Long-term outcomes of grade I/II skull base chondrosarcoma: an insight into the role of surgery and upfront radiotherapy

Hirotaka Hasegawa (hirohasegawa-tky@umin.ac.jp)
Mayo Clinic: Mayo Clinic Minnesota https://orcid.org/0000-0002-3585-2188
Kunal Vakharia
Mayo Clinic Minnesota
Christopher S Graffeo
Mayo Clinic Minnesota
Matthew L Carlson
Mayo Clinic Minnesota
Bruce E Pollock
Mayo Clinic Minnesota
Paul D Brown
Mayo Clinic Minnesota
Avital Perry
Mayo Clinic Minnesota
Jamie J Van Gompel
Mayo Clinic Minnesota
Colin L. W. Driscoll
Mayo Clinic Minnesota
Michael J Link
Mayo Clinic Minnesota

Research Article

Keywords: chondrosarcoma, radiotherapy, radiosurgery, proton beam, skull base tumor, surgical outcome, microsurgery

DOI: https://doi.org/10.21203/rs.3.rs-304906/v1

Abstract

Purpose

To clarify the need for post-operative radiation treatment in skull base chondrosarcomas (SBCs).

Methods

A retrospective analysis of patients with grade I or II SBC. Patients were divided according to post-surgical treatment strategies: (A) planned upfront radiotherapy and (B) watchful waiting. Tumor control and survival were compared between the treatment groups. The median follow-up after resection was 105 months (range, 9-376).

Results

Thirty-two patients (Grade 1, n = 16; Grade 2, n = 16) were included. The most frequent location was petroclival (21, 64%). A gross total resection (GTR) was achieved in 11 patients (34%). Fourteen (44%) underwent upfront radiotherapy (group A) whereas 18 (56%) were followed with serial MRI alone (group B). The tumor control rate for the entire group was 77% and 69% at 10- and 15-year, respectively. Upfront radiotherapy (P = 0.25), extent of resection (P = 0.11) or tumor grade (P = 0.83) did not affect tumor control. The majority of Group B patients with recurrent tumors (5/7) obtained tumor control with repeat resection (n = 2), salvage radiotherapy (n = 2), or a combination of both (n = 1). The 10-year disease-specific survival was 95% with no difference between the group A and B (P = 0.50).

Conclusion

For patients with grade I/II SBC, a reasonable strategy is deferral of radiotherapy after maximum safe resection until tumor progression or recurrence. At that time, most patients can be successfully managed with salvage radiotherapy or surgery. Late recurrences may occur, and life-long follow-up is advisable.

Introduction

Skull base chondrosarcoma (SBC) is a cartilaginous malignant neoplasm arising from a synchondrosis of the skull base. Conventional chondrosarcomas are histopathologically classified into grade I, II, and III based on mitotic rate, cellularity, and nuclear size.[1] Typically, grade I and II tumors behave indolently, while grade III tumors typically exhibit a more aggressive disease course.[2-4] There are also 5 non-conventional variants: juxtacortical, clear cell, myxoid, mesenchymal, and dedifferentiated, in which the first 3 subtypes are presumed to be indolent and thus behave similarly to grade I–II SBCs, while the other 2 are considered high-grade.[5-8] The majority of SBCs are grade I or II, thus expected to exhibit indolent behaviors.[2,4,9,10]

SBC is extremely rare; the incidence is reported to be less than 0.8–1 per million per year,[11] representing approximately 0.1% of all brain neoplasms.[3,4] Due to this rarity, the optimal treatment strategy remains

debatable. In general, maximal safe resection is the preferred treatment strategy; however, the location and infiltrative nature of the tumor into the skull base and possible involvement of critical adjacent neurovascular structures makes surgery challenging in many cases resulting in a low rate of gross total resection (GTR).[10,12] Additionally, it may be difficult on postoperative imaging to be confident GTR was achieved.

These facts, in combination with a lack of effective chemotherapy, and the relatively abundant experience with radiotherapy,[13-19] often lead physicians to recommend upfront radiotherapy following resection. However, even though radiotherapy seems effective based on single-arm prospective/retrospective studies, there is a lack of an appropriate comparison between patients with and without radiotherapy. In other words, the net benefit of the strategy involving surgery and radiotherapy versus surgery alone, remains to be elucidated. The primary goal of this study was to evaluate the role of upfront radiotherapy for the management of SBC, and try and discern if an optimal treatment strategy exists.

Methods

A retrospective study was performed involving patients with histopathologically confirmed grade I or II SBC treated at the authors' institution between January 1991 and March 2020. Patients who were referred after 2 or more recurrences were excluded to focus on the effect of the first surgical intervention with or without radiotherapy. Since mesenchymal/dedifferentiated/grade III SBCs are known to be far more aggressive,[7] they were excluded from this analysis. Extent of resection (GTR or non-GTR) was determined based on surgeon's estimation and postoperative imaging.

Statistical analysis

After data collection, patients were classified into 2 groups according to their post-surgical treatment strategies: (A) upfront radiotherapy and (B) watchful waiting. Patients received or did not receive adjuvant radiotherapy after maximally safe resection based on patient and treating physician preferences and recommendations without a standardized protocol at our institution. Baseline demographic and tumor characteristics were summarized and compared between groups. The Wilcoxon rank-sum test was used to compare continuous variables, whereas Fisher's exact test was used for categorical variables. Second, cumulative tumor control rate (TCR) and disease-specific survival (DSS) were calculated using the Kaplan-Meier method, and the curves were compared using the log-rank test. Failed tumor control was defined as radiographic evidence of tumor growth or recurrence, in the case of GTR. Patients were censored at the end of their radiographic follow-ups. Failed DSS was considered as any mortality that was presumed to be related to the tumor or associated intervention(s). Patients were censored at the end of their clinical follow-up or when they died without evidence of recurrence. In both TCR and DSS, the date of initial surgery was set as zero time. If an initial surgery was biopsy alone and immediately followed by another curative surgery, the date of the curative surgery was considered as zero time. Factors that potentially affected tumor control were tested using the Cox proportional hazard analysis. Finally, the entire clinical courses of the 2 groups were described in detail with an analysis on radiation-induced

complications. Common Terminology Criteria for Adverse Events (CTCAE) v5.0 was used to grade radiation-related complications. The study was approved by Institutional Review board. Informed consent was waived given the retrospective non-invasive nature of the study. All statistical analyses were performed using JMP 14.0 (SAS Institute, Cary, NC, USA). A P-value of < .05 was considered significant.

Results

Baseline characteristics

Thirty-two (17 females and 15 males) patients with a mean and median postoperative clinical follow-up period of 120 and 105 months (range, 9–376 months), respectively, were identified and included in the analysis (**Table 1**). The median age at initial surgery and maximal tumor diameter were 47 years (range, 12–76 years) and 35 mm (10–66 mm), respectively. Twenty-one (66%) tumors involved the petroclival synchondrosis, 7 (22%) the anterior skull base-sinonasal region, and 4 (13%) the cavernous sinus-middle fossa. One patient suffered from Maffucci syndrome. All patients underwent surgical resection as the first intervention. As initial surgical approach, transcranial approaches were used in 22, transnasal approaches in 3, 2-staged transcranial and transnasal approaches in 3, maxillectomy in 2, and combined bifrontal craniofacial approach and lateral rhinotomy in 2. Gross total resection (GTR) was achieved in 11 (34%) cases based on intraoperative impression and 3-month f/u MRI scan. Histopathologically, 16 had grade I and 16 had grade II tumors.

Postoperatively, 14 patients underwent upfront radiotherapy and 18 were managed with close surveillance; they were accordingly allocated to group A and B, respectively. The mean and median clinical follow-up periods were 71 months and 44 months, respectively in group A, and 157 months and 154 months, respectively in group B. The mean and median radiographical follow-up periods were 65 months and 40 months, respectively in group A, and 136 months and 140 months, respectively in group B. The clinical (P = 0.014) and radiographical (P = 0.044) follow-up periods were longer, and the rate of GTR was higher (P = 0.008) for group B (**Table 2**).

Tumor control

Among all patients, tumor recurrence after initial intervention was observed in 8 (25%) patients at a median of 48 months (range, 16–225 months). The 5-, 10-, and 15-year cumulative TCRs in the entire cohort were estimated as 77%, 77%, and 69%, respectively (**Fig1a**). Per groups, the 5-, 10-, and 15-year cumulative TCRs were 100%, 100%, and 67%, respectively in group A, and 64%, 64%, and 64%, respectively in group B. Early recurrence occurred less frequently in group A, but the difference was not statistically significant (P = 0.250; **Fig1b**). When stratified with the other factors including extent of resection (GTR vs. non-GTR, P = 0.111; **Fig1c**), histopathological grade (I vs. II, P = 0.831; **Fig1d**), maximal diameter (< 35 mm vs. ≥ 35 mm, P = 0.259; **Fig1e**), or age (< 45 years vs. ≥ 45 years, P = 0.902; **Fig1f**), no significant difference in TCR was observed.

The results of univariate Cox-proportional hazard analysis for factors potentially associated with tumor control are summarized in **Table 3**; although there was better tumor control when comparing group A to B (P = 0.278, hazard ratio [HR] for failed tumor control 0.30, 95% confidence interval [CI] 0.04–2.61), and GTR to non-GTR (P = 0.136, HR 3.64, 95%CI 0.66–19.95), this was not statistically significant. Since the extent of surgery seemed to be significantly associated with the subsequent treatment strategies, we performed multivariate analysis adjusted with extent of resection (**Table 3, model 1**). Neither treatment strategy (group A vs. B) nor extent of resection was associated with tumor control. We also performed the other multivariate analysis including treatment strategy and tumor grade (I vs. II); neither of them was significantly associated with tumor control (**Table 3, model 2**).

Overall outcome and detailed clinical course

One patient died in follow-up of causes unrelated to SBC, and one patient died of complications directly related to SBC. This patient was a 73-year woman with an extensive SBC involving the lateral posterior skull base, extending to the suboccipital subcutaneous tissues down to the upper cervical region. After partial removal and obtaining a diagnosis of grade I chondrosarcoma, she elected for watchful observation. She underwent radiotherapy elsewhere (details not available) at 2 years due to tumor progression. However, she began having recurrent aspiration pneumonia and lower cranial nerve dysfunction approximately 1 year after radiotherapy, and the tumor showed definite radiographic progression 1.5 years after radiotherapy. She eventually died of aspiration pneumonia at the age of 78 years (5 years from initial surgery). Thus, the 5-, 10-, and 15-year cumulative DSSs in the entire cohort were 100%, 95%, and 95%. No significant difference was observed between group A and B (P = 0.497). Despite several recurrences and subsequent interventions as described below, all the tumors were under good control at the last follow-up visit except for the above-mentioned patient with tumor-related mortality (**Fig2**).

In group A, upfront radiotherapy was performed at a median of 6 months postoperatively (range, 2–19 months). Proton radiotherapy was performed in 11, Gamma Knife (Elekta AB, Stockholm, Sweden) with external beam radiotherapy in 2, and Gamma Knife alone in 1. No recurrence was observed in 13 (93%) patients at a median of 33 months (4–148 months) following radiotherapy. In 1 (7%) patient who was initially treated with gamma knife (prescription dose, 17 Gy to the 50% isodose line; at 3 months following resection), tumor recurrence was confirmed at 136 months after radiotherapy, which was subsequently treated with proton radiotherapy. The patient was 7 months from the last treatment, and no progression was observed at last follow-up.

In group B, no recurrence was observed in 11 (61%) patients at a median of 47 months (10–183 months) following initial surgery; whereas recurrence was confirmed in 7 (27%) patients at a median of 38 months (16–225 months) following initial surgery. Regarding salvage intervention, radiotherapy alone was used in 3, surgery alone in 3, and surgery followed by radiotherapy in 1. Following salvage intervention, further progression was confirmed in 2 patients. One patient experienced tumor progression and subsequently died, as explained above. Another patient, who had sinonasal SBC spanning from ethmoid and maxillary

sinuses down to the hard palate and was treated with surgery alone, experienced 2 further recurrences, which were subsequently treated with additional surgeries alone without recurrence at the last follow-up. The other 5 patients had no further recurrence at a median follow-up of 135 months (48–234 months) following additional intervention.

Complications associated with additional interventions

Among 4 patients who underwent repeat surgery, no postoperative complications were observed. Among 18 patients who underwent radiotherapy (proton-based radiotherapy in 11, gamma knife and/or photon-based radiotherapy in 6, and detail not available in 1), tumor control was achieved in 16 patients (89%). Radiation-induced adverse events were observed in 7 (39%) patients; hypopituitarism in 3, moderate to severe hearing loss in 2, temporal lobe edema in 2, shoulder weakness due to accessary nerve dysfunction in 1, decreased taste in 1, radiation-induced meningioma in 1, and basal ganglia infarction in 1 (3 patients had more than one complication). The infarction caused left hemiparesis with dysarthria, and thus graded as CTCAE grade 3; this was due to middle cerebral artery occlusion at the M1 segment that was originally in contact with the tumor and thus included in the irradiation field. One hearing loss was graded as 3 but not debilitating. Otherwise, all complications were graded as 1 or 2 and non-debilitating.

Discussion

In this single-center retrospective study, we comprehensively analyzed treatment outcomes of 32 patients with grade I or II SBCs focusing on a management strategy with or without radiotherapy after maximal safe resection. Our results suggest that radiotherapy may contribute to favorable short- to intermediate-term tumor control even though the difference was not statistically significant. On the other hand, late recurrence, albeit rare, is possible and thus periodic surveillance imaging should be continued indefinitely. Although the recurrence rate seemed to be higher without upfront radiotherapy, recurrent tumors were generally manageable with a single surgery or radiotherapy or a combination after recurrence/progression was documented, and the final tumor control status was satisfactory and very similar to the cohort that received planned postoperative radiotherapy. Moreover, the majority (61%) of patients who had not undergone upfront radiotherapy did not experience recurrence. Hence, considering even the low risk of radiation-induced adverse events into account, radiotherapy may not be necessary in all cases.

It would be of importance to select which patients would benefit most from radiotherapy. Simon et al. found that upfront radiotherapy did not show any benefit in survival. Our data largely corroborate their conclusion; however, there does seem to be benefit regarding short- and mid-term tumor control with radiotherapy.[10] If a tumor is located at an area where repeat surgery would likely jeopardize neurological function (such as brainstem and cavernous sinus) or the treatment team feels patient compliance with close surveillance is unlikely, upfront radiotherapy is recommended. If the location allows surgeons to perform repeat resection without a high risk of additional morbidity (such as midline

clivus, anterior skull base, and nasal cavity/paranasal sinuses) or close surveillance is feasible, watchful waiting and salvage intervention upon recurrence is an acceptable approach. Adding upfront radiotherapy may cause undesirable radiation-induced complications.[20] Indeed, one debilitating stroke developed after proton beam radiation in our series. Nevertheless, as previous studies have demonstrated, the probability of debilitating complications is generally low, and favorable tumor control should be expected.[10,14,21] Simon et al. reported that complications graded as CTCAE grade 3 or higher were observed in 25% after proton beam radiation and found that upfront proton beam radiation (as opposed to surgery alone) was associated with an increased risk of treatment-related complications.[12] Notwithstanding, not all CTCAE grade 3 complications are debilitating, as seen in our cohort.

Safe maximal resection is an important first step for treatment strategy for SBC. Paradoxically, however, in our results the TCR after non-GTR was marginally better than after GTR; this seems to be because patients with non-GTR were more likely to undergo upfront radiotherapy than GTR. In other words, the true benefit of GTR remains to be determined, and tumor recurrence was not uncommon even after GTR, especially when patients did not undergo upfront radiotherapy. There are 2 recent studies reporting a similar trend.[7,12] Therefore, it may not be beneficial to pursue GTR at the cost of patients' neurological function. Of note, Raza et al reported that GTR may be beneficial for mesenchymal/dedifferentiated tumors,[22] suggesting that such aggressive subtypes require more radical treatment due to their extremely high tendency of recurrence. Theoretically, GTR should be performed from a standpoint of reducing tumor burden; however, in grade I/II SBCs, this is true only if safely possible without jeopardizing neurologic function.

It is of interest that no significant difference in tumor control was observed between grade I and II tumors. In some studies grade II tumors are grouped as "aggressive",[3,23] however, no consensus exists in the literature.[12,22,24] In 1977 Evans et al. demonstrated clear differences in survival by tumor grades,[1] and a recent SEER-based survey did confirm difference in tumor control between "well (-differentiated)" and "moderately (-differentiated)"[25]; however, these studies were mostly based on skeletal chondrosarcomas, and only a subset had SBCs. While it may be possible that the behavior of grade I/II SBCs is somewhat different from those of extracranial chondrosarcomas, the difference could also be related to the small numbers in our cohorts. Based on past experience, we have also seen moderate variability in classifying grade I and II tumors among centers, as discrepancies are sometimes reported on secondary review of outside pathological specimens.

The strength of our study lies in its simple and straightforward comparison. To discuss the real benefit of radiotherapy over a watchful observation strategy, comparisons should be made with an appropriate control cohort, which is in fact carried out only in few recent studies[12,22] among the literature (**Table 4**).[12,20,22-24,26-32] Moreover, aggressive SBCs (grade III, mesenchymal, and dedifferentiated) should be excluded from analysis to discuss treatment strategy for non-aggressive SBCs, as the treatment strategy for such aggressive SBCs is essentially different and radiotherapy is recommended regardless of surgical results.[7,10,12,22,33,34] Furthermore, cases with multiple recurrence, a known risk for failed tumor control due to scarring in the surgical site as well as narrower therapeutic/approach options,[12] may

complicate analysis and thus would better be excluded. Since we excluded such cases in this series, our results are readily applicable to those with newly-diagnosed grade I/II SBCs. Nevertheless, this study has several notable limitations. Even though the follow-up period was one of the longest, SBC is indolent, and there remains a chance of recurrence even decades after treatment. Therefore, especially given the relatively shorter observation period in the patients treated with upfront radiotherapy, longer follow-up would support more robust comparisons. Nevertheless, we must have somehow addressed this issue using survival curve analysis which enabled us to handle short-term dropouts in a statistically appropriate way. Moreover, although the number of study participants is one of the largest among studies involving only patients grade I/II SBCs, it is relatively a small number, and thus our statistical analyses might have been underpowered. Future study with further case accumulation would be desirable to reexamine our findings.

Conclusions

Radiotherapy following maximally safe resection for grade I or II SBC may decrease short- to intermediate-term recurrence, though late recurrence remains possible and thus life-long follow-up is needed. Given that recurrent tumors were generally manageable with surgery or radiotherapy, or a combination, without incurring greater long-term morbidity, and that the final tumor control was satisfactory, watchful observation after maximal safe resection is a reasonable consideration. This is especially true, for tumors in locations where repeat surgery is feasible and resultant deficits are unlikely.

Declarations

Acknowledgments

None.

References

1. Evans HL, Ayala AG, Romsdahl MM (1977) Prognostic factors in chondrosarcoma of bone: a clinicopathologic analysis with emphasis on histologic grading. Cancer 40 (2):818-831
2. Weber AL, Brown EW, Hug EB, Liebsch NJ (1995) Cartilaginous tumors and chordomas of the cranial base. Otolaryngol Clin North Am 28 (3):453-471
3. Awad M, Gogos AJ, Kaye AH (2016) Skull base chondrosarcoma. J Clin Neurosci 24:1-5. doi:10.1016/j.jocn.2015.10.029
4. Bloch OG, Jian BJ, Yang I, Han SJ, Aranda D, Ahn BJ, Parsa AT (2009) A systematic review of intracranial chondrosarcoma and survival. J Clin Neurosci 16 (12):1547-1551. doi:10.1016/j.jocn.2009.05.003
5. Mokhtari S, Mirafsharieh A (2012) Clear cell chondrosarcoma of the head and neck. Head Neck Oncol 4:13. doi:10.1186/1758-3284-4-13

6. Nakashima Y, Unni KK, Shives TC, Swee RG, Dahlin DC (1986) Mesenchymal chondrosarcoma of bone and soft tissue. A review of 111 cases. Cancer 57 (12):2444-2453. doi:10.1002/1097-0142(19860615)57:12<2444::aid-cncr2820571233>3.0.co;2-k
7. Ma XJ, Meng GL, Wang K, Li D, Wang L, Li H, Zhang JT, Zhang LW, Wu Z (2019) The Differences Between Intracranial Mesenchymal Chondrosarcoma and Conventional Chondrosarcoma in Clinical Features and Outcomes. World Neurosurgery 122:E1078-E1082. doi:10.1016/j.wneu.2018.10.230
8. Amer KM, Munn M, Congiusta D, Abraham JA, Basu Mallick A (2020) Survival and Prognosis of Chondrosarcoma Subtypes: SEER Database Analysis. J Orthop Res 38 (2):311-319. doi:10.1002/jor.24463
9. Korten AG, ter Berg HJ, Spincemaille GH, van der Laan RT, Van de Wel AM (1998) Intracranial chondrosarcoma: review of the literature and report of 15 cases. J Neurol Neurosurg Psychiatry 65 (1):88-92
10. Carlson ML, O'Connell BP, Breen JT, Wick CC, Driscoll CL, Haynes DS, Thompson RC, Isaacson B, Gidley PW, Kutz JW, Jr., Van Gompel JJ, Wanna GB, Raza SM, DeMonte F, Barnett SL, Link MJ (2016) Petroclival Chondrosarcoma: A Multicenter Review of 55 Cases and New Staging System. Otol Neurotol 37 (7):940-950. doi:10.1097/MAO.0000000000001037
11. Gatfield ER, Noble DJ, Barnett GC, Early NY, Hoole ACF, Kirkby NF, Jefferies SJ, Burnet NG (2018) Tumour Volume and Dose Influence Outcome after Surgery and High-dose Photon Radiotherapy for Chordoma and Chondrosarcoma of the Skull Base and Spine. Clin Oncol (R Coll Radiol) 30 (4):243-253. doi:10.1016/j.clon.2018.01.002
12. Simon F, Feuvret L, Bresson D, Guichard JP, El Zein S, Bernat AL, Labidi M, Calugaru V, Froelich S, Herman P, Verillaud B (2018) Surgery and protontherapy in Grade I and II skull base chondrosarcoma: A comparative retrospective study. PLoS One 13 (12):e0208786. doi:10.1371/journal.pone.0208786
13. Weber DC, Badiyan S, Malyapa R, Albertini F, Bolsi A, Lomax AJ, Schneider R (2016) Long-term outcomes and prognostic factors of skull-base chondrosarcoma patients treated with pencil-beam scanning proton therapy at the Paul Scherrer Institute. Neuro Oncol 18 (2):236-243. doi:10.1093/neuonc/nov154
14. Holtzman AL, Rotondo RL, Rutenberg MS, Indelicato DJ, Mercado CE, Rao D, Tavanaiepour D, Morris CG, Louis D, Flampouri S, Mendenhall WM (2019) Proton therapy for skull-base chondrosarcoma, a single-institution outcomes study. J Neurooncol 142 (3):557-563. doi:10.1007/s11060-019-03129-8
15. Koga T, Shin M, Saito N (2010) Treatment with high marginal dose is mandatory to achieve long-term control of skull base chordomas and chondrosarcomas by means of stereotactic radiosurgery. J Neurooncol 98 (2):233-238. doi:10.1007/s11060-010-0184-y
16. Uhl M, Mattke M, Welzel T, Oelmann J, Habl G, Jensen AD, Ellerbrock M, Haberer T, Herfarth KK, Debus J (2014) High control rate in patients with chondrosarcoma of the skull base after carbon ion therapy: first report of long-term results. Cancer 120 (10):1579-1585. doi:10.1002/cncr.28606
17. Amichetti M, Amelio D, Cianchetti M, Enrici RM, Minniti G (2010) A systematic review of proton therapy in the treatment of chondrosarcoma of the skull base. Neurosurg Rev 33 (2):155-165.

doi:10.1007/s10143-009-0234-0

18. Sahgal A, Chan MW, Atenafu EG, Masson-Cote L, Bahl G, Yu E, Millar BA, Chung C, Catton C, O'Sullivan B, Irish JC, Gilbert R, Zadeh G, Cusimano M, Gentili F, Laperriere NJ (2015) Image-guided, intensity-modulated radiation therapy (IG-IMRT) for skull base chordoma and chondrosarcoma: preliminary outcomes. Neuro Oncol 17 (6):889-894. doi:10.1093/neuonc/nou347
19. Mattke M, Vogt K, Bougatf N, Welzel T, Oelmann-Avendano J, Hauswald H, Jensen A, Ellerbrock M, Jakel O, Haberer T, Herfarth K, Debus J, Uhl M (2018) High control rates of proton- and carbon-ion-beam treatment with intensity-modulated active raster scanning in 101 patients with skull base chondrosarcoma at the Heidelberg Ion Beam Therapy Center. Cancer 124 (9):2036-2044. doi:10.1002/cncr.31298
20. Tzortzidis F, Elahi F, Wright DC, Temkin N, Natarajan SK, Sekhar LN (2006) Patient outcome at long-term follow-up after aggressive microsurgical resection of cranial base chondrosarcomas. Neurosurgery 58 (6):1090-1098; discussion 1090-1098. doi:10.1227/01.NEU.0000215892.65663.54
21. Lu VM, O'Connor KP, Mahajan A, Carlson ML, Van Gompel JJ (2020) Carbon ion radiotherapy for skull base chordomas and chondrosarcomas: a systematic review and meta-analysis of local control, survival, and toxicity outcomes. J Neurooncol 147 (3):503-513. doi:10.1007/s11060-020-03464-1
22. Raza SM, Gidley PW, Meis JM, Grosshans DR, Bell D, DeMonte F (2017) Multimodality Treatment of Skull Base Chondrosarcomas: The Role of Histology Specific Treatment Protocols. Neurosurgery 81 (3):520-530. doi:10.1093/neuros/nyx042
23. Sbaihat A, Bacciu A, Pasanisi E, Sanna M (2013) Skull base chondrosarcomas: surgical treatment and results. Ann Otol Rhinol Laryngol 122 (12):763-770
24. Vaz-Guimaraes F, Fernandez-Miranda JC, Koutourousiou M, Hamilton RL, Wang EW, Snyderman CH, Gardner PA (2017) Endoscopic Endonasal Surgery for Cranial Base Chondrosarcomas. Oper Neurosurg (Hagerstown) 13 (4):421-434. doi:10.1093/ons/opx020
25. Nie Z, Lu Q, Peng H (2018) Prognostic factors for patients with chondrosarcoma: A survival analysis based on the Surveillance, Epidemiology, and End Results (SEER) database (1973-2012). J Bone Oncol 13:55-61. doi:10.1016/j.jbo.2018.09.003
26. Hasegawa H, Shin M, Kondo K, Hanakita S, Mukasa A, Kin T, Saito N (2018) Role of endoscopic transnasal surgery for skull base chondrosarcoma: a retrospective analysis of 19 cases at a single institution. J Neurosurg 128 (5):1438-1447. doi:10.3171/2017.1.JNS162000
27. Samii A, Gerganov V, Herold C, Gharabaghi A, Hayashi N, Samii M (2009) Surgical treatment of skull base chondrosarcomas. Neurosurg Rev 32 (1):67-75; discussion 75. doi:10.1007/s10143-008-0170-4
28. Cho YH, Kim JH, Khang SK, Lee JK, Kim CJ (2008) Chordomas and chondrosarcomas of the skull base: comparative analysis of clinical results in 30 patients. Neurosurg Rev 31 (1):35-43; discussion 43. doi:10.1007/s10143-007-0099-z
29. Almefty K, Pravdenkova S, Colli BO, Al-Mefty O, Gokden M (2007) Chordoma and chondrosarcoma: similar, but quite different, skull base tumors. Cancer 110 (11):2457-2467. doi:10.1002/cncr.23073

30. Wanebo JE, Bristol RE, Porter RR, Coons SW, Spetzler RF (2006) Management of cranial base chondrosarcomas. Neurosurgery 58 (2):249-255; discussion 249-255. doi:10.1227/01.NEU.0000194834.74873.FB
31. Oghalai JS, Buxbaum JL, Jackler RK, McDermott MW (2005) Skull base chondrosarcoma originating from the petroclival junction. Otol Neurotol 26 (5):1052-1060. doi:10.1097/01.mao.0000185076.65822.f7
32. Crockard HA, Cheeseman A, Steel T, Revesz T, Holton JL, Plowman N, Singh A, Crossman J (2001) A multidisciplinary team approach to skull base chondrosarcomas. J Neurosurg 95 (2):184-189. doi:10.3171/jns.2001.95.2.0184
33. Frezza AM, Cesari M, Baumhoer D, Biau D, Bielack S, Campanacci DA, Casanova J, Esler C, Ferrari S, Funovics PT, Gerrand C, Grimer R, Gronchi A, Haffner N, Hecker-Nolting S, Holler S, Jeys L, Jutte P, Leithner A, San-Julian M, Thorkildsen J, Vincenzi B, Windhager R, Whelan J (2015) Mesenchymal chondrosarcoma: prognostic factors and outcome in 113 patients. A European Musculoskeletal Oncology Society study. Eur J Cancer 51 (3):374-381. doi:10.1016/j.ejca.2014.11.007
34. Strotman PK, Reif TJ, Kliethermes SA, Sandhu JK, Nystrom LM (2017) Dedifferentiated chondrosarcoma: A survival analysis of 159 cases from the SEER database (2001-2011). J Surg Oncol 116 (2):252-257. doi:10.1002/jso.24650

Tables

Tables not provided with this version.