# Treatment and Survival Outcomes of Primary Intracranial Squamous Cell Carcinoma

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BACKGROUND: **Primary intracranial squamous cell carcinoma (SCC) is a rare neoplasm associated with malignant transformation of benign epidermoid or dermoid cysts. The optimal treatment and prognosis of this rare disease are unclear.**

METHODS: **A comprehensive literature review identified all reports relevant to clinical presentation, treatment, and outcome of primary intracranial SCC. All available data were extracted from the included literature. Two patients diagnosed with malignant transformation of an epidermoid cyst in our institute were also included in the study. Survival analysis was conducted to determine the factors affecting patient outcomes.**

RESULTS: **A total of 62 cases were identified and selected for the present study. The median survival regardless of treatment was 12.8 months. Median survival for patients treated with surgery alone and surgery with radiotherapy was 5 months and 35 months, respectively ($P = 0.037$). Patients who underwent gross total resection showed relatively increased survival compared with those who underwent subtotal resection (median, 48 months vs. 25 months; $P = 0.067$). Patients with leptomeningeal carcinomatosis had a significantly decreased median survival of 10 months, as opposed to 41 months ($P = 0.005$).**

CONCLUSIONS: **Primary intracranial SCC shows poor prognosis, with controversial management. The results of this study indicate that complete resection of tumor when possible, followed by radiotherapy, is the optimal treatment for improving patient outcome.**

## INTRODUCTION

Primary intracranial squamous cell carcinoma (SCC) is an extremely rare neoplasm known to be associated with malignant transformation of benign epidermoid or dermoid cysts.[1-5]

The first description of primary intracranial SCC arising from an epidermoid cyst was provided by Ernst in 1912.[6] In 1981, Garcia et al.[1] defined this malignant transformation as follows: the tumor should be restricted to the intracranial intradural compartment without invasion of or extension beyond the dura and cranial orifices, connection with the middle ear, air sinuses, or sella turcica, and with no evidence of a nasopharyngeal tumor. Furthering that definition, Hamlat et al.[3] reported additional criteria as follows: the presence of a benign squamous cell epithelium within the malignant tumor and metastasis of carcinoma was excluded.

Since then, several reports of the disease have been published as case series with pathologic verification intraoperatively or at autopsy. However, clinical presentation, treatment, and prognosis of this rare disease are still unclear. The purposes of this study were to present the cases we encountered and to determine the optimal treatment and outcome of primary intracranial SCC through a review of the relevant literature.

## METHODS

A comprehensive literature review was conducted through PubMed, MEDLINE, and EMBASE databases to identify articles relevant to primary intracranial SCC that were published up to July 2018. The keywords "intracranial squamous cell carcinoma," "epidermoid," "dermoid," "malignant transformation," and "malignant degeneration" in various combinations were used. Additional relevant articles were identified through review of

**Key words**
- Epidermoid cyst
- Intracranial
- Malignant transformation
- Outcome
- Squamous cell carcinoma
- Treatment

**Abbreviations and Acronyms**
**CPA**: Cerebellopontine angle
**GTR**: Gross total resection
**HR**: Hazard ratio
**LC**: Leptomeningeal carcinomatosis
**MRI**: Magnetic resonance imaging
**SCC**: Squamous cell carcinoma
**SRS**: Stereotactic radiosurgery
**STR**: Subtotal resection

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references cited in selected articles. We included only English full-text articles in which the descriptive criteria of both Garcia et al.[1] and Hamlat et al.[3] were fulfilled. All available data were extracted from the included articles. Two patients diagnosed with intracranial SCC from malignant transformation of an epidermoid cyst at our institute were also included in the present study.

All statistical analyses were performed using SPSS version 18.0 (SPSS, Chicago, Illinois, USA). Survival analysis was performed using the Kaplan-Meier method, and the log-rank test was used to compare data between groups. Univariate Cox proportional hazard analysis was performed, and variables were considered for multivariate analysis to yield a hazard ratio (HR) only if they showed a P value of <0.1 in univariate analysis. Patient survival outcome was defined as the time from diagnosis of intracranial SCC to death or the last reported follow-up. For patients diagnosed by autopsy without surgery, the survival period was defined as the time from the onset of symptoms to death. Postoperative deaths that occurred within 1 month after surgery were excluded from the survival analysis. A P value <0.05 was considered statistically significant.

This study was approved by the institutional review board of Asan Medical Center. Because of the retrospective nature of the study, the need for informed consent was waived.

## RESULTS

### Illustrative Patients

***Case 1.*** A 71-year-old man presented with progressive hearing loss on the right side accompanied by facial weakness and sensory change 16 months before admission. Magnetic resonance imaging (MRI) showed a heterogeneous enhancing extra-axial mass in the right cerebellopontine angle (CPA) with invasion of the Meckel cave (Figure 1A). In March 2018, the patient underwent surgery, and subtotal resection (STR) of the tumor was performed because of high adherence of the tumor to the cranial nerves and brainstem. Results of histopathologic analysis were consistent with a diagnosis of malignant transformation of a benign epidermoid cyst to SCC. To rule out the possibility of intracranial metastasis of SCC, the patient underwent a systemic workup, which yielded negative results. The immediate postoperative course was uneventful. However, 1 month after surgery, the patient developed a refractory fever associated with chemical meningitis. Three months after the initial surgery, the patient required a ventriculoperitoneal shunt for communicating hydrocephalus. One month after the shunt operation, the patient was stable and was discharged without any evidence of recurrence.

***Case 2.*** A 50-year-old man visited the outpatient clinic of our oncology department in January 2018. The patient, whose case history had been reported by Chon et al.,[7] had undergone surgery for an epidermoid cyst in the right CPA, along with surgery and 3 stereotactic radiosurgeries (SRSs) for intracranial SCC in the left CPA. The survival reported in the case series was 34 months. Subsequently, chemotherapy consisting of 5-fluorouracil and cisplatin was administered, and the patient underwent a fourth SRS for tumor recurrence in June 2017 at another institution. MRI showed postoperative changes in the right CPA with no evidence of recurrence of SCC in the left CPA (Figure 1B). The patient was self-sufficient with mild neurologic deficit; however, he was lost to further follow-up.

### Literature Review

In total, 62 cases of primary intracranial SCC including the patients presented here were identified (Table 1).[2,4,5,8-62] The

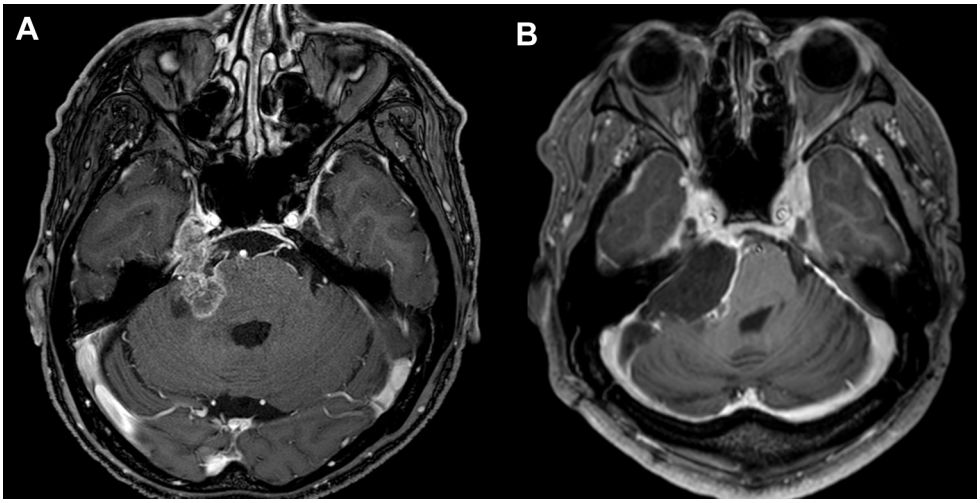


**Figure 1.** (**A**) Magnetic resonance imaging showed a heterogeneous enhancing extra-axial mass in the right cerebellopontine angle (CPA) with invasion of the Meckel cave. (**B**) Magnetic resonance imaging showed postoperative change in the right CPA with no evidence of tumor recurrence in the left CPA.

**Table 1.** Cases of Primary Intracranial Squamous Cell Carcinoma Reported in the Literature

| Reference/Year | Sex/Age (Years) | Location | Treatment | Interval from Benign Cyst to Malignant Transformation (Months) | Rec/LC | Survival |
|---|---|---|---|---|---|---|
| Yamanaka et al., 1955[8] | M/57 | Base of brain | Medical | | LC | Died 8 months |
| Davidson and Small, 1960[9] | M/46 | Frontal | S + RT | | | UD |
| Landers and Danielski, 1960[10] | F/73 | Cerebellar | Medical | | LC | Died 1 month |
| Fox and South, 1965[11] | M/43 | Temporal | S | 90 | LC | Died 1.5 month |
| Toglia et al., 1965[12] | F/53 | Base of brain | S | 12 | | POD 1 day |
| Salyer and Carter, 1973[13] | F/58 | Pituitary gland | S + RT | | | Died 1.25 months |
| Dubois et al., 1981[14] | M/53 | Fourth ventricle | S | | | Died 2 months |
| Garcia et al., 1981[1] | M/61 | CPA | S + RT | | | Died 25 months |
| Lewis et al., 1983[15] | F/53 | Parasellar, temporal | S | | | Died 1 month |
| Bondeson and Fält, 1984[16] | F/56 | CPA | Medical | | LC | Died 0.75 months |
| Giangaspero et al., 1984[17] | M/45 | Parieto-occipital | S + RT | | Rec | Died 8 months |
| Goldman and Gandy, 1987[2] | F/59 | Lateral ventricle | S + RT | 396 | Rec | Alive 36 months |
| Salazar et al., 1987[18] | M/49 | CPA and pons | S + RT | 3 | | Alive 10 months |
| Abramson et al., 1989[19] | M/37 | CPA | S | 24 | | UD |
| Nishiura et al., 1989[20] | M/38 | CPA | S + CT | 6 | | Alive 24 months |
| Knorr et al., 1991[21] | M/74 | CPA | S + RT | 13 | Rec | Died 3.75 months |
| Tognetti et al., 1991[22] | F/67 | Frontotemporal | S | 372 | | Died 1 month |
| Acciari et al., 1993[23] | M/62 | Parasellar | S | | | POD 10 days |
| Kobayashi et al., 1993[24] | F/59 | Frontal | S + RT + CT | | | Died 7 months |
| Nishio et al., 1998[25] | M/57 | CPA | S + RT | | | Alive 30 months |
| | M/42 | Middle and posterior fossa | S + RT | 9 | | Died 3.5 months |
| Uchino et al., 1995[26] | M/57 | CPA | S + RT | | | Alive 4 months |
| Mohanty et al., 1996[27] | M/20 | Cerebellar | S + RT | | LC | Died 13 months |
| Bayindir et al., 1996[28] | F/67 | Lateral ventricle | S | 10 | | Alive 36 months |
| Ogata et al., 1996[29] | F/63 | Dorsolateral pons | S | | Rec | Alive 46 months |
| Murase et al., 1999[30] | F/50 | CPA | S + SRS + CT | 120 | | Alive 60 months |
| Tsugu et al., 2001[31] | M/47 | Cerebellar | S + RT | | | Alive 72 months |
| Asahi et al., 2001[32] | F/55 | CPA | S | 156 | LC | Died 3 months |
| Khan et al., 2001[33] | M/53 | Prepontine | Shunt | | LC | Died 10 months |
| Nawashiro et al., 2001[34] | M/46 | Temporal | S | UD | | UD |
| Oertel et al., 2002[35] | F/54 | Cerebellar | S | | | Alive 3 months |
| Link et al., 2002[36] | F/67 | CPA | S + RT + SRS | 12 | Rec | Died 35 months |
| Park and Park, 2003[37] | F/65 | CPA | S + RT | | | Alive 6 months |
| Shirabe et al., 2003[38] | M/49 | Ventral pons | S + RT | UD | LC | Died 42 months |
| Akar et al., 2003[39] | F/UD | CPA | S | 18 | Rec | Died 5 months |

Rec, recurrence; LC, leptomeningeal carcinomatosis; M, male; S, surgery; RT, radiotherapy; UD, undetermined; F, female; CPA, cerebellopontine angle; CT, chemotherapy; POD, postoperative death; SRS, stereotactic radiosurgery.

Continues

**Table 1.** Continued

| Reference/Year | Sex/Age (Years) | Location | Treatment | Interval from Benign Cyst to Malignant Transformation (Months) | Rec/LC | Survival |
|---|---|---|---|---|---|---|
| Hamlat et al., 2003[40] | F/54 | Temporal | CT | 10 | LC | Died 6 months |
| Monako et al., 2003[41] | M/36 | Cisterna magna | S | | | Alive 24 months |
| Ozutemiz et al., 2003[42] | M/64 | Lateral ventricle | Medical | 144 | Rec | Alive 3 months |
| Guan et al., 2004[43] | F/42 | Temporal | S + RT | 132 | | Alive 12 months |
| Michael et al., 2005[4] | M/45 | Prepontine | S + RT + CT | | LC | Died 12 months |
| Tamura et al., 2006[5] | F/64 | Sphenoid | S + SRS | 96 | Rec | Alive 18 months |
| Agarwal et al., 2007[44] | M/45 | Posterior fossa | S | | | UD |
| Kodama et al., 2007[45] | M/67 | CPA | SRS | | | Died 11 months |
| Pagni et al., 2007[46] | F/65 | Pineal region | S | | LC | UD |
| Kim and Kim, 2008[47] | F/72 | CPA, brain stem | S + RT | | | Alive 12 months |
| Ge et al., 2009[48] | M/50 | Temporal | S | 72 | | UD |
| Kano et al., 2010[49] | F/64 | CPA | S + RT | 192 | LC | Died 25 months |
| Nakao et al., 2010[50] | F/74 | CPA | S + RT | 240 | | Alive 17 months |
| Hao et al., 2010[51] | F/61 | Prepontine | S | 72 | | Died 1.2 months |
| Lakhdar et al., 2011[52] | M/52 | CPA | S + RT | 6 | | Alive 3 months |
| Vellutini et al., 2014[53] | F/42 | CPA | S | 24 | | Died 1.3 months |
| Feng et al., 2014[54] | M/42 | CPA | S + RT | 24 | | Alive 6 months |
| Pikis and Margolin, 2016[55] | M/77 | CPA | S + RT | 9 | | Died 6 months |
| Solanki et al., 2016[56] | F/47 | CPA | S | 12 | | Died 1.5 months |
| Sun et al., 2016[57] | F/22 | CPA and prepontine | S + RT + SRS | | Rec | Died 41 months |
| Ding et al., 2016[58] | F/55 | Temporal | S | UD | | Died 13 months |
| Raheja et al., 2016[59] | F/54 | Prepontine | S | | LC | UD |
| | F/37 | CPA | S + RT + CT | | Rec/LC | Died 11 months |
| Roh et al., 2017[60] | F/53 | CPA | S + RT | | | Died 48 months |
| Mascarenhas et al., 2017[61] | F/35 | CPA | S | 60 | | UD |
| Badat et al., 2018[62] | M/70 | CPA | Medical | | LC | Died 12.75 months |
| Present case 1 | M/71 | CPA | S | | | Alive 4 months |
| Present case 2 | M/43 | CPA | S + SRS + CT | 5 | Rec | Alive 81 months |

Rec, recurrence; LC, leptomeningeal carcinomatosis; M, male; S, surgery; RT, radiotherapy; UD, undetermined; F, female; CPA, cerebellopontine angle; CT, chemotherapy; POD, postoperative death; SRS, stereotactic radiosurgery.

mean age at diagnosis of malignancy was 53.6 ± 12.2 years, and 32 (51.6%) patients were women. The most common location of tumor was the CPA (n = 29), followed by the temporal lobe (n = 7), prepontine area (n = 5), and cerebellum (n = 4).

In most cases, malignant transformation was associated with a benign epidermoid cyst (n = 56); 4 malignancies originated from a dermoid cyst,[24,25,31,35] 1 from an endodermal cyst,[41] and 1 from craniopharyngioma.[13] Malignant transformation from a previously diagnosed benign cyst was reported in 31 patients (50.0%). The median time interval from a benign intracranial cyst to malignant transformation was 24 months (range, 3–396 months).

The median survival regardless of treatment was 12.8 months (range, 0.75–81 months; mean, 28.5 ± 5.0 months). There was no statistical difference in median survival regarding age, sex, tumor location (supratentorial vs. infratentorial), or type of previous benign cyst.

Surgery was the main treatment in most cases, with only 5 patients being palliatively treated. Surgical resection was performed in 55 patients, and postoperative adjuvant treatment was

used in 31 patients. Adjuvant treatment included radiotherapy only (n = 22), SRS only (n = 1), radiotherapy plus SRS (n = 2), chemotherapy only (n = 1), and multimodality adjuvant treatment combined chemotherapy with radiotherapy (n = 3) or SRS (n = 2).

Outcomes were well documented in 54 reported cases, and survival was compared according to treatment modalities (Figure 2). Patients who underwent surgical treatment had significantly better prognosis than those who were palliatively treated (median survival, 25 months vs. 8 months; P = 0.010; Figure 2A). The median survival for patients treated with surgery alone and surgery plus radiotherapy or SRS was 5 months and 35 months, respectively. The difference between the groups was statistically significant (P = 0.037; Figure 2B). There was no difference in median survival between patients treated with surgery plus radiotherapy or SRS with or without chemotherapy (35 months vs. 12 months; P = 0.676; Figure 2C). Patients who underwent gross total resection (GTR) showed relatively increased survival compared with those who underwent STR (median, 48 months vs. 25 months; P = 0.067; Figure 2D).

Preoperative or postoperative chemical meningitis occurred in 10 patients (16.1%), including the first patient presented in current study.[11,19,22,27,32,39,40,51,59] Of 55 patients who underwent surgical treatment, 11 (20.0%) developed local recurrence. The mean interval to recurrence was 17 months (range, 2–36 months). The median survival of patients with and without recurrence did not differ (35 months vs. 13 months; P = 0.630; Figure 3A). The median survival after recurrence was 5 months. Leptomeningeal carcinomatosis (LC) was reported in 16 patients, with a significantly decreased median survival of 10 months as opposed to 41 months (P = 0.005; Figure 3B).

Variables including age, sex, tumor location, type of previous benign cyst, adjuvant radiotherapy after surgery for treatment modality, recurrence, and presence of LC were analyzed using univariate Cox proportional hazard analysis. Among the variables, increased survival was correlated with adjuvant radiotherapy after surgery (HR, 0.365; P = 0.024) compared with surgery alone. Presence of LC (HR = 2.292; P = 0.089) showed a relatively significant correlation.

## DISCUSSION

Primary intracranial SCC is extremely rare, and only a few cases have been reported in the literature. These neoplasms seem to represent malignant transformation from benign epidermoid or dermoid cysts. In general, primary intracranial SCC is known to have a poor prognosis, with the longest reported survival being 60 months.[30]

The pathogenesis of malignant transformation from benign epithelial cyst is believed to be associated with chronic local inflammation from repeated irritation by cyst rupture,

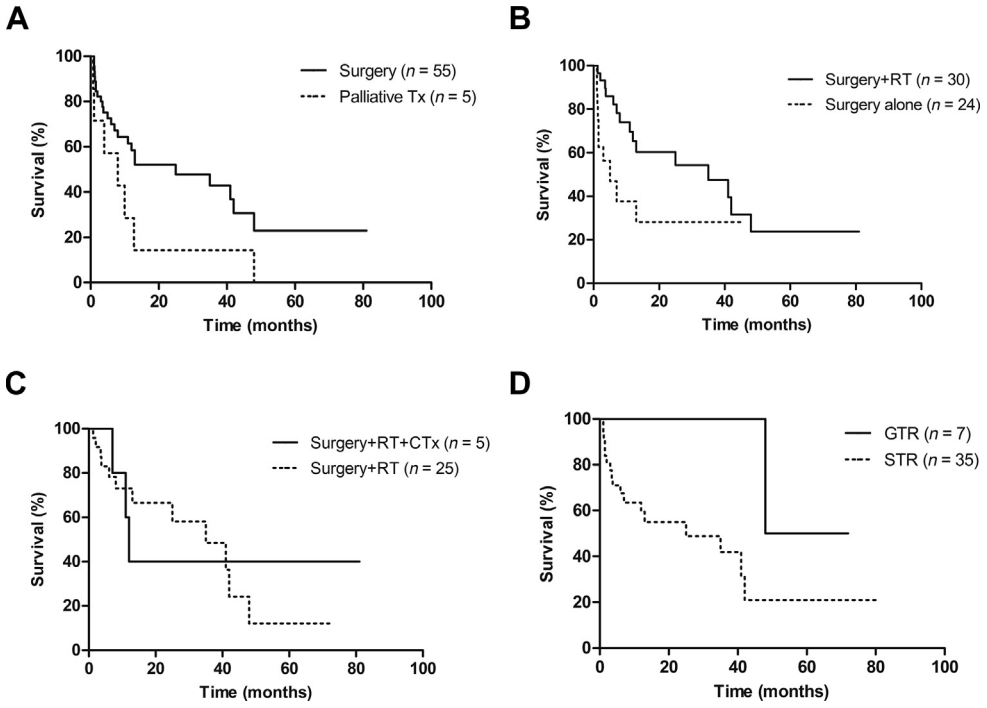


**Figure 2.** Kaplan-Meier survival curves for patients with primary intracranial squamous cell carcinoma according to different treatment groups. (**A**) Palliative treatment (Tx) versus surgery, $P = 0.010$. (**B**) Surgery alone versus surgery plus radiotherapy (RT) or stereotactic radiosurgery (SRS), $P = 0.037$. (**C**) Surgery plus RT versus surgery plus RT plus chemotherapy (CTx), $P = 0.676$. (**D**) Gross total resection (GTR) versus subtotal resection (STR), $P = 0.067$.

desquamating material, or STR.[19,22,50] The introduction of foreign materials during surgical resection may be another contributor to this process.[25]

The symptoms of primary intracranial SCC vary depending on tumor location and size. Because benign epidermoids have slower growth, a rapid progression of symptoms and signs is an important clinical indicator of malignant transformation.[20] The duration of symptoms in patients included in our review varied from 10 days[17] to 33 years[2]; most patients experienced rapid symptomatic progression within 6 months of diagnosis.

Radiologic evaluation also plays an important role in the diagnosis of intracranial SCC. Conventionally, benign epidermoids are avascular and do not enhance on intravenous contrast administration.[36,63-65] Contrast enhancement has been reported as a key finding of carcinomatous change in an epidermoid tumor.[4,26,36] Of the 62 patients included in the present study, MRI scans were obtained for 43, and 40 tumors showed enhancement after contrast injection. In addition, computed tomography scans showed 17 enhancing tumors in 19 patients who underwent postcontrast scan.

Surgical resection is accepted as the standard of care for the treatment of benign epidermoids. However, there is no established therapy once malignant degeneration of the lesions has occurred. Our literature review showed that 5 patients with primary intracranial SCC received palliative care without surgery, and the median survival in this group was 8 months, significantly shorter than the survival of surgically treated patients. However, because all of these patients were diagnosed with autopsy and the survival was assessed from the onset of symptoms, an accurate comparison between the 2 groups was not possible.

Because surgery alone is not curative and often limited to STR, postoperative radiotherapy has been widely used, and the benefit of radiotherapy in intracranial SCC has been well documented.[3,5,66] In our review, the median survival of patients treated with adjuvant radiotherapy after surgery was 35 months, which was significantly higher than the survival of those receiving surgery alone. In a previous study of malignant epidermoid tumor comparing 2 treatment groups, the average survival of patients who had undergone surgery alone ($n = 13$) and those who had undergone adjuvant radiotherapy ($n = 17$) was 6.6 months and 12.7 months, respectively (log-rank test, $P < 0.003$).[66] Similarly, Hamlat et al.[3] reported an increased median survival of 26 months in patients who had undergone surgery plus radiotherapy ($n = 24$) compared with patients treated with surgical resection only ($n = 9$; 3 months; log-rank test, $P = 0.077$). The dose used for radiotherapy was documented in 21 cases, with a mean dose of 52.0 Gy (range, 36.0–67.2 Gy) and did not correlate with survival outcome (correlation coefficient = 0.243; $P = 0.288$).

Recent studies have reported the effectiveness of SRS for treating intracranial SCC.[5,67] Tamura et al.[5] compared the survival of 24 patients with intracranial malignant epidermoid cysts according to treatment modalities. The median survivals of patients treated with surgery alone ($n = 9$), surgery plus radiotherapy ($n = 11$), and surgery plus SRS ($n = 4$) were 1, 18, and 44 months respectively (log-rank test, $P < 0.004$). The patients who underwent SRS were identified in 65 cases in our review, with marginal treatment doses of 12–15 Gy. The median survival of patients who underwent SRS was 41 months (range, 11–81 months), which was superior to the survival of patients who received other treatments. However, each patient was treated with a different combination of modalities; SRS only in 1 patient, SRS after surgery in 1 patient, combined SRS with surgery and radiotherapy in 2 patients, and combined SRS with surgery and chemotherapy in 2 patients. The heterogeneity of treatment modalities used and the small number of cases limited the effective analysis of SRS. Therefore, we grouped the patients who received SRS together with those who received radiotherapy in the present study, rather than analyzing them separately.

Chemotherapy was applied in 7 reported cases. Patients were treated with chemotherapy alone ($n = 1$), chemotherapy with surgery ($n = 1$), and combined chemotherapy with radiotherapy or SRS after surgery ($n = 5$). Nagasawa et al.[67] reported the outcome of patients treated with chemotherapy, either alone, with surgery, or with radiotherapy, and suggested an increased survival in these patients compared with those who were treated with surgery alone. However, because the effectiveness of surgery followed by

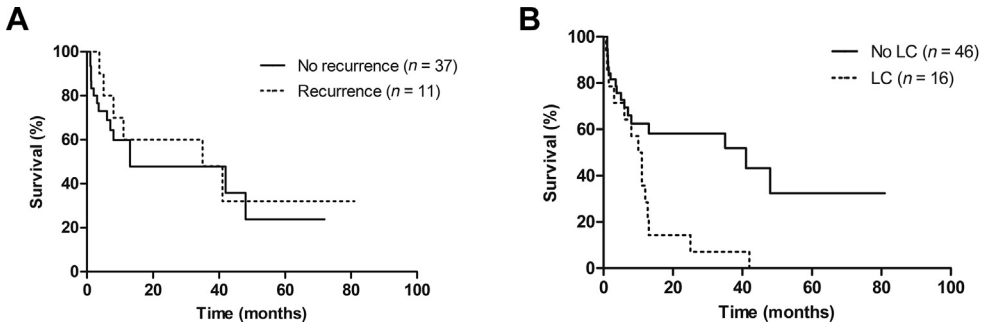


**Figure 3.** Kaplan-Meier survival curves for patients with primary intracranial squamous cell carcinoma. (**A**) Patients with recurrence versus patients without, $P = 0.630$. (**B**) Patients with leptomeningeal carcinomatosis (LC) versus patients without, $P = 0.005$.

radiotherapy in treating intracranial SCC has been well documented,[3,5,66] we assessed whether adjuvant chemotherapy offers better control of malignancy in patients who received radiotherapy after surgery. The survival of patients treated with adjuvant chemotherapy was not superior to that of those treated with surgery plus radiotherapy. However, the number of analyzed cases was small, and the protocols used for chemotherapy varied, making it difficult to draw meaningful conclusions.

In the present study, the median survival for patients treated with surgical resection only was 5 months from the time of operation (range, 1–46 months). The poor surgical outcomes may be the result of the infiltration of malignant cells into the normal brain parenchyma adjacent to the tumor.[55] In most cases, the tumor had invaded into vital neurovascular structures with tight adherence, making complete resection unfeasible. The extent of resection was specified in 42 of 55 patients who underwent surgery and GTR was implemented in only 7 patients.[9,29,31,41,48,52,60] In particular, in patients in whom the tumor was located in the CPA, only 2 out of 29 patients underwent complete resection because of severe adhesion to the brainstem. It has not yet been established whether GTR of the tumor would increase patient survival compared with STR. According to our study, patients who underwent GTR showed relatively increased survival compared with those who underwent STR, although this was not statistically significant. For accurate diagnosis and proper treatment, the tumor should be removed to the greatest extent possible, particularly regions showing contrast enhancement, although aggressive resection of these tumors can result in postoperative mortality.[15,22,23]

In addition, complete resection can diminish the risk of postoperative chemical meningitis, which is a well-recognized complication of epidermoid tumors.[27,39,68] Spillage of the highly irritative cyst contents into the subarachnoid space during STR can cause chemical meningitis; this occurs in an estimated 40% of patients with epidermoid tumor who undergo STR.[39,68,69] Akar et al.[39] reported that of 28 patients with epidermoid tumor, 3 cases of aseptic meningitis were identified in the postoperative period. All were diagnosed from 7 incompletely resected tumors.

Hamlat et al.[3] reviewed the malignant transformation of intracranial epithelial cysts and classified them into 5 types (Table 2). According to the classification, 26 reported cases were diagnosed at the first surgery or autopsy, and 30 patients were classified as having malignant transformation from a previously diagnosed epidermoid cyst. The median survival of the 2 groups was 11 months and 25 months, respectively ($P = 0.473$). Six patients were diagnosed with malignant transformation from benign cysts other than epidermoid, with a median survival of 7 months. The survival was not significantly different from that of SCC originating from epidermoid cysts (12.75 months, $P = 0.818$).

LC after malignant transformation of tumor was reported in 16 cases. They were diagnosed at autopsy[8,10,11,27] or identified by cerebrospinal fluid cytology[16,33,40,46] and MRI.[4,45,46,49,59] Patients with LC have a poorer prognosis with rapid progression, and most patients were reported to have died. An effective treatment for LC has not yet been reported. Nagasawa et al.[67] reviewed 12 patients with LC and compared survival outcomes between patients who underwent surgery alone ($n = 5$) and those who received adjuvant therapy ($n = 7$). Patients treated with surgery alone had an average survival of 1.6 months, whereas those treated with adjuvant therapy with or without surgery showed a statistically significantly increased survival of 14.6 months (log-rank test, $P < 0.001$). However, all patients who received adjuvant therapy had different therapeutic modalities (chemotherapy, radiotherapy, or SRS) either alone or in combination. Furthermore, because of the scarcity of patients, future investigation is needed for better disease management.

**Table 2.** Classification of Malignant Transformation of Intracranial Epithelial Cysts[3]

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|---|
| 1) Initial malignant transformation of an epidermoid cyst |
| 2) Malignant transformation from a remnant epidermoid cyst |
| 3) Malignant transformation from other benign cysts |
| 4) Malignant transformation with leptomeningeal carcinomatosis |
| 5) Other malignancies arising from benign cysts |

The present study had several limitations. First, because the study relies on an analysis of data extracted from various other sources, publication bias cannot be excluded, and undescribed data could not be obtained. Second, the number of included patients was relatively small because of low prevalence of the disease and scarcity of data, limiting the power to generate statistical significance. Third, the survival of patients receiving palliative care was assessed from the onset of symptoms, which may have affected the outcome of group comparison. In addition, it was not possible to eliminate the possibility that patients with a poor condition tend to receive palliative treatment. Different treatment modalities were used in various combinations; this heterogeneity may have affected the results.

## CONCLUSIONS

Primary intracranial SCC that arises from benign epidermoid or dermoid cysts is rare and has a poor prognosis, with controversial management. Malignant transformation should be considered in cases of rapid progression of symptoms or enhancement within the cyst. Although patients with LC showed worse prognosis, the results of this study indicate that complete resection of the enhancing tumor whenever possible, followed by radiotherapy, may improve patient outcomes.

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