

Outcomes of chordomas of the sacrum and mobile spine: Clinical series with average 6-year follow-up

ABSTRACT

Study Design: Retrospective clinical series.

Purpose: To search for spinal chordoma's survival rates, recurrences, and complications and compare sacral and mobile spine chordomas.

Overview of Literature: The primary spinal chordoma treatment is mainly considered radical surgery, although recurrence rates are pretty high. Radical surgery with extra marginal resection is possible with significant neurologic deficits and very high complication rates.

Materials and Methods: This study reviews 48 spinal chordoma patients (sacrum 28, mobile spine 20) surgically treated between 1995 and 2019. Follow-up times ranged between 12 months and 238 months (average 6.16 years). Six patients were lost to follow-up after at least 1 year of control; three died 30 days after surgery.

Results: Surgery for sacrum tumors was an extra marginal resection (sacrectomy) in 19 patients, while nine patients had intralesional surgery. There were 13 cervical chordomas and seven thoracolumbar chordomas. Although we tried marginal resections for cervical chordomas, all had positive margins, and we accepted them as intralesional. Surgery for thoracolumbar chordomas was total spondylectomy in four cases and intralesional excision in three patients. Because of recurrences, the average surgery per patient was 3.45. It was more common in mobile spine chordomas (average 4.2) than sacral chordomas (average 2.92). Surgical complications of mobile spine chordomas (15/20; 75%) were also more than sacral chordomas (16/28; 57%). Chordomas of the mobile spine had no metastasis, while sacral chordomas had a 21% (6/28) metastasis rate. The recurrence rates of sacral chordomas (16/21; 76%) were not significantly different from the mobile spine (15/18; 83%). Among sacral chordomas, in all five cases who had no recurrence, the level of sacrectomy was S2 and below.

Conclusions: Recurrence and survival rates of mobile spine and sacral chordomas are not different. Sacral chordomas tend to metastasize. Sacrectomy is successful for sacral chordomas at S2 and below.

Keywords: Chordoma, metastasis, mobile spine, sacrum, spine tumor

INTRODUCTION

Chordoma is a histologically benign, nevertheless clinically aggressive tumor which is believed to arise from remnants of notochord, usually located in the sacrum (50%), skull base (30%), and mobile spine (20%).^[1] The approximate incidence is 0.1/1,000,000 individuals per year.^[2] Although chordoma is a slow-growing tumor, the average recurrence rate is 50%.^[3] The preferred treatment for chordoma is primarily surgical resection followed by radiotherapy.^[4] However, chordomas are highly resistant to chemotherapy and radiotherapy, decreasing overall survival time.^[5] The average life expectancy of chordoma patients is 6 years, with a

5-year survival rate of 70% and a 10-year survival rate of 40%.^[6] To provide a local control, new treatment modalities have recently been proposed, such as carbon-ion and proton beam

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radiotherapy, yet the recurrence rate of chordomas remains the same.^[7] In the advanced stages of the disease, 30%–40% of the patients have metastasis, and common metastatic sites are lung, liver, bone, lymph nodes, and other sites.^[1]

This study aims to retrospectively analyze the chordoma patients, which the senior author operated on between 1995 and 2019. We included 48 patients (28 sacral, 20 mobile spine) and compared them by the number of surgeries, complications, metastasis, recurrence rates, and outcomes.

MATERIALS AND METHODS

Between 1995 and 2019, the senior author has managed 61 chordoma patients (sacral 40, C2 10, subaxial cervical 4, thoracolumbar 7). We excluded the cases with insufficient data and lost to follow-up after primary surgery. We reviewed the remaining 48 patients (sacral chordoma 28, mobile spine chordoma 20) retrospectively.

We conducted this study in compliance with the principles of the Declaration of Helsinki. Institutional review board approval was not necessary for this study at our institution. Informed consent was waived.

Statistical analysis was performed using independent *t*-test, Chi-square test, Mann–Whitney U test, and Kaplan–Meier test.

RESULTS

Five patients of the mobile spine chordomas were below 40 years old, while there were no patients in the sacral chordoma group below 40 years old. The male-to-female ratio was 31/17. The age range was 28 and 82 (mean 54.8). The location of the tumors is summarized in Table 1.

Surgical treatment

The type of surgery varies according to the tumor's location, tumor dimensions, and patient's approval of deficits in the case of radical surgeries [Table 2].

Sacral chordomas

Our policy was to offer a radical surgery for sacral chordomas. However, we did not attempt radical surgery if the patient had previous surgery, if the tumor is in huge dimensions, and if the patient did not accept morbidity of surgery.

Sacrectomy

Nineteen patients had extra marginal resections, or the so-called sacrectomy: Three at the L5-S1 level, four at the

S1 level, 10 at the S2 level, one at S3, and one at S4 level. All sacrectomies at L5-S1 and S1 levels and 3 of S2 levels needed anterior-posterior combined surgeries. We had three early deaths (the 1st month after surgery). Seven patients had only one surgery. The average number of surgeries was 2, 8.

Survivals ranged between 12 and 180 months. The average survival time is 68 months.

Four patients are still living—one with lung metastasis, one with lung and liver metastasis, and two without any recurrence and metastasis.

Posterior intralesional surgery

Nine patients had intralesional surgery. One patient had one surgery only. The average number of surgery was 3.

Table 1: Location of tumors

| Location | n |
|------------------------|----|
| Cervical chordoma | 13 |
| C2 | 9 |
| Subaxial | 4 |
| Thoracolumbar chordoma | 7 |
| Thoracic | 1 |
| Lumbar | 6 |
| Sacral chordoma | 28 |
| Total | 48 |

Table 2: Type of surgeries in the first surgical approach

| C2 chordomas (n: 9) (all intralesional) | n |
|--|----|
| Anterolateral retropharyngeal excision | 2 |
| Combined anterior-posterior approach | 6 |
| Transoral | 4 |
| Transmandibular | 1 |
| Anterolateral retropharyngeal | 1 |
| Posterior excision and fixation | 1 |
| Subaxial cervical chordomas (n: 4) (all intralesional) | |
| Anterolateral corpectomy, graft, plate | 2 |
| Posterolateral excision and fixation | 1 |
| Combined approach | 1 |
| Thoracolumbar chordomas (n: 7) | |
| Total spondylectomy | 4 |
| T3-4 | 1 |
| L1 | 1 |
| L5 | 2 |
| Intralesional excision, combined surgery | 3 |
| L2 | 1 |
| L3-4 | 1 |
| L5 | 1 |
| Sacral chordomas (n: 28) | |
| Sacrectomy | 19 |
| L5-S1 level | 3 |
| S1 level | 4 |
| S2 level | 10 |
| S3 level | 1 |
| S4 level | 1 |
| Posterior intralesional excision | 9 |

Of nine patients, two had metastasis. Survivals ranged between 27 and 238 months. The average survival time is 92.1 months. One patient is still living after 72 months with metastasis.

Mobile spine chordomas

Thirteen cervical chordomas (9 at C2, remaining four at subaxial levels). Although we tried marginal resections, all had positive margins, and we accepted them as intralesional. The follow-up times range between 12 and 133 months, average 74.1 months. On the last evaluation, there were no cervical chordoma patients alive.

There were seven thoracolumbar chordomas; two died, three are alive, and two were lost on follow-up. The follow-up times range between 19 and 142 months, with an average of 82.6 months.

The cervical chordomas have undergone more repeat surgeries, up to 10 surgeries in one case. Average surgeries are 5 for cervical chordomas, while it was 2.7 in thoracolumbar chordomas.

It seems that thoracolumbar chordomas have better outcomes than cervical chordomas.

We compared the results of mobile spine chordomas with sacral chordomas in Table 3. The number of surgeries ranged between 1 and 10, and the average number was 3.3.

Complications

In general, complication rates increased with multiple surgeries. Thirty-one of 48 patients had at least one complication (64.5%). Only 12 patients had one surgery. Because of recurrences, the average surgery per patient was 3, 45. It was more common in mobile spine chordomas (average 4.2) than sacral chordomas (average 2.92).

Surgical complications of mobile spine chordomas (15/20; 75%) were also more than sacral chordomas (16/28; 57%).

Sacral chordomas had more wound-related complications (8) or excessive bleeding.^[3] In five patients, rectum perforations were observed. Other complications were ureteral injury (1), partial sciatic nerve injury (1), Cerebrospinal fluid (CSF) fistula (1), gluteal artery injury (1), and cardiac problem (1).

Mobile spine chordoma had more dural laceration (7), CSF fistula treated with external lumbar drainage (2). Other complications were neurologic worsening (4), cervical epidural hematoma of which needed reoperation (1), excessive bleeding (1), bleeding from tracheostomy (1),

respiratory distress (1), vertebral artery injury resulting pseudoaneurysm and hematoma (1), jugular vein injury (1), iliac artery injury (1), iliac vein injury (1), ureteral injury (1), deep vein thrombosis (1), and facial nerve palsy (1).

Adjuvant therapies

Twenty-one patients did not receive any radiation. Conventional radiotherapy was applied in 23 patients, proton beam radiation in one, and cyberknife in three patients. Chemotherapy was used in three cases only: Two patients received imatinib, one patient received palbociclib.

Metastasis

We did not see any metastasis in the chordomas of the mobile spine. However, six of 28 (21%) patients with sacral chordomas had metastasis: Lung and liver metastasis 2, single vertebral metastasis 1, multiple vertebral metastases 2, and lung, vertebra, and gingiva metastasis all together 1. Thus, the presence of metastasis is statistically significant compared to sacral and mobile spine chordoma.

Table 3: Comparison of sacral chordomas and mobile spine chordomas

| | Sacral chordomas (n=28) | Mobile spine chordomas (n=20) | P |
|-----------------------------|-------------------------|-------------------------------|-------|
| Age, mean (minimum–maximum) | 56.1 (40-78) | 53 (28-81) | 0.459 |
| Sex (male/female) | 19/9 | 12/8 | 0.575 |
| Number of surgeries (mean) | 2.8 | 4.2 | |
| 1 surgery | 9 | 3 | 0.124 |
| 2 surgeries | 6 | 4 | |
| 3 surgeries | 3 | 4 | |
| 4 surgeries | 7 | 1 | |
| 5 surgeries | 2 | 2 | |
| 6 surgeries | 1 | 1 | |
| 7 surgeries | 0 | 2 | |
| 8 surgeries | 1 | 1 | |
| 9 surgeries | 0 | 1 | |
| 10 surgeries | 0 | 1 | |
| Complications | | | |
| None | 12 | 5 | 0.202 |
| At least one | 16 | 15 | |
| Metastasis | | | |
| None | 22 | 20 | 0.34 |
| Yes | 6 | 0 | |
| Recurrence | 76% (16/21) | 83% (15/18) | 0.702 |
| Radiotherapy | 57% (12/21) | 61% (11/18) | 0.802 |
| Outcomes and survival times | | | |
| Early death | 3 | 0 | 0.967 |
| Death on follow-up | 16 | 15 | |
| Living | 5 | 3 | |
| Lost | 4 | 2 | |
| Follow-up duration | 12-238 months | 12-142 months | |
| Average follow-up | 76 months | 76.5 months | |

Outcomes

Follow-up times ranged between 12 months and 238 months (average 74.65 months, i.e. 6, 16 years). Six patients were lost to follow-up after at least 1 year of control; three died 30 days after surgery. The mean survival time of sacral chordomas is 76 months (range 12–238 months), the mean survival time of mobile spine chordomas is 76.5 months (range 12–142 months). Kaplan–Meier analysis of mobile spine chordomas and sacral chordomas is depicted in Figure 1.

Tumor recurrence

After removing early deaths and lost to follow-up cases after 12 months, sacral chordomas' recurrence rates were 76% (16/21), of mobile spine chordomas 83% (15/18).

We also examined if a more radical surgery (such as sacrectomy) justifies less recurrence. For sacral tumors, nine patients had intralesional surgeries. Two were lost to follow-up, remaining seven patients had all recurrences. They had an average of three surgeries. Nineteen patients had sacrectomy. Two were lost on follow-up. Nine patients had recurrences (64%), but five patients had no recurrence. On the other hand, three patients who had high sacral amputations

had early deaths. In all five cases that had no recurrence, the level of sacrectomy was S2 and below (S2 three cases, S1 one case, and S4 one case).

Radiotherapy

Twelve of 21 sacral chordomas had radiotherapy. Mean overall survival of sacral chordoma patients who had no radiotherapy (55, 8) was less than those who had radiotherapy (91, 2), although statistically not significant (*P* value 0.156). Eleven of 18 mobile chordoma patients had radiotherapy. Mean overall survival of mobile spine chordoma patients who had no radiotherapy (71, 7) was not different than those who had radiotherapy (79, 5) (*P* value 0.697). Figure 2 depicts the effect of radiotherapy on Kaplan–Meier analysis for both groups.

Sample cases

Case 1

Giant sacral chordoma [Figure 3]. This is a neglected sacral chordoma that reached gigantic dimensions (more than 25 cm diameter) and involving L5 level. Even with such dimensions, she had 6 years of survival with four intralesional surgeries.

Case 2

Sacrectomy at S2 level [Figure 4]. This is a huge sacral chordoma below S2 level (dimensions 20 cm × 12 cm) a sacrectomy at S2 level with combined anterior-posterior approach could be done after a prophylactic colostomy. Excessive bleeding could be controlled by leaving an abdominal gauze ventrally.

Case 2

C2 chordoma with recurrent surgeries [Figure 5]. This patient had nine surgeries and lived 8, 5 years. During recurrences, repeat surgeries caused complications such as vertebral artery occlusion, CSF leakage, and pseudomeningocele.

Case 3

Thoracic chordoma, posterior spondylectomy [Figure 6]. This patient with chordoma involving T3 and T4 bodies and

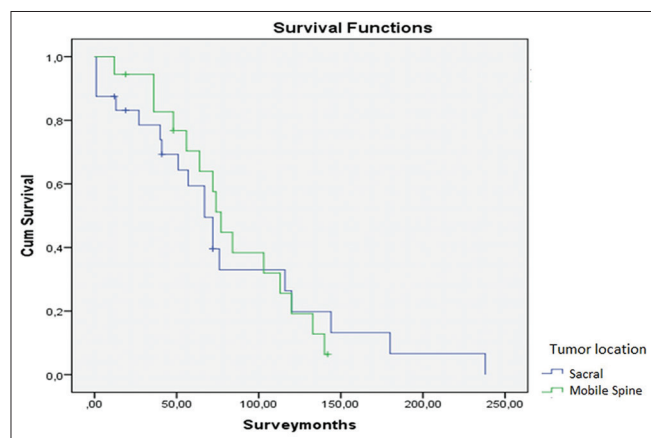


Figure 1: Kaplan–Meier analysis of survival times of sacral chordomas and mobile spine chordomas

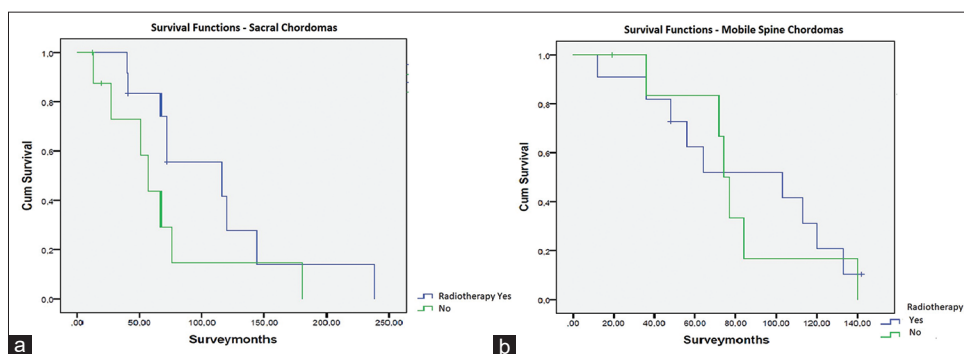


Figure 2: Kaplan–Meier analysis of the patients who had radiotherapy and no radiotherapy, and comparing sacral chordomas (a) and mobile spine chordomas (b)

two previous intralesional surgeries had a radical surgery by removing two vertebra and three ribs, is still living without recurrence 16 years after en-bloc spondylectomy, 26 years after primary surgery.

DISCUSSION

Ahmed *et al.* have examined survival rates of 49 patients with a mean follow-up period of 6.3 years.^[8] The locations were 30 skull base/clival, 12 vertebral columns, and seven sacrum. They reported a better prognosis with gross total resection and high-dose stereotactic fractionated radiotherapy. Sacral chordomas had a worse prognosis.

Mobile spine chordomas

Although reports are describing en-bloc resection of cervical chordomas,^[9-11] en-bloc resection is not feasible in most cases.^[12] This is due to the tendency of chordomas to involve multiple compartments at the time of diagnosis. Gokaslan's group has also reported that en-bloc resection of chordomas involving the upper cervical spine (C1-2) compared to subaxial cervical spine is associated with poorer outcomes, such as less favorable margins, higher rates of complications, and increased tumor recurrence.^[13] Therefore, our policy for whole cervical chordomas has been marginal resections, resulting in Enneking positive margins. We always stopped at the dura, preserved eloquent roots, and vertebral artery. The type of primary surgeries is shown in Table 2.

However, for thoracolumbar chordomas, we always tried extra marginal resections. En-bloc resection was possible in

four cases, but the remaining three patients have intralesional excisions with combined anterior-posterior surgery. The decision for intralesional surgery depends on the dimensions of the tumors, invasion of the tumor to surrounding tissues (especially great vessels and eloquent nerves), and the patient's approval of deficits and complications.

Sacral chordomas

As we can expect, the distal sacral chordomas are more amenable to total removal. In all five cases that had no recurrence, the level of sacrectomy was S2 and below. Although the margins were free on pathological examination in high sacral chordomas, they all recurred in the long term. Hence, sacrectomy is more feasible for sacral chordomas at S2 and below.

Sacral tumors at the level of S2 and below can be removed by a posterior-only approach. However, tumor dimensions, intrapelvic component, and invasion to the rectum are also essential factors in deciding an anterior dissection.

Bakker *et al.* have reported a systematic review on chordomas.^[14] This review reports prognostic factors that influence disease-free survival are female gender, a history of prior resection, and surrounding muscle invasion. Conversely, significant adverse prognostic factors for overall survival are local recurrence, metastasis, a history of the previous resection, and a high-grade lesion.^[14,15]

Stener and Gunterberg^[16] advocated a more aggressive approach for en-bloc removal of the sacrum, although mid

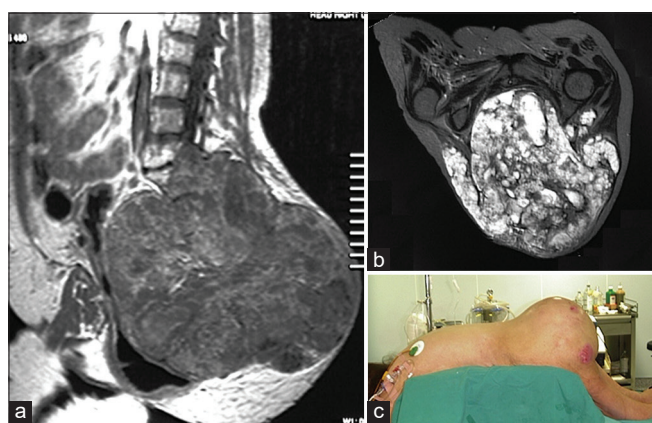


Figure 3: Giant sacral chordoma. A 56-years-old female patient admitted with pain in perianal area and left leg. Perianal sensory loss and urinary incontinence for 2 years. Additional psychosis has caused a neglect of treatment. Magnetic resonance images revealed a giant sacral tumor (a and b). Sacrum tumors may remain w/o symptoms for long periods, they reach big dimensions at the time of diagnosis. September 2009 biopsy chordoma. Significant blood loss during intralesional resection of big mass in October 2009 (c). Total four surgeries and radiotherapy, died in 2015 (6 years - 72 months survival)

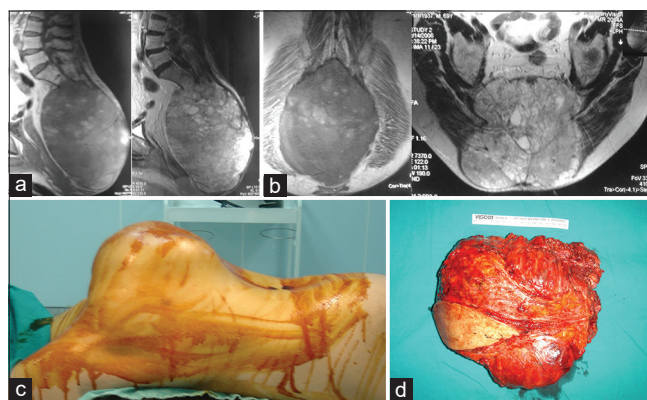


Figure 4: Sacrectomy at S2 level. A 67-years-old male urinary and bowel disfunction and prominent tumor at the back of sacrum. Magnetic resonance images show huge sacral chordoma below S2 level (dimensions 20 cm × 12 cm) (a and b). In 2006, we performed a sacrectomy at S2 level with combined anterior-posterior approach. (c and d) Since the rectum was invaded by the tumor, a prophylactic colostomy opened. After posterior osteotomies excessive bleeding caused immediate closing by leaving an abdominal gauze ventrally. The abdominal gauze and drains were removed 2 days later. Postoperative deep wound infection needed a revision surgery with irrigation drains. He was lost to follow-up after 1 year

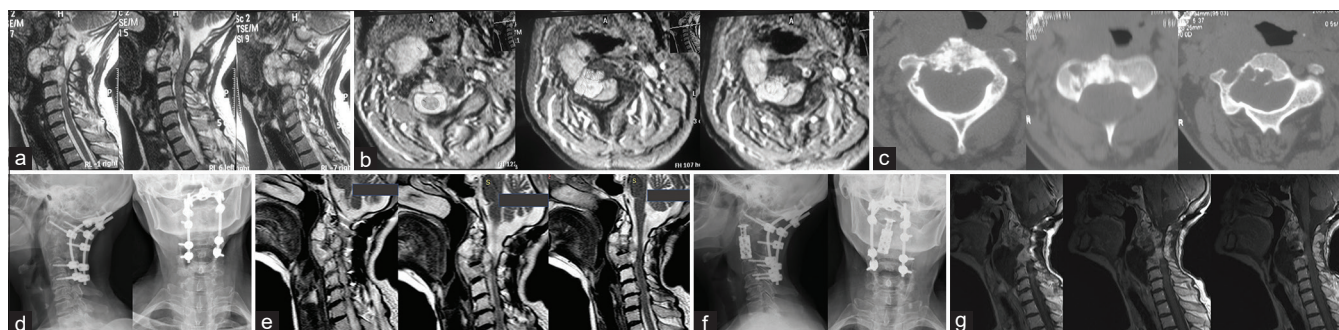


Figure 5: C2 chordoma with recurrent surgeries. A 60-years-old female presented with severe neck pain and restriction of neck movements. Biopsy in 2009 revealed chordoma (a-c). She had anterolateral retropharyngeal approach, subtotal tumor removal, occipitocervical fixation (d). Right vertebral artery occluded during surgery. After another recurrence (e), she had C2 and C3 corpectomy and cage surgery in 2016 (f). In magnetic resonance images in 2017, tumor recurrence and cerebrospinal fluid collection on retropharyngeal area are seen (g). She had one more anterolateral surgery to remove recurrent tumor and repair cerebrospinal fluid leakage. She had total nine surgeries and radiotherapy. She died in 2018, 8,5 years (103 months) after primary surgery

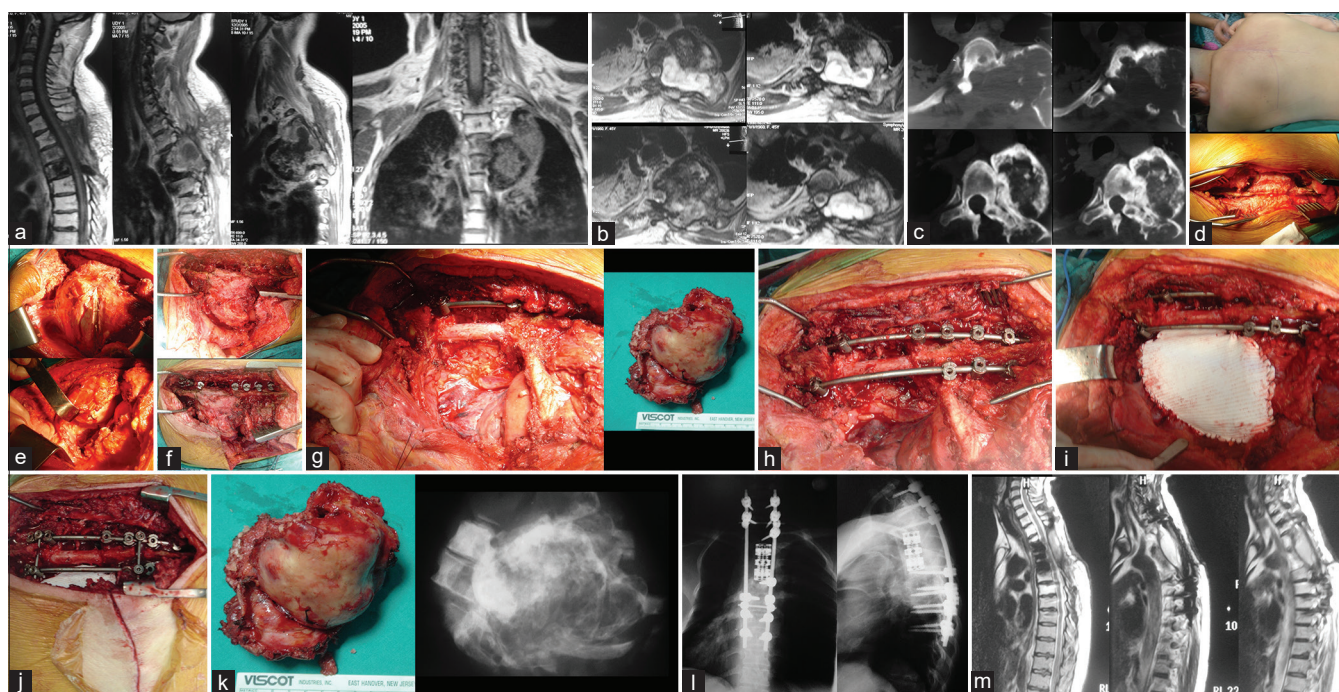


Figure 6: Thoracic chordoma, posterior spondylectomy. A 46-years-old female, presented with paraparesis 12 years before. She had T3-4 chordoma, and had two previous surgeries in 1994, and 2005 in another center. Radiotherapy (46 Gy) also applied. At the time, we evaluated she had no neurological deficits, local swelling at the back. Magnetic resonance images (a and b) and computed tomography scans (c) showed a T3-4 left paravertebral tumor invading 3 ribs, >10 cm diameter. Surgery in December 2005: C6-T7 midline and T-shaped incision (d). Posterior thoracotomy. 3, 4 and 5th ribs resected (e). Ossified tumor was released from the lung aorta by chest surgeons (f). After the right T3 and T4 hemilaminectomy and sacrificing right T3 and T4 roots, right pedicle screws from C7 to T7 and a rod placed. T2 and T3 bodies were released, and two adjacent bodies with tumor and ribs were resected totally (g). Left side screws, rod and a vertebral body cage between T2 and T5 are placed (h). Chest wall defect (appr. 10 cm) was repaired using polytetrafluoretilen (PTFE) dual mesh (i). A thoracic tube and external lumbar drainage are placed (j). En-bloc specimen and its radiogram show removal of two bodies (k). Duration of surgery was 750 minutes, total bleeding was 1100 ml. She had wound revision surgery one month later. Postoperative radiograms (l) show the construct design. Control magnetic resonance images 1 year after surgery show no remnant tumor (m). She is still alive, has no neurology, no recurrence after 2005 (16 years after en-bloc spondylectomy, 26 years after primary surgery)

to high sacrectomy would lead to loss of bowel, bladder, and sexual function. However, more recent series reported a wide resection could be obtained in only 50% of cases and, more importantly, disease-free survival was only 50% at 10 years even after wide resection.^[17] The reason for tumor recurrence even after a wide resection is the presence of tumor cells outside the central mass of the tumor (skip metastases), even

2 cm outside in 43% of cases.^[18] The skip metastases caused poor local control in that series.

Prevention of complications must be a great concern for sacral chordomas.^[19] The contribution of the plastic surgeons by different flap techniques can avoid very common skin problems.^[20] Besides, excessive bleeding can be controlled

by transient occlusion of the abdominal aorta by a balloon dilation catheter.^[21]

Varga *et al.*^[22] have published a multicenter retrospective review of prospectively collected data containing 173 sacral chordomas. The average follow-up was 3.2 years (range 5 days–16.2 years). The local recurrence was 35% ($n = 57$), death occurred in 30% of the patients ($n = 50$) during the study period. The median overall survival was 6 years postsurgery, and local recurrence-free survival was 4 years. The authors conclude that en-bloc resection reduces local recurrence but does not influence overall survival.

Denaro *et al.*^[23] have also done a systematic review of 58 studies. The recurrence rate ranged from 25% to 60% for cervical chordomas and from 18% to 89% for sacrococcygeal chordomas.

Adjuvant therapies

The best treatment strategy for improved long-term survival in chordoma was a combination of surgical resection and radiation therapy.

Zhou *et al.*^[24] have reported 60 patients (skull base/clivus, $n = 24$; vertebral column, $n = 5$; sacrum, $n = 31$) with a mean follow-up time of 7, 7 years. The overall 10-year survival rate (58%) of the patients treated with surgery alone was significantly different from those treated with a combination of surgery and radiation (73%). The long-term prognosis of sacral chordoma was the worst (10-year survival rate = 48%). Our study could not find significant difference in survival rates with and without conventional radiotherapy.

A position paper by the Chordoma Global Consensus Group was published in 2017.^[3] In recurrence, we must choose between surgery alone, surgery and RT, and RT alone individually. However, a salvage resection with curative intent can be feasible for patients with isolated disease, a long disease-free interval, good performance status, and a reasonable likelihood of acceptable morbidity.

Surgical resection is accepted as a cornerstone of management in most chordomas. Other than radiotherapy, immunotherapy agents are being explored in chordomas as well as many different cancer types. In chordoma, brachyury has been identified as a prominent biomarker and potential molecular immunotherapy target, as well as PD-1 inhibition.^[25]

This study has limitations such as retrospective nature, limited numbers, although long follow-ups and various surgical approaches are used in individual cases. Besides, most cases

had mainly surgical treatment and this series does not involve radiosurgery applications.

CONCLUSIONS

The management of sacral and mobile spine chordomas is challenging, and recurrences occur very often. The average survival is 6, 16 years, but there are some cases alive after almost 20 years. Recurrence and survival rates of mobile spine and sacral chordomas are not different. Sacral chordomas tend to metastasize, while mobile spine chordomas do not. We do not think an extra marginal resection of cervical chordomas is possible without significant deficits and complications. We must also select the participants for sacrectomy, since recurrence after total sacrectomy is common. Sacrectomy is successful for sacral chordomas at S2 and below.

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Conflicts of interest

There are no conflicts of interest.

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