Surgery for Chordomas of the Craniocervical Junction: Lessons Learned

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ABSTRACT

We investigated the outcomes of chordomas of the craniocervical junction after surgery including complication rates, survival, associated adverse factors, and quality of life. We present our results and lessons learned from surgeries performed between 1982 and 2007 in the National Hospital for Neurology and Neurosurgery, London. Patients undergoing transfacial, transoral, and transmandibular surgeries for chordomas of the craniocervical junction were enrolled in this study. Chi-square, Fisher exact tests, and log-rank survival analysis were used to determine significant adverse factors ($p < 0.05$). In our series, 80 operations were performed in 66 patients; 37 patients were male, 29 female. Age at presentation was commonly 40 to 60 years. After surgery, pain was the same or better in 98.1% of patients; 18.6% of patients presented with myelopathy, of whom 27.8% improved, 44.4% remained unchanged, 27.8% deteriorated. Complication rates were as follows: velopharyngeal incompetence 2%, dysphagia 3%, failure of fixation 2%, sepsis 5%, meningitis 5%, wound infection 3%, chest infection 6%, cerebrospinal fluid leakage 5%. Five- and 10-year overall survivals were 62% and 39%, respectively. Complication rates for these major operations can be minimized in specialist centers, with careful patient selection and counseling. Quality of life and survival are significantly improved after surgery.

KEYWORDS: Chordoma, clivus, craniocervical junction, surgery

Chordomas are rare tumors that arise from remnants of the notochord—a structure that induces and coordinates the formation of the vertebral column during development of the embryo. By week 10 in utero, however, the notochord normally degenerates and only persist in the nucleus pulposus of the cartilaginous discs.

Chordomas arise commonly in the clivus and sacrum with an incidence of 0.5 per million in Europeans¹ and were probably first described by Virchow in 1857.² They account for 1 to 8% of primary malignant bone tumors and 20% of those arising in the spine³ and are slowly growing tumors that infiltrate local bone and

soft tissues, with a high chance of local recurrence or seeding after resection. Because they are often midline tumors, most can be approached by midline transoral, transmaxillary, and transmandibular approaches, as well as high anterolateral retropharyngeal and lateral approaches to the upper cervical spine and subtemporal or lateral petrous approaches for upper clival tumors. These approaches are often difficult and associated with significant morbidity and mortality, and therefore surgery needs to be justified by an improved quality of life and survival. In this article, we review the outcomes of 41 male and 25 female patients and present the

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lessons learned from decades of chordoma surgery in our unit.

MATERIALS AND METHODS

Surgical Approaches

Craniocervical chordomas are usually midline tumors, involving the clivus and atlantoaxial vertebrae. Surgery has a beneficial effect on life expectancy, although the potential risks should be considered for each case. Mean survival without surgery in one series was less than 1 year.¹ Chordomas may be excised by anterior midline approaches (transoral, transmandibular, and transfacial), posterior suboccipital approaches, transpetrous surgery, lateral atlantoaxial approaches, and pterional or middle fossa craniotomies, or any combination of these, depending on the exact position of the tumor and probably more often on the surgeon's experience and preference. We prefer the extradural ventral midline approaches, as developed by James and Crockard.^{4,5} The standard transoral approach is rarely sufficient for excision of chordomas due to the extensive nature of these tumors, and usually an "open door" maxillotomy is needed to access the upper clivus, or mandibulotomy for tumors extending lower than C2–3. The anatomy of ventral midline approaches is usually consistent and familiar to the suitably trained surgeon; direct exposure of the clivus is possible, unhindered by cranial nerves or major blood vessels. This is particularly true for primary ventral midline tumors that are confined to the defined safe anatomic boundaries of the clivus. Disadvantages of this approach include working down a deep and narrow space, and for intradural tumors, it can be difficult to close the dura, thus increasing the risk of cerebrospinal fluid (CSF) leakage and infection. A nasogastric tube is inserted in standard transoral surgery when gastric emptying and tube-feeding are required only for a short time after the operation, or a percutaneous gastrostomy is placed preoperatively in those with a bulbar palsy or when planning an extended transoral approach. If the tumor transgresses the dura, a lumbar drain is often used for up to 5 days postoperatively to allow healing and minimize the risk of CSF fistulae and infection. If the tumor does not breach the dura, inadvertent opening of the dura should be avoided as this is associated with a much higher incidence of meningitis (23% in our series) compared with when the dura remains intact (0%, $p < 0.05$). If the dura is opened, it can be repaired using a combination of artificial dura, fibrin glue, dermal fat graft, and flaps of nasal septal mucosa.⁶ After extensive anterior resection, stability of the craniocervical junction often needs to be restored by posterior occipitocervical instrumentation, with or without supplementary anterior stabilization. In our series of 66 patients with clival tumors, 16 had standard transoral operations, 16 had

transoral surgeries with splitting of the soft palate, 27 received "open-door" maxillotomies, four had transmandibular procedures, and three received midface degloving approaches.

The overall mortality and complication rates of different approaches, whether anterior midline or lateral, are similar when comparing the outcomes of larger series.^{6–9} Rather than be dogmatic about the ideal approach, it is more important to achieve maximum tumor excision by whichever approach the surgeon is experienced with. Carpentier et al described their preference for lateral approaches to the craniocervical junction,¹⁰ and subtemporal, frontotemporal, transpetrous, or transcavernous approaches were favored by Gay et al and Tzortzidis et al.^{7,8}

RESULTS

Complications and Quality of Life

There are no published series of quality of life or cost-effectiveness after surgery for skull base chordomas. More recently, surgeons have started to use outcome measures such as Medical Outcome Study 36-Item Short Form and Euroqol Eq. 5D questionnaires in many conditions, but data for patients with chordomas are lacking and limited by the low incidence of these tumors. Quality of life, however, can be inferred to a certain extent by looking at the complications and relative improvement of symptoms after surgery.

In our series, patients reported an improved quality of life after surgery due to the relief of pain. Pain was the same or better in 98% of patients, and 75% of patients did not have any complications and felt that they were the same or improved as a result of surgery. Overall complication rates are shown in Table 1. Quality of life generally varies inversely with complications, and we have therefore analyzed our data to identify factors that might be associated with complications and their avoidance. Complication rates were higher in patients with recurrent tumor and revision surgeries, compared with first-time operations (chi-square test, $p = 0.05$). However, there was no significant difference in overall

Table 1 Surgical Complications

Velopharyngeal incompetence (%)	2
Failure of fixation (%)	2
Dysphagia (%)	3
Wound infection (%)	3
Systemic sepsis (%)	5
Meningitis (%)	5
CSF leakage (%)	5
Chest infection (%)	6
Mortality within 1 mo from surgery (%)	0

CSF, cerebrospinal fluid.

survival between those patients who had complications and those who did not (log-rank test, $p = 0.21$).

Dysphagia was significantly associated with transmandibular surgery, but there was no association with tracheostomy or occipitocervical fixation. The incidence of velopharyngeal incompetence was not significantly different between the various extents of surgery, but there was a trend to a higher incidence after open-door maxillotomy. There was no significant difference after standard transoral surgery with or without division of the soft palate, implying that the most important factor leading to palatal incompetence was likely to be the loss of bulk of the posterior pharyngeal wall, which would be greater after the more extensive resections possible with maxillotomy, rather than soft palate scarring. We now attempt to improve the posterior pharyngeal bulk by using dermal fat grafts to fill the defect adjacent to the dura after tumor excision. The rates of local infection, systemic sepsis, and meningitis were not related to the type of surgery but were significantly associated with longer periods in the intensive care unit. Meningitis was significantly more common when the dura had been breached, and this should therefore be avoided when possible ($p < 0.05$); if the tumor does not transgress the dura, then durotomy and intradural exploration should be discouraged.

In their series of 53 patients, Colli and Al-Mefty recorded a complication rate of 60%, mainly comprising neurological complications (28.6% permanent, 22.2% transient) and cranial nerve palsies, but also a 7.9% incidence of CSF leakage, 4.8% incidence of hydrocephalus, 3.2% incidence of meningitis, and 3.2% incidence of oronasal fistulae.⁹ They found that larger extents of tumor resection were not associated with greater complications, but that there was a correlation with better survival with excision of more than 90% of tumor. A higher rate of CSF leakage (30%) was seen in another series of 60 patients, probably due to a greater proportion of patients who presented with tumor penetrating the dura.⁷ They also did not find any differences in complication rates between those patients receiving complete excision and those receiving partial debulking, further adding to the argument for attempting as complete an excision as possible at first presentation.⁷ In a smaller series, Carpentier et al described three postoperative deaths, three CSF leaks, and one case of meningitis in their series of 36 patients.¹⁰ Pallini et al had 17 significant complications in 26 patients including three CSF fistulae,¹¹ and Harbour et al documented three postoperative deaths in 11 patients.¹²

Survival

The assessment of survival is a rather blunt tool for the benchmarking of outcome after surgery; it is perhaps better to have a shorter survival with good quality of life,

Figure 1 Survival of patients with chordoma, after surgery.

rather than a longer survival that is punctuated by complications and pain. Survival is, however, a straightforward yardstick that may be used to assess the efficacy of different treatments. Survival data for our whole group are shown in Fig. 1. Excluding chondrosarcomas and cartilaginous tumors, our median survival was 122 months, and mean survival 100 months from the date of surgery, with 5- and 10-year survivals of 62% and 39%, respectively. We found that patients could broadly be separated into two groups: those with a shorter life expectancy, with tumor recurrence and death within 4 years from initial surgery, and those with higher long-term survival and indolent disease.

This is in keeping with Watkins et al's series of 38 patients who received surgery between 1958 and 1988, in which patients either died within 5 years of surgery or had an almost normal life expectancy.¹³ Our 5- and 10-year survival times were 62% and 39%, respectively, falling within the range of previously published survival times. Forsyth et al had very similar 5- and 10-year overall survivals of 51% and 35% after surgery, with disease-free survivals of 33% and 24%,¹⁴ and Carpentier et al found a significant difference between primary surgery cases (80% and 65% survivals at 5 and 10 years) and in cases of recurrent tumor (50% and 0%, respectively), as in our series.¹⁰ Colli and al-Mefty⁹ documented a longer 5-year survival of 85.9%, but their series included chondroid chordomas, which have often been misdiagnosed in the past and may represent chondrosarcomas, which are associated with a better prognosis.¹³

DISCUSSION

Importance of Correct Histological Diagnosis

It can sometimes be difficult to distinguish between chordomas and chondrosarcomas using conventional hematoxylin and eosin stains. Up to 25% of chondroid chordomas or chondrosarcomas can be misdiagnosed as

chordomas if immunohistochemical labeling is not used, and we recommend that diagnosis is confirmed by using a panel of antibodies including S100, cytokeratin, epithelial membrane antigen, carcinoembryonic antigen, and vimentin.¹³ In one study, seven tumors that were morphologically chondroid chordomas were found to be chondrosarcomas with more critical immunohistological analysis.¹⁵ If chondroid tumors are incorrectly diagnosed as standard chordomas, then this will create bias in survival and confound the results of outcome studies after surgical or radiation treatments.

Differences in survival are largely influenced by the extent of tumor resection but may also be explained in part by altered expression of chordoma genes. Tumor volume greater than 70 mL is associated with shorter survival, but there is also a greater chance of recurrence in patients with an increased tumor expression of human telomerase reverse transcriptase mRNA and mutation of p53 protein.^{11,16} The Ki67 proliferation index, histological subtype of the tumor, and degree of necrosis are perhaps less reliable predictors of outcome, probably due to heterogeneous expression throughout the tumor and sampling error.^{10,11} Although a low Ki67 index does not necessarily imply a good prognosis, there is, however, a good correlation between rapid tumor recurrence and a Ki67 greater than 6%, and also in older age groups.^{17,18}

Multidisciplinary Approach

Our management protocol relies on close cooperation between the allied specialties of neurosurgery, spinal surgery, maxillofacial surgery, otolaryngology, radiology, radiotherapy, anesthetics, and pathology.⁶ The overriding goal since 1986 has been to perform maximal tumor excision at the time of first presentation and either observe if the tumor has been excised completely using postoperative imaging or use radiotherapy if there is residual tumor or after surgery for recurrence.

Dedicated anesthesia is required for these difficult skull base lesions, often requiring placement of a tracheostomy. The surgical team should be experienced, or have access to experienced, surgeons who are able to instrument the craniocervical junction, because after these operations the occipital condyles or apical-alar ligament complex may be disrupted. Stabilization is most often by posterior occipitocervical or atlantoaxial fixation techniques, which can be supplemented by anterior instrumentation. Occasionally stability can be maintained, especially in younger patients, despite odontoidectomy and section of the apical and alar ligaments, but this should be monitored with dynamic X-rays over time.

First Operation—Aim for Complete Resection

Treatment should start with maximal tumor resection at first presentation, as suggested by our data (Fig. 2) in

Figure 2 Survival of patients after primary radical surgery, compared with patients who underwent primary debulking surgery and later presented to our unit for revision surgery. First operation—black. Surgery for recurrence—gray.

which better survival was seen in patients who underwent radical surgery from the outset, compared with patients who presented to our unit and received surgery for recurrence after suboptimal primary resection. This is in keeping with the opinion of Crockard et al: “The best outlook was associated with the greatest extent of tumor removal achieved during the first operation.”⁶

Carpentier et al compared a smaller group of 22 patients who underwent primary surgery in Paris and 14 who were treated for recurrence after primary surgery elsewhere, and likewise found a significant difference in outcome between the two groups (log-rank test, $p = 0.049$), further supporting the role for aggressive surgery from the outset.¹⁰ However, our philosophy for the treatment of recurrent tumors differs. Subsequent operations for recurrence should aim to excise the greatest quantity of tumor by the most direct surgical path while maintaining quality of life. Because prognosis is worse after tumor recurrence, maintaining quality of life is paramount. Overambitious second surgeries, with increased risk of complications, should be discouraged.

CONCLUSION

Our present recommendations are for a radical excision at first presentation, with or without adjuvant radiation treatment, depending on the extent of resection. Biopsy alone and conventional radiotherapy techniques are associated with a worse prognosis.^{1,6} Chordomas are complex tumors that are difficult to treat and therefore require close interaction between different medical specialties to achieve the best results. Correct immunohistochemical identification of the tumor is important for prognosis and management. Although the complication

rate for these major operations can be minimized in specialist centers, careful patient selection and counseling is advisable before performing such surgery. Looking to the future, proton beam therapy,^{19,20} carbon ion therapy,²¹ cyberknife,²² and the novel approach of endoscopic skull base surgery^{23,24} show potential in the treatment of chordomas. Whether outcomes, quality of life, and survival can be unquestionably improved by these modalities remains to be established, although early results show much promise.

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