contain critical necessary information, these questions remain unanswered.

Through the publication of clinical series from 1993 to 2005, we have shared our experiences regarding the prognostic factors of skull base chordomas treated with resection at a skull base center in China. Since this report was published, more comprehensive and meaningful results have been obtained as we have introduced endoscopic surgeries, intraoperative neuromonitoring, and navigation systems. In addition, we have improved the techniques of skull base repair. In this study, we retrospectively reviewed the cases of 238 patients with skull base chordomas that were resected at our medical center in the last 10 years. We propose new MRI-based classifications for tumor location and bone invasion, which are also related to clinical features and chosen surgical strategy. We evaluated the results of our surgical techniques, focusing on the extent of tumor resection, surgical complications, and follow-up outcomes. We then examined the factors that may influence marginal tumor resection and long-term outcome.

**Methods**

**Patient Population**

Patients with either primary or recurrent skull base chordomas, who were consecutively treated between February 2005 and December 2014 in the Skull Base Ward of the Neurosurgery Department at the Beijing Tiantan Hospital of Capital Medical University, were included. For those who underwent more than surgery, details about their initial procedure performed at our center were collected and analyzed in the present study. Patients without certain pathological diagnoses, without a history of tumor resection, and without adequate neuroimaging and clinical information were excluded.

We identified 238 patients who met the inclusion criteria and retrospectively reviewed their inpatient records for demographic data, clinical symptoms and signs, duration of the initial symptoms, previous surgery and radiotherapy, surgical approaches, operative details, dura mater integrity, repair of the cranial base, blood loss, surgery duration, complications, preoperative and postoperative Karnofsky Performance Scale (KPS) scores, and duration of hospital stay. All of these parameters were reviewed and recorded separately by 2 members of the study team (K.T. and J.M.). This study was certified by the ethics committee of Beijing Tiantan Hospital, Capital Medical University.

**Imaging and Classification Criteria**

Preoperative MR images were evaluated by the study team to assess the following: 1) maximum tumor diameter, which was recorded by comparisons among the longest diameters (D1, D2, and D3) in 3 dimensions (sagittal, coronal, and axial); and 2) tumor volume, which was approximately calculated by the cubature formula \( V = (D1 \times D2 \times D3)\pi/6 \).

Because remnants of the notochord, as the precursors of chordoma, occasionally exist among the sutures of the skull base, we speculated that chordomas should also be closely related to these bony connections. We proposed a modified classification of tumor location composed of 6 types, of which are shown in Fig. 1 (left).

We also proposed a classification system for the extent of bone invasion, which included endophytic and exophytic types. The intrinsic type, which was relatively rare, was represented by inner bony lesions with neither extraosseous nor intraosseous invasion trends, as demonstrated in Figs. 1 (right) and 2. It is worth noting that a distinction of benign notochord cell tumors or eckhordosis physaliphora from the intrinsic chordoma should be made. These imaging evaluations were performed by 2 members of the study team (L.W. and K.T.), and any differences were resolved by discussion.

**Surgical Principles and Dural Repair**

Our surgical treatment strategy was to perform radical resection whenever possible. For patients with poor physical or physiological statuses, especially those with repeated tumor recurrence, a less aggressive tumor resection would be preferred on the basis of an adequate decompression of vital structures, such as the brainstem and visual pathway. No patients in this series were intended to undergo a 2-stage operation.

At the conclusion of tumor resection through the lateral approaches, free fat grafts were used to repair the dural defect in the skull base, regardless of whether it was caused by tumor destruction or surgical incision. The fat grafts were placed into the dural defect like a “bath plug” or sutured with the nearby skull base dura. Free fat grafts were also used in the anterior midline approach when CSF leakage was suspected.

**Extent of Resection**

All patients underwent postoperative MRI within 2 weeks of surgery, and these images were reviewed with their respective preoperative MR images. The degree of tumor resection was evaluated based on the postoperative MR images with operative records used for reference. GTR was defined as the entirety of the tumor that was removed, followed by drilling the bony tumor margins until normal-appearing bone fracture was reached and an absence of residual tumor was apparent on the postoperative MR image. Near-total resection (NTR) was defined as an absence of tumor as observed by microscope or endoscopy, with radiological evidence that > 90% of tumor was removed. In cases in which only a residual tumor was present, subtotal resection (STR) was defined as having > 70% of the tumor resected, and partial resection (PR) was defined as having ≤ 70% of the tumor resected. For the sake of comparison, GTR and NTR were collectively classified as marginal resection (MargR), and STR and PR were correspondingly labeled as intralesional resection.

**Patient Follow-Up**

We recommended that all patients be evaluated on an
outpatient basis at 3 months for the initial follow-up, at 6 months for the second follow-up, and annually for life thereafter. Radiation therapy was recommended to patients who had obvious and active remnants at the first follow-up, or those with locally advanced lesions not amenable to surgery. The radiation therapy was recommended to patients who had obvious and active remnants at the first follow-up, or those with locally advanced lesions not amenable to surgery. Two researchers (K.T. and K.W.) attempted to acquire the most recent status of enrolled patients either from patients or their legal guardians through telephone interviews in April 2015.

The primary end point was overall survival (OS), defined as the time from the start of follow-up to the date of death from any cause. The secondary end point was progression-free survival (PFS), defined as the time from the start of follow-up to the time of the first event (progression or death). The diagnosis of progression, including recurrence and regrowth, was made on the basis of complaints about progressive clinical manifestations in combination with newly discovered abnormalities on MRI, which could only be explained by tumor relapses in the primary site or adjacent regions during outpatient follow-up. Patients with no events were censored at the date of their last follow-up.

**Statistical Analysis**

After descriptive statistical analyses were performed, we analyzed the contributions of the clinical and radiological factors to the extent of tumor resection. The Pearson $\chi^2$ test was used for categorical variables, and the ANOVA test was used for normally distributed continuous variables. The rank test was applied in the analysis of abnormally distributed data. A binary logistic regression analysis was used to study the risk factors associated with MargR. The OS and PFS rates were estimated by the Kaplan-Meier method, and a 2-sided log-rank test was used to look for significant differences between groups, which were classified by the key factors in this study including therapeutic history, classification of tumor location, extent of bone invasion, and extent of tumor resection.

A $p$ value $< 0.05$ was considered statistically significant. Statistical software used for this study included SPSS version 13.0 and IBM SPSS version 19. The statistical analysis was performed separately by 2 authors (L.W. and Z.W.).

**Results**

**Clinical Features**

One hundred forty males and 98 females (male/female ratio of 1.4:1) were included in this study. The mean age of patients at their first operation performed in our center was 38.1 years (median 40 years, range 5–76 years). One hundred eighty-three patients (76.9%) with primary tumors underwent initial operations at our skull base clinical center. Among the 55 patients with recurrent tumors, 46 had received a total of 62 tumor resections, including 34 patients (73.9%) who underwent initial operations at other institutions; 9 cases had received radiotherapy only. Gamma Knife surgery was the most common choice of...
radiotherapy in this series, accounting for 36 courses of radiotherapy (85.7%). One patient had a family history of chordomas, and 2 patients had chordomas associated with a pituitary adenoma and an ipsilateral epidermoid cyst, respectively. The average duration of the initial symptoms was 14.4 months (median 6 months, range 0.5–120 months). The most common initial symptoms included headache and neck pain (33.2%), diplopia (29%), visual impairment (11.3%), and dysphagia and dyspnea (7.5%).

Radiological Features

The mean tumor maximum diameter was 42.9 mm (SD 12.5 mm, range 15–85.9 mm), and the mean tumor volume was 28.3 cm$^3$ (median 22.8 cm$^3$, SD 23.2 cm$^3$, range 1.9–139.4 cm$^3$). With respect to tumor location, most were classified as the sphenoclival (SC) type (141 cases comprising 59.2%), followed by occipitocervical (OC) (41 cases comprising 17.2%). Sphenopetrous (SP), petrous-occipital (PO), ethmoid-sphenoid (ES), and extensive types were present in 10.1%, 6.3%, 1.7%, and 5.5% of patients, respectively. In terms of initial symptoms associated with different tumor locations, diplopia was the most common for SC- and SP-type tumors, accounting for 38.3% and 41.7% of these groups, respectively; headache and neck pain was the most frequent initial symptom for OC-type tumors (60.9%); dysphagia and hypacusis were the 2 main symp-
approach in 31 cases, the zygomatic–extended middle fossa approach in 28 cases, the anterior transpetrous approach in 25 cases, and the crano-orbitozygomatic approach in 7 cases. The infratentorial subgroup included the far lateral transcondylar approach in 43 cases, the extreme lateral paracondylar approach in 12 cases, and the retrosigmoid approach in 3 cases.

The surgical approaches were mainly selected according to tumor location, as demonstrated in Fig. 3 (lower). For SC-type tumors, either the microscopic or endoscopic transsphenoidal approach was used in cases with extracranial growth patterns, and lateral approaches, such as the transpetrosal presigmoid, anterior transpetrous, or modified anterior transpetrous approaches, were chosen for tumors in which the main body was intracranial with an obvious compression of the brainstem. For OC-type tumors, we typically used the far lateral transcondylar approach, whereas the retrosigmoid or extreme lateral paracondylar approaches were used for PO-type tumors. In such cases, extradural resection with or without the assistance of endoscopic surgery was viewed as the first option. For SP-type tumors, the crano-orbitozygomatic, zygomatic–extended middle fossa, or modified anterior transpetrous approaches were selected, and an epidural route to reach a tumor located in the cavernous sinus or the petrous apex was also occasionally attempted. The transmaxillary approach, which is another midline approach, was performed for a few extensive-type recurrent cases, in cooperation with oral and maxillofacial surgeons.

The integrity of the dura was determined during surgery and recorded as a key component of each patient’s operative records. Ninety-three cases (39.1%) showed intraoperative evidence of tumors breaking through the dura, and these cases were classified as the intradural sub-
group. The remaining 145 cases (60.9%) were classified as the extradural subgroup. Regarding the type of operation, 67 tumors (28.2%) were resected through epidural routes without opening of the dura, and 162 cases (68.1%) underwent intradural procedures including either subdural exposure or resection. In 9 patients (3.8%), after the extradural portion of the tumor was resected, we continued to open the dura for GTR once it was verified that the dura had been broken through. At the end of surgery, we repaired dural defects in the skull bases of 101 patients (42.4%) with free fat grafts (82 cases), other autologous tissues (4 cases), or artificial dura (15 cases).

Degree of Tumor Resection

A GTR was achieved in 28 cases (11.8%), and NTR in 129 cases (54.2%). STR and PR were performed in 61 (25.6%) and 20 (8.4%) patients, respectively. As shown in Table 1, MargR was achieved in 73.9% of patients who had no prior surgery, which was 2.3 times higher than in patients with a surgical history (p < 0.001). None of the patients with histories of radiotherapy underwent GTR, and only 25.9% of these patients received PR, which was significantly different from the number of patients without prior radiotherapy who received PR (p = 0.001). As for tumor location, SC-type (73.8%) and PO-type (73.3%) tumors had higher rates of GTR and NTR; however, patients with OC-type (56.1%) and extensive-type (61.6%) tumors were more likely to receive STR and PR (p = 0.034). MargR was achieved in 86.4% of the exophytic-type tumors, which was much higher than the MargR rates for the endophytic- and intrinsic-type tumors (p < 0.001). In this series, MargR was achieved in only 49% of patients who received the anterior midline approaches, whereas the MargR rate reached 76.0% for those who received lateral approaches (p = 0.025). A combination of extradural and intradural routes seemed to achieve higher rates of GTR (33.3%; p = 0.037) than extradural or intradural approaches.

The mean maximum diameters of the GTR, NTR, STR, and PR groups were 33.4 ± 9.9, 41.7 ± 11.1, 48.5 ± 14.3, and 47.7 ± 9.5 mm, respectively, and this value was significantly smaller in the GTR group than in the other 3 groups by multiple comparisons (p = 0.005, p < 0.001, and p < 0.001, respectively). Moreover, the mean maximum diameter was also significantly smaller in the NTR group than in the STR and PR groups (p = 0.002 and p = 0.005, respectively). Although tumor volume was analyzed by rank test because the values were not normally distributed, it was significantly different among the different degrees of tumor resection (p < 0.001). There were no significant differences among the different degree of resection groups when sex (p = 0.390), age (p = 0.737), blood loss (p = 0.425), surgical duration (p = 0.293), and duration of the initial symptoms (p = 0.875) were considered.

Based on the aforementioned results, tumor volume, therapeutic history, preoperative KPS score, tumor location, and extent of bone invasion were included in the multivariable analysis of risk factors for MargR. As a result, recurrent tumor (OR 5.721, 95% CI 2.797 to 11.700; p < 0.001) and tumor volume ≥ 40 cm³ (OR 3.166, 95% CI 1.640 to 6.110; p = 0.001) were verified as 2 risk factors for MargR, as illustrated in Table 2.

Surgical Complications and Management

The mean hospital stay was 21.8 days (median 20 days, range 7–92 days). As indicated in Table 3, the most common surgical complication was meningitis (8%), all cases of which were secondary to the open surgery. The second most common complication was CSF leakage (3.8%), in all 9 cases of which the patient underwent lumbar spinal drainage as the initial treatment. Lumbar spinal drainage was not successful in 4 patients who underwent surgical repair. It was noteworthy that all 9 patients with postoperative CSF leakage belonged to the open surgery group, and no CSF leaks occurred after the transsphenoidal surgery. Cerebral infarction occurred in 3 patients; brainstem infarction also occurred in 3 patients, causing hemiparesis and even quadriplegia. Hydrocephalus developed in 4 patients, and 3 of these cases were resolved by ventriculoperitoneal shunt. Five cases of wound effusion and 1 case of subdural effusion were also present and required either lumbar spinal or subdural drainage. Debridement was performed in 3 patients who had wound infections. Pulmonary infection occurred in 8 patients who had open surgeries, and 5 received tracheotomies due to permanent lower cranial nerve palsy. One patient died as the result of sudden brainstem hemorrhage 10 days after surgery.

The KPS score was used to assess functional status during the perioperative period, as used by others. The average KPS score was 76.4 ± 12.1 preoperatively and 75.4 ± 17.9 postoperatively before discharge. There was no significant difference between these values (p = 0.702), which may imply that surgery could not improve the postoperative short-term functional outcome of the patients as a whole. There were 4 patients with an extremely poor postoperative KPS score of 20. These individuals suffered from severe neurological or systemic complications; after they were discharged and transferred to their local neurosurgical institutions, all of them died as a result of further deterioration.

Outcomes of Follow-Up

Initial follow-up data were available for 234 of 238 patients, including 180 patients with primary tumors. Forty-six patients died during follow-up (19.7%), including the aforementioned 4 patients whose postoperative KPS score was 20. Tumor progression was detected in 82 of 180 patients with primary tumors (45.6%). The mean follow-up was 43.7 months (median 41 months, range 4–127 months). The OS rates at 3, 5, and 7 years were 81%, 76%, and 71%, respectively; the PFS rates at 3, 5, and 7 years were 51%, 45%, and 31%, respectively. The mean PFS was 56.9 months (median 39 months, 95% CI 49.7–64.1 months), and the mean OS was 94.7 months (95% CI 87.6–101.8 months).

Patients with primary lesions had significantly longer OS and PFS, with PFS rates at 3 and 5 years of 61% and 51%, respectively, when compared with patients with recurrent lesions, whose PFS rates at 3 and 5 years were only 23% and 14%, respectively, as demonstrated in Fig. 4A and B.

The number of prior operations was also shown to be associated with both OS and PFS (Fig. 4C; p < 0.001), whereas PFS for patients with different types of tumor location and bone invasion was significantly different (Fig. 4D, Table 4; p = 0.023 and p = 0.020, respectively).
Regarding the degree of resection, patients with GTR gained obviously longer OS and PFS compared with other degrees of resection (Fig. 4E). The median PFS was 68.9 and 34.1 months for the groups that underwent MargR and intralesional resection (Fig. 4F; p < 0.001), which were performed in 154 and 80 cases, respectively, and the corresponding OS was 102.1 and 74.9 months, respectively (Table 4; p = 0.002).

Discussion

Skull base chordomas are locally invasive tumors with a slight male predilection, as shown in Table 3, in which the constituent ratio of males ranged from 49% to 70%.2,6,16,20,22,23,24,28,33 There was a very wide spread of age at diagnosis in our series, ranging from 5 to 76 years, with a peak incidence in the fourth decade of life. This corresponded to the average age reported in most surgical series, except for that described by Jahangiri et al. (59 years).16,20,22,23,24,33 The mean time from initial symptoms to diagnosis is usually longer than 1 year23,27 and was 18.8 months and 14.4 months in our present study and in a previously reported series, respectively.33 Chordomas are indolent and slow-growing tumors that are often clinically silent until the late stages of disease.29

Headache and neck pain, as well as diplopia, were the most common initial symptoms, and the latter has been
thought to be more characteristic of skull base chordomas, occurring in 28%–64% of skull base chordoma cases according to various reports. In addition, the results from this series verified that the initial clinical presentation varies according to different tumor locations (Fig. 3 [upper]). For the SC and SP types, diplopia was often the earliest and most frequent symptom, whereas dysphagia and head and neck pain were more common in the OC and PO types.

**Modified Classifications**

There have been several different types of tumor classification based on anatomical locations proposed since 1997, when al-Mefty and Borba described a surgical classification for skull base chordomas based on the lesions’ patterns of extension through the skull base. Pallini et al. adopted this classification for their series, described in 2003. This classification was not widely adopted due to its abstract and difficult-to-remember details. Thereafter, several other classification methods were described in different surgical series. Some of these classification schemes were relatively simple and not comprehensive, whereas others were relatively complex and unsuitable for clinical application, and still others were without specific definitions.

The classification of tumor location in this report was modified from what we used in our previously reported series, which included sellar, middle fossa, clival, cranio-cervical junction, and extensive types. Because the histopathogenesis features of chordomas are similar to those of skull base chondrosarcomas, it is suspected that chordomas are closely related to the sutures of skull base bones. These bony connections are the most probable sites for the remnants of the notochord, which are chordoma precursors. This classification system was named using the connection between 2 pieces of adjacent bone, which represented not only the specific location of its main body but also the potential histogenetic site. In this classification system, the ES, SC, and OC tumor types represented the midline components in the cephalocaudal direction, which accounted for more than three-quarters of the patient series (77.8%, Fig. 1 [left]). It was consistent with the consensus that chordomas are prone to arise from the midline of the cranial base. The SP and PO tumor types represented the lateral components in either middle or posterior cranial fossa. Large lesions, especially those that were recurrent, were often classified into the extensive category and were usually difficult cases. This classification mainly demonstrated its clinical value in selecting surgical approaches, and to some extent seemed to be associated with patients’ initial symptoms and PFS.

In our previous series, a classification system to describe bone invasion was proposed, but was not able to clinically distinguish different cases. A modified classification system, which was intended to describe the variations of bone invasion, was used in this report. Patients with exophytic chordomas in this series were all operated on through lateral approaches, gained more satisfying degree of resection, and consequently attained longer PFS than patients with the other 2 types of tumors. The intrinsic chordomas, a newly described tumor type, may act as the precursor of either exophytic or endophytic chordomas.

**Selection of Surgical Approach**

Over the past decade, the endoscopic endonasal ap-
Approach (EEA) and expanded EEA have gradually gained ground in the field of cranial base surgery, with increasing indications and satisfactory outcomes.\(^{15,20}\) Thus, comparisons between the EEA and open cranial base surgery, and debates on which surgical strategy is better, have increased.\(^{19}\) We believe that both strategies have their own advantages, which may be complementary to each other. The lateral open approaches can provide better control of the vessels and a better view of the brainstem-tumor interface, which allows for a more secure dissection.\(^{24}\) On

### TABLE 4. Patient characteristics and univariable analysis of the prognostic factors associated with OS and PFS using the Kaplan-Meier method

<table>
<thead>
<tr>
<th>Factor</th>
<th>No.</th>
<th>OS (mos)</th>
<th>p Value*</th>
<th>PFS (mos)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male vs female)</td>
<td>137/97</td>
<td>96.8 vs 88.5</td>
<td>0.511</td>
<td>59.3 vs 54.0</td>
<td>0.475</td>
</tr>
<tr>
<td>Duration of initial symptoms (≤12 vs &gt;12 mos)</td>
<td>139/95</td>
<td>86.8 vs 101.5</td>
<td>0.248</td>
<td>49.3 vs 62.7</td>
<td>0.252</td>
</tr>
<tr>
<td>Primary (yes vs no)</td>
<td>180/54</td>
<td>103.4 vs 61.2</td>
<td>&lt;0.001</td>
<td>66.9 vs 29.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. of prior ops (0/1/2/3)</td>
<td>189/36/3/6</td>
<td>100.8/73.5/30.5/28.8</td>
<td>&lt;0.001</td>
<td>65.0/31.2/30.5/11.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Tumor location (SC/OC/SP/PO/ES/E)</td>
<td>138/41/24/14/13</td>
<td>—</td>
<td>0.716</td>
<td>47.6/57.1/57.5/88.0/31.0/28.8</td>
<td>0.023</td>
</tr>
<tr>
<td>Bone invasion type (I/II/III)</td>
<td>190/7/37</td>
<td>—</td>
<td>0.191</td>
<td>52.3/44.8/79.2</td>
<td>0.020</td>
</tr>
<tr>
<td>Dural invasion (yes vs no)</td>
<td>92/142</td>
<td>91.6 vs 94.8</td>
<td>0.592</td>
<td>64.6 vs 51.6</td>
<td>0.551</td>
</tr>
<tr>
<td>MargR (yes vs no)</td>
<td>154/80</td>
<td>102.1 vs 74.9</td>
<td>0.002</td>
<td>68.9 vs 34.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Extent of resection (GTR/NTR/STR/PR)</td>
<td>28/126/60/20</td>
<td>110.9/98.6/80.0/42.1</td>
<td>0.001</td>
<td>91.7/53.9/36.7/19.8</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* Statistically significant values (p < 0.05) are in boldface type.
the other hand, the EEA can provide a direct route to the tumor using natural orifices. In this study, surgeries using lateral approaches had more aggressive tumor resection and gained a higher rate of GTR, which may be explained as follows: 1) the lateral approaches are indeed safer for dissection of the interface between the tumor and brainstem, and allow for better tumor resection in certain situations, especially for exophytic chordomas; or 2) the learning curve for the EEA, which has only been used by our team for a few years, had a negative influence on the extent of tumor resection in this series. Last year, in some cases of OC- and PO-type tumors, we attempted lateral open resection combined with endoscopically-assisted surgery with satisfactory resection results. Therefore, there is no comparative superiority among any of these approaches. We select approaches on the basis of tumor classifications regarding location and bone invasion, the surgeon's experience, as well as the patient's preference.

Compared with the previous cohort,33 we have gradually realized that it is vital to keep the skull base dura intact, because it acts as an important barrier against the tumor. Therefore, we advocated the extradural route whenever possible in this series. However, 42 (17.6%) patients with epidural tumors were misdiagnosed as having subdural tumors on the basis of their preoperative MRIs, and vice versa in 9 (3.8%) patients. Thus, using preoperative MR images was not reliable for estimating whether the dura had been broken through.

Factors Associated With Extent of Resection

Because the definitions of resection degree are varied,16,20,22,23,24,28,33 the rates of MargR from different reports cannot be rigorously compared. Compared with our previous report,33 the overall MargR rate slightly declined in the present series. There may be 2 reasons for this observation: 1) the surgeons were still learning the EEA procedure, and thus, the MargR rate for the EEA in this series was not as stable as that of the lateral approaches; and 2) the ratio of patients with recurrent tumors in this series was higher than in the previous one (23.1% vs 20.8%), and prior surgery is associated with a lower chance of radical excision.21,23,24,28,29

In this article, we performed for the first time an analysis of multivariable factors related to the extent of resection. On the basis of previous reports,9,20,23,24,28 and the results of this series, we determined that tumor resection is easier for a primary neoplasm than for a recurrent tumor. The difficulty of reoperation is doubled due to the more tangled anatomy and tougher texture. It can also be stated that patients with larger tumors (tumor volume ≥ 40 cm³) had a significantly lower likelihood of MargR.

Role of Tumor Resection on Survival

The results of survival rates in this series showed a slight improvement compared with our prior series, in which the 5-year OS rate was 67.6%,53 and were similar to the results presented by the 10-year meta-analysis, in which the weighted average 5-year OS and PFS rates were 78.4% and 50.8%, respectively.17 This can partly be attributed to improvement in physicians’ understanding of this tumor, as well as our consistent surgical philosophy, which is similar to the philosophy of other authors1,5,9,21,23 that radical resection should be performed when feasible.

Although a chordoma cannot be regarded as a surgically curable tumor, the importance of tumor resection to patients’ survival cannot be overemphasized. According to the results in this series, it is of vital importance to attain GTR in the initial operation for patients with primary chordoma for a better long-term outcome. If it was not realistic to remove both tumor and the surrounding suspected bone due to the tumor’s lobular characteristic and the limited field of view, MargR proved to be an acceptable option. For recurrent tumors, the goal of surgery is to prolong the intervals between reoperations. Thus maximally safe cytoreductive surgery is still needed rather than merely palliative intrasional debulking surgery. The use of neuronavigation, intraoperative neurophysiological monitoring, and neuroendoscopy can be helpful to some extent.

Complication Rates

The reported complication rates after surgery range from as low as 16% to as high as 60%.22 Meningitis and CSF leakage ranked as the most common complications, and brain infarctions often led to severe functional deterioration. The incidence of CSF leakage was obviously less in this series than in the previous report,33 which was due to some extent to technical improvements in skull base repair. For the last decade, free fat grafts have gradually been used to repair dural defects. In addition to being a material with excellent histocompatibility to prevent CSF leakage, free fat grafts can act as barriers to protect the brainstem from exposure to radiation and to prevent the regrowth of skull base chordomas along the initial weak points in the dura.

Nonetheless, it is important to mention that selection biases, which were frequently encountered in the observational analyses, could have had an impact on the results of this study. Furthermore, because the intergroup sample sizes of tumor location, bone invasion, and number of prior operations had obvious differences, their associations with long-term outcome still need to be further verified.

Conclusions

Two modified classification systems demonstrated clinical value in describing the radiological features of chordomas and in guiding the choice of surgical approach. We found that MargR was more likely to be achieved for primary lesions with smaller volumes. We also found that MargR, and GTR when possible, of primary lesions seemed to be associated with better long-term outcomes. In addition, CSF leakage declined due to improved dural repair with free fat grafts.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions


Correspondence

Junting Zhang. Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, Tiantan Xili 6, Dongcheng District, Beijing 100050, People's Republic of China. email: zhangjunting2003@aliyun.com.