REVIEW

Surgical management of chordoma: A systematic review

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Context: Chordomas are rare primary tumors of bone characterized by local aggressiveness and poor prognosis. The surgical exeresis plays a critical role for their management.

Objective: The aim was to provide an overview of the surgical management of chordomas of the mobile spine and sacrum, describing the most common surgical approaches, the role of surgical margins, the difficulties of en bloc resection, the outcomes of surgery, the recurrence rate and the use of associated therapies.

Methods: We performed a systematic search using the keywords “chordoma” in combination with “surgery”, “spine”, “sacrum” and “radiotherapy”.

Results: Fifty-eight studies, describing 1359 patients with diagnosis of chordoma were retrieved. 17 studies were performed on subjects with cervical chordomas and 49 focused on patients with sacrococcygeal chordomas. The remaining studies included patients with chordomas in cranial region and/or mobile spine and/or sacrococcygeal region. The recurrence rate ranged from 25% to 60% for cervical chordomas, and from 18% to 89% for sacrococcygeal chordomas.

Conclusion: Despite the remarkable advances in the local management of chordoma performed in the last decades, the current results of surgery alone are still unsatisfactory. The radical en bloc excision of tumour is technically demanding, particularly in the cervical spine. Although radical surgery must still be considered the gold standard for the management of chordomas, a multidisciplinary approach is required to improve the local control of the disease in patients who undergo both radical and non-radical surgery. Adjuvant radiation therapy increases the continuous disease-free survival and the local recurrence-free survival.

Level of evidence: Systematic review; level III.

Keywords: Chordoma, Surgery, Spine, Sacrum, Radiotherapy

Introduction

Chordomas are rare primary tumors of bone that arise from embryonic remnants of the notochord. Recently, it has been recognized that chordomas can also derive from intraosseous benign notochordal cell tumors that undergo malignant transformation.¹ The incidence of chordoma is estimated to be approximately 1 per 1,000,000 people,² accounting for 4% of malignant bone tumors. Chordomas are topographically classified into four groups: skull base (25-35%), cervical spine (10%), thoraco-lumbar spine (5%), and sacral (50 to 60%).³ Chordomas typically occur in adults between ages 40 and 70, affecting males twice as often as

females.² However, cranial chordomas are more like to arise in female and younger subjects and may even occur in children and adolescents.⁴

Chordomas are slow-growing tumor, with a high tendency to local relapse, but low initial propensity for metastasis. However, metastasis to bone, lungs and liver have been found up to 43%.⁵⁻⁷ Chordomas are complex to treat due to the involvement of critical structures such as the brainstem, spinal cord, and nerves and arteries.

The gold standard treatment for chordomas of the mobile spine and sacrum is complete en bloc resection of the tumor with clean margins and postoperative external-beam radiation therapy. It provides the longest survival in most of the data.⁸

Prognosis is typically poor, current series suggest that 5-year survival is 50% to 68% and 10-year survival is 28% to 40%.^{2,9} Poor prognostic factors include large

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size, subtotal resection, microscopic necrosis, and Ki-67 index greater than 5%.⁹

In this systematic review of the literature, we aimed to describe the surgical management of chordomas of the mobile spine and sacrum to address the following research questions:

- which surgical approaches are commonly used?
- do surgical margins affect the results?
- what are potential difficulties of en bloc resection?
- how is the outcome of surgery and the reoccurrence rate?
- when associated therapies are used?

Materials and methods

Literature search and data extraction

We performed a systematic search using the keywords “chordoma” in combination with “surgery”, “spine”, “sacrum” and “radiotherapy”, with no limit regarding the year of publication. The following databases were accessed on April 2017: PubMed, Medline, Cochrane, CINAHL, Google scholar, and Embase.

Articles were included if they reported on five or more cases of chordomas of the mobile spine or sacrum treated with surgery. Exclusion criteria were the following: case reports, studies with inconsistent or inadequate data collection, studies that did not report on the surgical management and outcomes of chordomas cases specifically, review articles without quantitative data, and articles in languages other than English.

Two authors (U.G.L. and M.C.) independently read the abstract of each publication. The reference section of the identified publications was studied to ascertain whether other relevant material could be found. If deemed relevant, all publications were retrieved. Most articles were excluded on the basis of information provided by the title or abstract.

From the included articles, the following data were extracted: chordoma localization, surgical approach, surgical margins, associated therapy, outcomes and recurrence rate.

Results

1027 papers reporting data on the management of chordomas were identified. Of these, only 139 were potentially eligible and underwent full text review. We excluded 81 articles for the following reasons: case reports, non-surgical treatment and qualitative reviews (Figure 1).

Finally, we included 58 articles describing 2065 patients with diagnosis of chordoma (Table 1). The site of primary tumor was the sacrococcygeal region in 1346 (67%) patients, the mobile spine in 646 (30%),

and cranial region in 73 (3%). Among 646 patients with chondroma of the mobile spine, cervical spine was affected in 320 (50%) patients, the thoracic spine in 135 (21%), and the lumbar spine in 251 (39%).

Which surgical approaches are commonly used?

Surgical approaches were performed according to the site of the tumor mass.

Seventeen studies^{9–25} reported several approaches to cervical chordomas. Barrenechea *et al.*¹¹ used posterior or combined anterior and posterior approach; Choi and Wang *et al.*^{12,15} used standard transoral, extended transoral, transmandibular, transfacial or anterior approach and posterior approach; Hsieh *et al.*¹³ used anterior approach or combined transmandibular or submandibular and posterior approach; Murali *et al.*¹⁰ used transoral or anterior or posterior approach.

Four^{10,11,13,15} of these studies provided a detailed description of surgical excision. Barrenechea *et al.*¹¹ managed 74 cases of chordoma of the cervical spine using a retrocarotid approach with mobilization of the vertebral artery. When the tumor could not be completely resected via the initial anterior approach, a subsequent posterior resection was performed. Tumor resection was intralesional in all cases, and gross-total tumor resection was achieved in six cases. Hsieh *et al.*²⁶ performed multistage procedures to achieve marginal en bloc tumor excision in their five consecutive cases. Murali *et al.*¹⁰ reported a subtotal resection of the tumor in 2 patients and a total resection in 5 patients. Wang *et al.*¹⁵ reviewed 14 cases with primary cervical chordomas and reported 5 wide resections and 9 intralesional resections.

Forty-seven studies focused on patients with sacrococcygeal chordomas. Different surgical approaches have been described according to the localization of the tumoral mass. Eighteen^{27–44} studies reported the approach performed in 442 operations. The posterior approach was performed in 244 (55%) cases and the combined anterior and posterior approach was performed in 198 (45%) cases.

Twenty-six^{14,27,28,31–39,41–55} of 47 studies provided a detailed description of surgical excision. On 548 resections, the exeresis was wide in 330 (60%), marginal in 82 (15%), intralesional in 110 (20%), and wide contaminated (wide margin excision with intraoperative contamination of healthy tissue) in 26 (5%) cases.

To make easier and safer the surgery of chordomas, newer surgical techniques have been developed. Yang *et al.*³⁸ proposed the pre-operative use of transcatheter arterial embolization (TAE). According to their outcomes, pre-operative TAE can decrease intraoperative

Figure 1 Flow diagram of the literature search.

blood loss, make the surgical field clear, decrease the need for anterior approaches and facilitate the maximal removal of the sacral chordoma. Xue-Song *et al.*³⁷ suggested to perform a surgical excision of extensive sacrococcygeal chordomas assisted by occlusion of the abdominal aorta. The reported advantages are: less blood loss, more clear view of the surgical field allowing for better managing of pelvic organs and sacral nerve roots, shorter operating time. The authors also supported the idea that the more is the volume of blood loss, the higher is the risk of tumor cells metastasizing, for this reason the occlusion of the abdominal aorta may decrease the rate of recurrence and metastasis.

Do surgical margins affect the results?

Studies about thoracic and thoraco-lumbar chordomas reported that wide excision margins achieve better results when compared to intralesional and marginal excision margins.^{17,18,23}

Although the wide resection represents the gold standard, contrasting data have been published about its role in the reduction of the local recurrence rate in the sacrococcygeal region. After wide resection, some authors^{9,30} reported a local recurrence rate ranged from 5% to 17%, whereas intralesional or marginal resections are

associated with a local recurrence rate ranged from 71% to 81%. Other authors^{31,35} demonstrated no correlation between negative margins and better outcomes relatively to local recurrence rate and survival. However, Schawb *et al.*³⁵ demonstrated the negative effect of the intralesional margins, despite they did not find an increased rate of local control or survival with wide margin.

What are the potential difficulties of en block resection?

The main problem to achieve a wide en-bloc exeresis of cervical chordomas was the surrounding vital organs such as the vertebral artery (VA) and nerve roots. Barrenechea *et al.*¹¹ suggested not to sacrifice the VA to obtain an en-bloc removal of the tumor, because in case of tumor recurrence on the side of the contralateral artery, successive surgery is greatly limited by the subverted vascular anatomy. Isolation and mobilization of the VA allows the same objective and offers the possibility for subsequent surgery. Hsieh *et al.*¹³ recommended to perform a preoperative assessment of the intracranial vascular blood supply with a cerebral angiogram and to evaluate the tolerance of VA sacrifice with a temporary balloon occlusion test. Moreover, Hsieh *et al.* sustained the sacrifice of C1-C4 nerve

Table 1 Details of included studies.

STUDY	CHORDOMA LOCALIZATION	SURGICAL APPROACH	SURGICAL MARGINS	ASSOCIATED THERAPY	OUTCOME	RECURRENCE RATE
Ahmed 2009 ⁴⁵	Sacral chordomas (18)	-	Wide (8); marginal (8); intralesional (2)	Adjuvant RT (6); adjuvant RT + CT (2)	The 5-, 10- and 15-year survival rates were 81, 70, and 33%, respectively.	33% (6)
Atalar <i>et al.</i> 2006 ²⁷	Sacroccocygeal chordomas (11)	8 patients underwent a total of 12 operations: anterior and posterior (4); posterior (8); inoperable sacroccocygeal chordomas (3)	Marginal (8); intralesional (3)	Adjuvant RT (5); adjuvant RT + CT (2); RT (3 inoperable patients)	-	89%
Azzarelli <i>et al.</i> 1988 ¹⁶	Sacroccocygeal chordomas (27); cervical chordoma (1); lumbar chordomas (2); sapheno-occipital chordomas (3)	-	Sacral chordomas: radical (5); marginal (3); intralesional (11); inoperable sacroccocygeal chordomas (8); Non sacral chordomas: no radical surgery (3); inoperable sacroccocygeal chordomas (3)	Sacral chordomas: adjuvant RT (5); RT (1 inoperable patients); Non sacral chordomas: adjuvant RT (3); RT (2 inoperable patients) Adjuvant RT (10)	Sacral chordomas: 24 (2-80) months of disease free interval	Sacral chordomas: 48% (13: adequate surgery 2; adequate surgery + RT 1; inadequate surgery 9; inadequate surgery + RT 1;)
Baratti <i>et al.</i> 2003 ²⁸	Sacral chordomas (28)	Posterior approach (26);	Wide (11); marginal (13); intralesional (4)	RT (2 inoperable patients) Adjuvant RT (10)	Disease-free survival at 5 and 10 years was 60.6% and 24.2% respectively. Overall survival was, respectively, 87.8% and 48.9% at the same interval	18% (5)
Barrenechea <i>et al.</i> 2007 ¹¹	Cervical chordomas (7)	combined abdominal and posterior approach (2) Posterior approach (2); combined anterior and posterior approach (5)	Intralesional (7)	Adjuvant proton beam RT (3); adjuvant proton beam RT + CT (2)	2 died and 5 free of disease, with a median follow-up duration of 23 months (range 7–169 months)	28% (2)

Bergh <i>et al.</i> 2000 ⁹	Sacrococcygeal chordomas (30); cervical chordomas (5); thoracic chordomas (1); lumbar chordomas (3)	-	Wide (23); marginal or intralesional (16)	Adjuvant RT (4 sacral and 1 cervical chordoma)	23 patients were disease free at the last follow-up (mean follow-up: 8 years; range, 1 month to 23 years)	44% (17)
Bjornsson <i>et al.</i> 1993 ¹⁷	Cervical chordomas (19); thoracic chordomas (7); lumbar chordomas (14)	-	-	Adjuvant RT (29)	17 patients died and 23 were alive 5 years after surgery.	75% (30)
Boriani <i>et al.</i> 2006 ¹⁸	Cervical chordomas (15); thoracic chordomas (7); lumbar chordomas (30)	-	Intralesional excision (20, 8 of them with extracapsular excision); en bloc resection intralesional or contaminated (8); en bloc resection wide margin or marginal (10); palliative surgery (10)	Adjuvant RT (16 with intralesional excision, 8 with en-bloc excision, 10 palliative surgery)	continuously disease free: 3 patients treated with intralesional excision and RT for an average of 52 months; 8 patients treated with wide margin en-bloc excision for an average of 70 months and 4 patients treated with for an average of 10 months.	66% (100% of patients following RT alone, palliative, or intralesional intracapsular excision; 75% of patients following extracapsular excision and RT; 50% of patients following en bloc with inadequate margin and RT; 20% of patients following en bloc resection with appropriate margin)
Chandawarkar 1996 ²⁹	Sacrococcygeal chordomas (50)	Posterior approach (22); combined abdominal and	-	Adjuvant RT (24 patients with a positive or close-cut margin (< 2 cm) and those with a history of surgery)	The average disease-free survival was 63 months, and the overall survival was 7 years	-
Chen <i>et al.</i> 2010 ⁴⁰	sacral chordoma	posterior approach (28) posterior approach (36)	-	-	5-year and 10-year actuarial CDFS were 59.3 and 42%, respectively 10-year actuarial CDFS were 59.3 and 42%, respectively	Local recurrence 44.4% (16/36)
Cheng <i>et al.</i> 1999 ⁷²	Sacral chordomas (19); lumbar chordomas (4)	-	Wide (7); intralesional microscopic disease remaining: (5); intralesional macroscopic disease remaining (11)	Adjuvant RT (13 patients with positive margin)	continuously disease free survival was 58% (13 patients) and the 10-year was 22% (5 patients)	-

Continued

Table 1 Continued.

STUDY	CHORDOMA LOCALIZATION	SURGICAL APPROACH	SURGICAL MARGINS	ASSOCIATED THERAPY	OUTCOME	RECURRENCE RATE
Choi <i>et al.</i> 2010 ¹²	Craniocervical junction and upper cervical spine (C1-C3) chordomas (97)	Standard transoral (40) or extended transoral (16) or transmandibular (53) or transfacial (4) or anterior (11) approach and posterior approach for fixation (97)	-	-	The 5- and 10-year survivals were	25%
De Santis <i>et al.</i> 1990 ¹⁹	Cervical chordomas (2); lumbar chordomas (6); sacral chordomas (3)	-	Non radical surgery	-	55% (53 patients) and 36% (35 patients) The 5- and 10-year survivals of	-
Dhawale <i>et al.</i> 2014 ⁴¹	sacral chordoma (21)	combined anterior-posterior resection (14); posterior resection alone (7)	positive (5), marginal (6), and wide (10)	Adjuvant RT (18)	36% (4 patients) and 18% (2 patients), respectively Median survival was 7.2 years for overall. 3.4 years for those with local recurrence or metastatic disease	Local recurrence 40% (8/21), metastatic disease 19% (4/21)
Eid <i>et al.</i> 2011 ²⁰	Cranial base chordomas (7); cervical chordomas (6); lumbar chordomas (1); sacral chordomas (16)	Surgery (24); CT-guided biopsy (6)	Wide Wide resection (12); subtotal resection (12)	Adjuvant radiotherapy/radiosurgery (12 patients underwent subtotal resection); radiotherapy/radiosurgery (6)	At final follow-up (mean follow-up:78 months, ranging 24–178) 5 patients were continuously disease free; 2 patients showed no evidence of the disease, after a second wide excision; 16 were still alive with their disease. The overall survival rate was 96% at 5 years and 67% at 10 years	67% (20)
Eriksson <i>et al.</i> 1981 ⁶¹	Spheno-occipital chordomas (14); vertebral chordomas (8); sacrococcygeal chordomas (29)	Surgery (33); no surgery (9)	-	Adjuvant RT (16); RT (9)	Mean survival (years): surgery:5; surgery + RT:2.8; RT:3.4	-

Ferraresi <i>et al.</i> 2010 ⁶²	Skull base chordomas (1); vertebral chordomas (13); sacral chordomas (11)	Surgery (22)	Wide (5); intralesional (17)	adjuvant RT (3); palliative RT (8)	The 5-year and 10-year survival rate of the entire series was 76.7% and 59.7%, respectively	Local recurrence 20% (1) in wide resection group; local progression 94% (16) in intralesional resection group
Fourney <i>et al.</i> 2005 ⁴⁶	Sacral chordomas (16)	-	Wide (10); marginal (6)	-	-	40% in wide resection group; 67% in marginal resection group
Fuchs <i>et al.</i> 2005 ³⁰	Sacral chordomas (52)	Posterior approach (22); combined anterior and posterior approach (30)	Wide (21); marginal or intralesional (31)	Adjuvant RT (22)	The overall survival rate in the entire group was 74% at five years, 52% at ten years, and 47% at fifteen years	44% (23)
Gokaslan <i>et al.</i> 2016 ¹⁴	Cervical Chordoma (54) Thoracic Chordoma (24) Lumbar Chordoma (78)	-	Radical (58) Non radical (84)	Adjuvant RT (85)	Overall survival 7 years	35% (58)
Hanna <i>et al.</i> 2008 ⁴⁷	Sacral chordomas (18)	-	Wide (10); marginal (7); intralesional (1)	-	7 of 18 patients died of their disease at a median of 3 years; 5 of these patients local recurrence and metastases before death	67% (12)
Hsieh <i>et al.</i> 2009 ⁴⁸	Sacral chordomas (19)	-	Wide (8); marginal (5); intralesional (6)	-	The mean disease-free survival for patients with wide or marginal en bloc tumor excisions was 51 months, but only 17.5 months for patients who had contaminated/ intralesional resections	26% (5)
Hsieh <i>et al.</i> 2011 ¹³	Cervical chordomas (5)	Combined transmandibular (2) or submandibular (1) and posterior approach; anterior approach (2)	Wide (3); marginal (2)	-	The mean disease-free survival f was 84.2 months. Mean f-u:54,7 months.	40% (2)

Continued

Table 1 Continued.

STUDY	CHORDOMA LOCALIZATION	SURGICAL APPROACH	SURGICAL MARGINS	ASSOCIATED THERAPY	OUTCOME	RECURRENCE RATE
Hulen <i>et al.</i> 2006 ³¹	Sacral chordomas (16)	Sequential anterior and posterior approach (16)	Wide (9); marginal (4); intralesion (3)	Adjuvant RT (7); adjuvant CT (2)	-	75% (12: wide 6, marginal 3, intralesion 3)
Logroscino <i>et al.</i> 1998 ²¹	Clivus chordomas (1); cervical chordomas (2); thoracolumbar chordomas (8); sacral chordomas (4)	Clivus chordomas: transoral and extraoral excision (1); cervical chordomas: anterior approach (1), combined anterior and posterior approach (1); thoracolumbar chordomas: combined anterior and posterior approach (6), anterior approach (2); sacral chordomas: posterior approach (4)	Marginal (8); intralesional (5); palliative surgery (2)	Adjuvant RT (7)	At final follow-up 8 patients were alive, 6 died and 1 did not return to follow-up	-
Lopes <i>et al.</i> 1996 ⁶³	Sacroccoccygeal chordomas (20);	Sacroccoccygeal chordomas: surgery (12);	-	Sacroccoccygeal chordomas: adjuvant RT (8); adjuvant CT (5); RT (6); CT (1); clivus chordomas: adjuvant RT (1); RT (1); retroperitoneal chordomas: CT (1)	Five-year overall survival < 5%	-
	clivus chordomas (3); retroperitoneal chordomas (1)	no treatment (2);				
		clivus chordomas: surgery (2)				
Lybeert and Meerwaldt 1986 ⁶⁸	Sacroccoccygeal chordomas (14); clivus chordomas (3); lumbar chordomas (1)	Surgery (14)	-	Adjuvant RT (10); RT (4)	-	14% (2 of 14 underwent RT)
Meng T. <i>et al.</i> 2014 ⁵²	Mobile Spine chordoma (58) Sacral chordoma (95)	anterior (6) posterior (112)	subtotal (15) total piecemeal (80)	Adjuvant RT (14) Local treatment with cisplatin or methotrexate (107)	local relapse-free survival 66.7% Overall survival 50.1%	Local recurrence 33% (51)
		combined anterior and posterior (35) Surgery (23)	total en bloc (58)	Preoperative selective arterial embolism (64) Adjuvant RT (17): carbon ion therapy or proton therapy	local control (94%), overall survival (83%) and progression-free survival (68%)	local recurrence 17% (4/23)
Mima M. <i>et al.</i> 2013 ⁶⁴	sacral chordoma		-			

Moojen <i>et al.</i> 2011 ⁴⁴	Sacrococcygeal chordoma (15)	Posterior approach (12) Combined anterior and posterior approach (3)	Wide excision (10)	Neo Adjuvant RT (1), Adjuvant RT (4)	overall survival 8.2 years	80% (12/15)
Murali <i>et al.</i> 1981 ¹⁰	Cervical chordomas (8)	Anterior (3) or posterior (3) or transoral (1); no treatment (1)	Total resection (5); subtotal (2)	Adjuvant RT (1)	60% (3 of 5 patients)	-
Nishida Y. <i>et al.</i> 2009 ⁵³	Sacral Chordoma: Surgery alone (10), RT alone (7)	-	Wide resection (8) Intralesional resection (2)	-	Surgery group: 5-year disease-specific (85.7%) and local recurrence-free survival rate (62.5%) RT group: 5-year disease-specific (53.3%) and local recurrence-free survival rate (100%) The mean survival in patients with chordomas of the clivus was 7.7 years; in patients with sacrococcygeal chordomas was 7.2 years	Surgery group 30% (3,9 RT group 0%
O'Neil <i>et al.</i> 1985 ⁶⁵	Sacrococcygeal chordomas (18); intracranial chordomas (12); vertebral chordomas (4)	-	Subtotal resection (23); total resection (7)	Adjuvant RT (5 with total and 16 with subtotal excision)	The overall survival rates at 5, 10 and 20 years were 83.3, 55.6 and 55.6%, respectively	-
Osaka <i>et al.</i> 2005 ³²	Sacrococcygeal chordomas (12)	Combined anterior and posterior approach (6); posterior approach (6)	Wide (11); intralesional (1)	Adjuvant RT (1)	disease-free survival at 5 years: 68.8%, overall survival rate at 5 years: 81.3%	-
Osaka <i>et al.</i> 2014 ⁴²	Sacrococcygeal chordomas (15)	Combined anterior and posterior approach (8); posterior approach (7)	Wide (14)	Colostomy (6), musculocutaneous flap (2), Ethanol (1), RT (2)	At latest follow-up (mean follow-up 50 months, range 24–90 months), six patients showed no evidence of disease, one was alive with local disease, three had died of disease, and two had died of complications	Local recurrence 26% (4)
Ozaki <i>et al.</i> 1997 ⁴⁹	Sacrococcygeal chordomas (12)	-	intralesional (1) Marginal (6) (2 out of the 6 had contaminated margin); intralesional (5)	Adjuvant RT (1); RT (1)	At latest follow-up (mean follow-up 50 months, range 24–90 months), six patients showed no evidence of disease, one was alive with local disease, three had died of disease, and two had died of complications	50% (4 with intralesional resection, 1 with marginal resection, 1 with contaminated margins)

Continued

Table 1 Continued.

STUDY	CHORDOMA LOCALIZATION	SURGICAL APPROACH	SURGICAL MARGINS	ASSOCIATED THERAPY	OUTCOME	RECURRENCE RATE
Ozger <i>et al.</i> 2010 ³³	Sacroccocygeal chordomas (17)	Combined anterior and posterior approach (11); posterior approach (6)	Wide (14); marginal (1); intralesional (2)	Adjuvant RT (4)	The overall survival rate is 47% (8 alive and 9 dead) at a mean follow-up of 55.5 months. The five-year survival rate is 43%.	41% (7; 4 underwent only surgery and 3 underwent surgery + RT)
Park <i>et al.</i> 2006 ⁵⁸	Sacral chordomas (21)	-	Wide or marginal (5); intralesional (16)	Adjuvant RT (21)	-	-
Rich <i>et al.</i> 1985 ²²	Skull base chordomas (14); cervical chordomas (5); thoracic chordomas (3); lumbar chordomas (7); sacroccocygeal chordomas (19)	-	Total excision (16); subtotal excision (17); biopsy (15)	Adjuvant RT (17 with subtotal excision); preoperative RT (2 with total excision); RT (15)	The median survival is 7 and 5 years for surgery or radiation, respectively	46% (22)
Rotondo <i>et al.</i> 2015 ⁵⁴	Sacroccocygeal chordomas (71);	-	Wide (45)	Adjuvant RT (58)	5 years Overall Survival 81%,	Local recurrence 36% (46), Distant recurrence 20% (26)
	Lumbar chordoma (40)		Intralesional (79)	Neo Adjuvant and Adjuvant RT (60)		
	Thoracic chordoma (16)		Unknown (3)			
Ruggieri <i>et al.</i> 2010 ³⁴	Sacral chordomas (56)	Combined anterior and posterior approach (37); posterior approach (19)	Wide (31); wide-contaminated (11); marginal (9); intralesional (5)	-	Overall survival was 97% at 5 years, 71% at 10 years, and 47% at 15 years.	43% (24)
Ruosi <i>et al.</i> 2015 ⁴³	Sacral chordoma (14)	Posterior approach	Wide resection (8), intralesional resection (6)	-	Survival at 44 months was 100%, at 88 months was 71.43, and 57.14% at 132 months	Local recurrence 42% (6), Distant recurrence 25% (4)
Safwat <i>et al.</i> 1987 ⁶⁶	Sacroccocygeal chordomas (25); spheno-occipital chordomas (6); vertebral chordomas (6)	-	Wide (4); marginal (6); intralesional (17)	Adjuvant RT (15)	Overall survival was at 5 years 41% for radiation therapy; 33% for surgery and 50% for combined therapy	58% (21)
Samson <i>et al.</i> 1993 ⁵⁰	Sacral chordomas (21)	-	Wide (11); marginal (3); intralesional (7)	Adjuvant RT (16)	-	-
Schwab <i>et al.</i> 2009 ³⁵	Sacral chordomas (42)	Combined anterior and posterior approach (34);	Wide (27); wide-contaminated (8); marginal (3); intralesional (4)	Adjuvant RT (15)	The 5 and 10 year overall survival rates were 59% and 35%	36% (15: 9 with wide resection; 2 with wide-contaminated; 4 with intralesional resection)
		laparoscopic mobilization (8)				

Solini <i>et al.</i> 2009 ⁵¹	Sacral chordomas (9)	Combined anterior and posterior or single posterior approach	Wide resection (9)	-	-	27% (3)
Stacchiotti <i>et al.</i> 2010 ²³	Sacral chordomas (108); lumbar chordomas (21); cervical-dorsal chordomas (9)	-	Wide (48); marginal (35); intralesional (47); inoperable (8)	Adjuvant RT (42); adjuvant CT (5)	The 5- and 10-year Overall Survival were 78% and 54% respectively	59% (82 of 130 patients who received primary tumor surgery)
Sundaresan <i>et al.</i> 1979 ⁶⁷	Sacroccocygeal chordomas (36); lumbar chordomas (11); thoracic chordomas (2); cervical chordomas (5)	Surgery alone: 9 patients with sacroccocygeal chordoma. Surgery + RT: 17 with cervical and 20 with sacroccocygeal chordoma. Biopsy + RT: 9 patients with sacroccocygeal chordoma	-	Adjuvant RT (17 patients with cervical chordomas; 20 patients with sacroccocygeal chordomas)	The median survival for was approximately 6 years. The 5-year survival for the sacroccocygeal group was 66%, as opposed to 50% for the vertebral group. Approximately 40% of patients with sacral chordomas lived 10 years. The overall median survival was 60 months.	-
Sundaresan <i>et al.</i> 1987 ²⁴	Sacral chordomas (20); vertebral chordomas (12); skull base chordomas (2)	-	Wide (6); marginal (5); intralesional (20); biopsy (2)	Adjuvant RT (18); adjuvant CT (7)	The median progression-free and overall survival were 10 and 90 months, respectively	-
Thieblemont <i>et al.</i> 1995 ⁵⁹	Sacral chordomas (10)	-	Radical (1); subtotal (9)	Adjuvant RT (10)	5-year overall survivorship 81%	local recurrence 46% (53/115), distal metastases 17% (20/115) 40% (10)
Tao J. <i>et al.</i> 2016 ⁵⁵	sacral chordoma (115)	Surgery (115)	Adequate (77), Inadequate (38)	Adjuvant RT (31)	-	-
Volpe <i>et al.</i> 1983 ²⁵	Sacroccogygeal chordomas (13); lumbar chordomas (2); cervical chordomas (3); skull base chordomas (7)	Surgery (25)	-	Adjuvant RT (14); adjuvant CT (3)	No evidence of disease was found in all but 1 patient after a follow-up ranging 3.5 to 8.5 years.	20% (1)
Waisman <i>et al.</i> 1999 ³⁶	Sacral chordomas (5)	Posterior approach (5)	Wide excision (5)	Adjuvant RT (1)		

Continued

Table 1 Continued.

STUDY	CHORDOMA LOCALIZATION	SURGICAL APPROACH	SURGICAL MARGINS	ASSOCIATED THERAPY	OUTCOME	RECURRENCE RATE
Wang <i>et al.</i> 2012 ¹⁵	Cervical Chordoma (14)	Anterior approach (4), Transoral and posterior approach (1), anterior and posterior approach (9)	wide (5), intralesional (9)	Adjuvant RT (14)	5-year disease-free survival rates 50%	local recurrence 57% (8)
Xue–Song <i>et al.</i> 2010 ³⁷	Sacroccocygeal chordomas (9)	Posterior approach with occlusion of abdominal aorta	Wide (6); marginal (3)	Adjuvant RT (5)	During the follow-up period (range 10–57 months, mean 31.4 months), no patient developed local recurrence or metastatic spread of tumor	0
Yang <i>et al.</i> 2010 ³⁸	Sacroccocygeal chordomas (30)	Posterior approach after Transcatheter Arterial Embolization	Wide (30)	-	-	40% (12)
Yonemoto <i>et al.</i> 1999 ³⁹	Sacroccocygeal chordomas (13)	Combined anterior and posterior (10); posterior approach (2); unknown (1)	Wide (3); marginal (2); intralesional (8)	-	The 5-year survival rate was 81.8% and the 10-year survival rate was 29.1%. F-U: average 75,8; ranging 7-156 months. 7 patients died of the disease, 6 were alive without evidence of the disease at last f-u.	46% (6: 5 gluteal muscles, 2 sacral stumps)
York <i>et al.</i> 1999 ⁶⁰	Sacral chordomas (27)	-	Wide (15); marginal or intralesional (12)	Adjuvant RT (18); adjuvant CT (7)	The median (Kaplan-Meier) survival time for the entire group was 7.38 years (range, 4 months to 34 year) after the first operation	70%

(-) number of patients.

roots because it does not lead to significant neurological defects, whereas the sacrifice of C5-T1 nerve roots leads to severe neurological impairments of the upper limb.²⁶

A wide en-bloc exeresis of chordomas in the sacrum was linked with potential nerve roots lesions. In terms of complications, bladder and rectal functions were the most relevant surgical morbidities. There is a direct correlation between the number of preserved nerve roots and the neurological functions: when both the S2 roots are removed the functions are inexorably lost,^{24,56} if only one S2 root is preserved the urinary and rectal functions are occasionally recovered.²⁸ Finally, the bilateral preservation of S2 leads to neurological impairment, which can be recovered in up to 50% of patients.⁵⁰

Fatigue fractures seemed to be a less relevant surgical complication. Bergh *et al.*⁹ reported 6 fractures of the remnant sacrum on a total of 18 patients underwent high sacral amputation, while wound-related complications affected 53.5% of patients in the series of Baratti *et al.*²⁸

How is the outcome of surgery and the reoccurrence rate?

In studies focused on cervical chordomas, the recurrence rate after surgery ranged from 25%¹² to 60%,¹⁰ in those focused on chordomas of the sacrococcygeal region, the recurrence rate ranged from 18%²⁸ to 89%.²⁷

The most common site for tumor recurrence was the sacral remnant and the muscle tissue through neoplastic cells dissemination.^{16,51} It is recommended to observe an adequate osseous margin and to remove the surrounding soft tissue, such as part of the gluteus maxims or piriformis muscle, because chordoma has an infiltrating behavior.⁵¹ The protective role of pre-sacral lamina in terms of tumor spreading is debated. Baratti *et al.*²⁸ found that in most of cases this fascia is already infiltrated at the time of diagnosis, while Yonemoto *et al.*³⁹ sustain that the presacral lamina is able to stop the tumor spreading. However, when tumor recurs on rectal or bladder tissue the possibility for a tumor resection remains controversial. Accordingly to the general condition of selected non-metastatic patients, excision of the tumor recurrence may be useful in pain and impairments reduction.⁵⁷

When associated therapies are used?

Only three studies^{10,11,15} on cervical chordomas reported associated therapies after surgery, mainly radiotherapy, which were used in 14%¹⁰ and 71%¹¹ of patients respectively.

Twenty-eight (73%)^{27–33,35–37,41,42,44,45,49,50,54,55,58–68} studies on chordomas of the sacrococcygeal region

reported associated therapies, mainly radiotherapy. On 568 patients who underwent surgery, 272 (48%) received further treatments, including radiotherapy and/or chemotherapy.

Although chordoma has poor sensitivity to radiation therapy and to chemotherapy,^{29,69–71} there are evidences^{16,30,37,60,72} that adjuvant radiation therapy increases the continuous disease-free survival and the local recurrence-free survival when administered in patients who underwent inadequate tumor excision (marginal or intralesional) with micro- or macroscopic residual disease. On the other hand, there are no differences between wide excision and wide contaminated.^{34,35}

Discussion

This systematic review of the literature reports the state of the art of the surgical management of chordomas of the mobile spine and sacrum. We found that the sacrococcygeal region is the most frequent localization of chordomas, accounting for almost 70% of cases.³ On the other hands, the cervical spine is the most affected part of the mobile spine, accounting for 50% of cases.³

The following research questions have been addressed.

Which surgical approaches are commonly used?

The surgical approach is currently performed according to the site of tumor mass. In the cervical spine, the standard transoral or extended transoral or transmandibular or transfacial or anterior approaches can be used for chordomas of C1-C3; moreover, the posterior approach can be performed.¹² In the remaining levels, the anterior or posterior or combined anterior-posterior approaches can be used. After the exeresis of the tumor, the stability of the spine may be restored using fibular allograft bone or tricortical iliac crest for the anterior reconstruction.¹¹

Hsieh *et al.*¹³ proposed to classify cervical chordomas taking into account their anatomical site, in order to drive the planning of surgical approach. They distinguished three subgroups: high-cervical chordomas, arising from C1-C3; mid-cervical chordomas, involving C4-C6; and low-cervical chordomas, arising from the cervico-thoracic junction (C7-T1).

Sacrococcygeal chordomas can be classified in proximal sacrum chordomas, involving the first and second segment of the sacrum, and distal sacrum chordomas, arising from the other segments of the sacrum.³⁴ In terms of surgical management, the combined anterior and posterior approach is indicated for proximal sacrum chordomas, whereas the posterior approach is

suitable for distal sacrum chordomas.^{50,73–76} Approaching the tumor from anteriorly may be useful to separate the sacrum from the rectum avoiding the risk of rectal perforation.^{75,77} However, the combined anterior-posterior approach is time consuming and involves significant blood loss.³⁶

A controversial point about the management of sacrococcygeal chordomas is represented by the spinopelvic reconstruction after total or high proximal sacrectomy. Some authors recommend this procedure to prevent the complete dissociation between mobile spine and pelvis,^{78–81} other authors believe that it is not useful according with the acceptable ambulatory function of patients after surgery.^{34,82}

Do surgical margins affect the results?

According to the Enneking,⁸³ surgical margins can be defined: *intralesional*, if the resection passes through the lesion; *marginal*, if the dissection passes through the pseudocapsule or the reactive tissue; and *wide*, if the tumor is excised with a surrounding normal tissue. All the studies strongly recommend to perform a *wide excision* for both chordomas of the mobile spine and sacrum, when it is feasible, and reported better outcomes in patients who underwent a primary radical surgery. Thus, it is widely accepted that the wide en-bloc excision at primary surgery provides the best treatment option.

What are the potential difficulties of en bloc resection?

The surgery of cervical chordomas is technically demanding, because of the difficulty in achieving *en bloc* resection of the tumor. The main obstacle is due to the involvement of the vertebral artery (VA) and nerve roots. The resection of these structures can be associated with major complications, including strokes and marked neurologic impairment.^{11,13}

When the tumor is located highly in the sacrum or has considerable dimensions, many obstacles may be encountered in performing an extensive surgery: nerve roots resection may lead to neurological impairment relatively to urinary and bowel functions and to ambulation, but also fatigue fractures, pelvic instability, lumbar descent, intra-operative conspicuous blood loss and infections.²²

For this reason, surgical procedure, intended benefits and potential complications should be carefully discussed with the patient. This surgery is not easy to standardize and the experience of the surgeon is needed to adapt the surgical procedure to individual requirements. Therefore, surgical approach and type of fixation must be specifically adapted to the single patient.

How is the outcome of surgery and the reoccurrence rate?

The local control of the disease is one of the most important issues in the management of chordomas. The recurrence rate at about 5 years ranged from 25%¹² to 60%¹⁰ for cervical chordomas, and from 18%²⁸ to 89%²⁷ for sacrococcygeal chordomas. This data was strongly affected by surgical margins and association with adjuvant therapies. Indeed, it is currently accepted that the main positive predictive factors of local recurrence is surgical margins and positive history for previous intralesional surgery.^{27,30,34,39,47,49,60}

When associated therapies are used?

Historically, chordomas are resistant to radiation therapy and chemotherapy.^{29,69–71} However, adjuvant radiation therapy increases the continuous disease-free survival and the local recurrence-free survival when administered in patients who underwent inadequate tumor excision (marginal or intralesional) with micro- or macroscopic residual disease and radical surgery.^{16,30,37,60,72}

Adjuvant proton-beam therapy is routinely performed for the management of chordomas at many high-volume cancer centres. However, given its limited availability, the intensity-modulated radiation therapy (IMRT) and stereotactic delivery techniques have been also proposed as alternative treatments.⁸⁴ On the other hand, the evidence supporting the role of systemic therapy in the preoperative and adjuvant settings is scanty.

Conclusions

The ideal treatment for chordomas is an en bloc resection with clean margins and postoperative external beam radiation therapy.⁸ Radical surgery is technically demanding and the surgical approach needs to be accurately planned. The multidisciplinary approach is required to improve local control of the disease.

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