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# Analysis of Intracranial Meningioma Recurrence after Surgical Management

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## Abstract

**Background:** Meningioma is one of the well-known common primary brain neoplasms that account for more than 20% of intracranial tumors. Intracranial meningioma recurrence after surgery has long been recognized, although the mechanism of recurrence remains unclear.

**Objective:** To analyse impact of pre-operative and peri-operative measurements in relation to pathological outcome.

**Patients and Methods:** Retrospectively analysed 72 patients with meningiomas (45) female and (27) male who were treated surgically and re-operated again at our Hawler Teaching Hospital and West Emergency Hospital from June 2017 until June 2021 in Erbil Governorate in Northern Iraq. Clinical characteristics and demographics possibly associated with tumor recurrence were assessed, including gender, age, clinical symptoms, tumor location, pathology data, and radiotherapy and recurrence rate were closely studied.

**Results:** A total of 72 cases with meningioma included in the research, in which 17 cases recurrent cases were observed, in total of 72 cases 58 were benign (Grade I), and 14 were atypical/ malignant (Grade II/III). The mean age of patients (SD) was ± 51.2 years and a follow-up duration of 4 years. Overall recurrence rates 23.6% with Male to Female ratio of 0.55:1. Age, and gender could not be demonstrated as significant association factor in tumor recurrence. Factors significantly associated with tumor relapse in the analysis were tumor location at the Foramen magnum and Optic Nerve, both being (50%). The rates of recurrence were significantly high when the degree of removal (by Simpsons Classification) was for grade three (50%) and for grade four and five (70%), compared with 6.3% and 8.8% for grade one or two, respectively. A high recurrence rate was detected when the adjuvant was not received compared with the patients who received radiotherapy. Majority of patients had better outcome.

**Conclusion:** it was concluded from this study that Meningioma recurrence is well recognized and there are many factors including age, gender, extend of tumor resection, location, histological type of tumor and adjuvant therapy that would determine the pathological outcome and impact on patient's life.

**Keywords:** Meningioma, recurrence, Simpsons Classification, radiotherapy

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## Introduction

Meningioma is one of the prevalent intracranial tumors, accounting for nearly 20% of tumors in the central nervous system. It arises from the cells covering the arachnoid layer of the brain. They typically have a wide base of attachment to the dura, and may cause hyperostosis of subjacent bone or invade the bone. The prevalence peaks above 60 years, with a female: male ratio of 3:2. Nevertheless, the tumor may occur in children as well but to lesser extent.

Meningiomas are graded into (3) categories based on histological features based on the World Health Organization classification of tumors, [1]. Nearly 90% of meningiomas are benign (Grade I) that have slow growth, incidence increases with age [2]. However, some meningiomas are considered atypical (Grade II) and Malignant (Grade III), and 15 subtypes [3].

The intracranial meningiomas distribution is as follow: convexity (35%), parasagittal (20%), sphenoid ridge (20%), intraventricular (5%), tuberculum sellae (3%), infratentorial (13%), and others (4%). Surgical removal is considered the best treatment option for symptomatic meningiomas, with the objective of completely removing the tumor. Although individuals with benign meningiomas have a good survival rate, some patients with symptomatic meningiomas experience long-term impairment and problems after surgery [4, 5].

Even though meningiomas are usually benign histologically, the close skull can never be considered risk-free from any space-occupying lesions as rising intracranial pressure may lead to life-threatening complications. Because progression and recurrence are well recognized and not infrequent characteristics of meningiomas, a better understanding and thorough analysis of contributing factors are of paramount importance. In this literature review, we analyse some factors which may be predictive in tumor relapse, focusing on histological alterations, clinical manifestations, and risk factors related to the tumor treatment itself. Independent risk factors, like as gender and age, have also been analysed. Lastly, the extent of surgical removal reflected by the Simpson grade seems to be very closely associated with the risk of recurrence.

| Simpson Grade | Description |
|---|---|
| Grade 0 | Complete tumor removal, plus removal of an additional 2–3 cm from the tumor insertion site |
| Grade I | Complete tumor removal, including any dural attachments or abnormal bone |
| Grade II | Complete tumor removal with coagulation of dural attachment |
| Grade III | Complete tumor removal without resection or coagulation of its dural attachment |
| Grade IV | Partial tumor removal |
| Grade V | Biopsy only |

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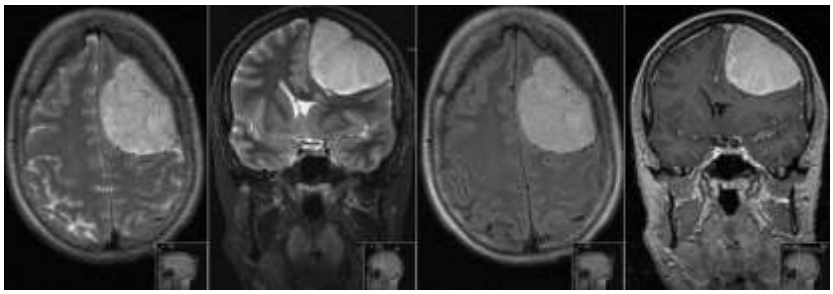

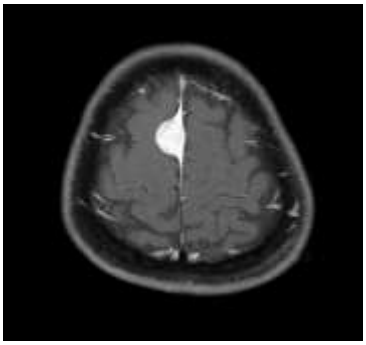

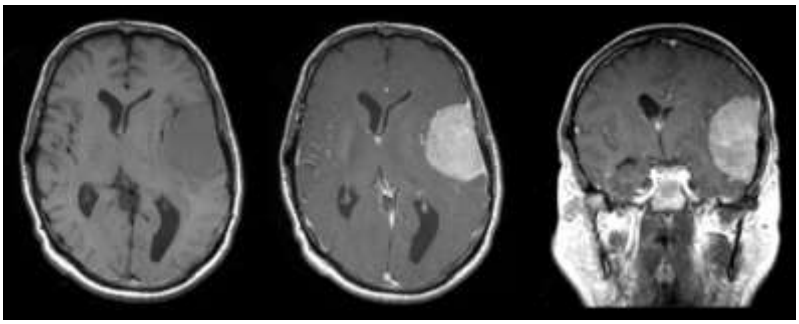

## Patients and Methods

We retrospectively reviewed the medical records of 79 patients underwent surgical removal of their intracranial meningiomas at Hawler Teaching Hospital and Rozhawa Emergency Hospitals from June 2017 until June 2021 in Erbil Governorate at Northern Iraq, 72 patients included in the study and their data analysed but only 17 cases had recurrence.

**The exclusion criteria:**Were multiple meningioma, recurrence of meningioma with presence of other malignancy and death.

All Patients diagnosed by different diagnostic methods, including skull X-ray, computerized tomography (CT) scan, magnetic resonance imaging (MRI) with contrast , and angiograms concerning tumor size , brain edema, tumor vascularity, associated bony changes.

The clinical and demographic parameters possibly linked with tumor recurrence were analysed, including gender, age, clinical symptoms, pathology data and receiving radiotherapy. Focal neurological deficit were defined as impaired function of cranial nerve,

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such as ptosis, facial palsy, hearing loss, anosmia.

Tumor location classified based on CT and MRI findings into convexity, parasagittal, olfactory, sphenoid ridge, supra-sellar, CPA, tentorium foramen magnum, optic nerve.

The extent of surgical excision of the tumor was categorized using Simpson's scale into five grades [6]. According to the WHO classification system.

The WHO's six criteria for histologic diagnosis of (benign, atypical, and malignant meningiomas) were used: hypercellularity, loss of architecture, nuclear pleomorphism, mitotic index, tumor necrosis, and brain invasion [7, 8].Our all laboratory histological diagnosis done in Erbil.

Seventeen cases out of 72 found to have recurrence and underwent second operation during follow up for 3 years diagnosis by MRI and CT scan , Different modalities of surgical approaches carried out for getting optimum view and access for total gross tumor resection including: Pterional, retrosegmoidal , supraorbital subfrontal , sub-occipital , supracerebellar trasn-tentorial …etc approaches.

## Statistical Analysis

Data were analysed using the Statistical Package for Social Sciences (SPSS, version 25). Fisher's exact test was used when the expected frequency (value) was less than 5 of more than 20% of the table's cells. The Chi-square test of association was used to compare proportions .The McNemar-Bowker test was used to compare the proportions (of histopathological diagnosis) of the same patients but on two different occasions. A p-value of $\leq 0.05$ was considered statistically significant.

## Results

Seventy-two patients diagnosed radiologically for having intracranial meningioma were included in the study. Forty five (62.5%) of cases were females and twenty seven (37.5 %) were males. Their mean age (SD) was ± 51.2 (12.9) years , range of age was from 14-71 years, and the median age was 53 years. It is shown in Table 1 (62.5%) of patients were aged 50 years and above which comprises majority of cases and (37.5%) were below age of 50, showing prevalence of meningioma being more common in elderly, The recurrence rate was (23.6%) among the patients, with the male-female ratio of 0.55:1, but overall no significant association was found between the rate of recurrence and age (p = 0.388) and gender (p = 0.830), as presented in Table [1].

**Table (1):** Age and gender distribution and their association with tumor recurrence

| | **Recurrence** | **No recurrence** | **Total** | |
|---|---|---|---|---|
| | No. (%) | No. (%) | No. (%)† | p |
| Age | | | | |
| < 40 | 5 (38.5) | 8 (61.5) | 13 (18.1) | |
| 40-49 | 3 (21.4) | 11 (78.6) | 14 (19.4) | |
| 50-59 | 3 (13.6) | 19 (86.4) | 22 (30.6) | |
| ≥ 60 | 6 (26.1) | 17 (73.9) | 23 (31.9) | 0.388* |
| Gender | | | | |
| Male | 6 (22.2) | 21 (77.8) | 27 (37.5) | |
| Female | 11 (24.4) | 34 (75.6) | 45 (62.5) | 0.830** |
| Total | 17 (23.6) | 55 (76.4) | 72 (100.0) | |

*By Fisher's exact test. **By Chi square test. †Column % was calculated

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Our study showed that the majority of meningioma were located in convexity (29 patients) followed by parasagittal and sphenoid ridge (11and 10) cases respectively, and least being located at foramen magnum and optic nerve (2 cases in each region), No significant association was found between the tumor location and the rate of recurrence (p = 0.427), as presented in Table [2].

**Table (2):** Rate of tumor recurrence by tumor location

| | | Recurrence | No recurrence | p |
|---|---|---|---|---|
| Tumor location | N | No. (%) | No. (%) | |
| Convexity | 29 | 4 (13.8) | 25 (86.2) | |
| Parasagittal | 11 | 2 (18.2) | 9 (81.8) | |
| Olfactory | 6 | 1 (16.7) | 5 (83.3) | |
| Sphenoid ridge | 10 | 4 (40.0) | 6 (60.0) | |
| Supra-cellar | 4 | 1 (25.0) | 3 (75.0) | |
| Cerebro-pontine angle | 5 | 2 (40.0) | 3 (60.0) | |
| Tentorium | 3 | 1 (33.3) | 2 (66.7) | |
| Foramen magnum | 2 | 1 (50.0) | 1 (50.0) | |
| Optic nerve | 2 | 1 (50.0) | 1 (50.0) | 0.427* |
| Total | 72 | 17 (23.6) | 55 (76.4) | |

*By Fisher's exact test

Majority (34) of cases have had grade two removal followed by grade one (16 cases), then grade three (12 cases) followed by grade four and five, each 10 cases. Of the cases which recur in each grade group , the rate of recurrence seen to be significantly (p < 0.001) high when the degree of removal was of grade three (50%) or grade four and five (70%), compared with (6.3%) and (8.8%) for grade one and two, respectively. Out of the 72 patients, 46 patients received radiotherapy compared to 26 patients who did not, A significantly (p = 0.001) high rate of recurrence was detected when the radiotherapy was not received (46.2%) compared with (10.9%) when the patients received radiotherapy Table (3).

**Table (3):** Rate of tumor recurrence by degree of removal** and radiotherapy

| | | Recurrence | No recurrence | |
|---|---|---|---|---|
| Degree of removal | N | No. (%) | No. (%) | p |
| One | 16 | 1 (6.3) | 15 (93.8) | |
| Two | 34 | 3 (8.8) | 31 (91.2) | |
| Three | 12 | 6 (50.0) | 6 (50.0) | |
| Four and five | 10 | 7 (70.0) | 3 (30.0) | < 0.001* |
| Radiotherapy | | | | |
| Received | 46 | 5 (10.9) | 41 (89.1) | |
| Not received | 26 | 12 (46.2) | 14 (53.8) | 0.001† |
| Total | 72 | 17 (23.6) | 55 (76.4) | |

*By Fisher's exact test. †By Chi square test. **By Simpsons classification

In the majority of cases, the pathological laboratory results showed to be benign meningioma followed by atypical and malignant meningioma respectively, In a total of 17 cases underwent second operation, their second pathological results showed;

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benign type (9) cases followed by atypical (5) cases. It is noticed that there was transition and histological change in one case of benign type to atypical type and another one benign case into malignant type. There was only one case diagnosed as malignant type had recurrence and on reoperation the laboratory study showed same pathological grading, No significant difference was detected between the grades of the pathological diagnosis of the first and the second meningioma (p = 0.368). As it is presented in Table [4].

**Table (4):** Association between the pathology of first and second meningioma

| | **Pathology of second meningioma** | | | |
|---|---|---|---|---|
| | Benign | Atypical | Malignant | P* |
| Pathology of first meningioma | No. (%) | No. (%) | No. (%) | |
| Benign | 9 (81.8) | 1 (9.1) | 1 (9.1) | |
| Atypical | 0 (0.0) | 5 (100.0) | 0 (0.0) | |
| Malignant | 0 (0.0) | 0 (0.0) | 1 (100.0) | 0.368 |
| Total | 9 (52.9) | 6 (35.3) | 2 (11.8) | |

*By McNemar-Bowker test

Variety of clinical presentations included in study but the most common clinical presentations of the patients who had edema were headache (44.4%) and seizure (25.0%). As it is illustrated in Table [5].

**Table (5):** Clinical presentations by brain edema

| | **Brain edema** | **No brain edema** | **Total** | **p** |
|---|---|---|---|---|
| Clinical presentation | No. (%) | No. (%) | No. (%) | |
| Headache | 21 (42.9) | 11 (47.8) | 32 (44.4) | |
| Seizure | 14 (28.6) | 4 (17.4) | 18 (25.0) | |
| Motor deficit | 5 (10.2) | 2 (8.7) | 7 (9.7) | |
| Vomiting | 4 (8.2) | 1 (4.3) | 5 (6.9) | |
| Dizziness | 1 (2.0) | 2 (8.7) | 3 (4.2) | |
| Visual disturbance | 2 (4.1) | 0 (0.0) | 2 (2.8) | |
| Others | 2 (4.1) | 3 (13.0) | 5 (6.9) | 0.519* |
| Total | 49 (100.0) | 23 (100.0) | 72 (100.0) | |

*By Fisher's exact test

Clinical presentation by tumor volume showed majority of cases had headache (44.4%) and seizure (25%) , it is obvious in the results shown in Table [6] that there is correlation between tumor volume changes and clinical presentations of patients , those had tumor volume (1-2 cm) experienced headache, seizure and other complains only (46.2%) , (46.2%) and (7.7%) respectively without having other complains, and those had tumor volume (< 4) cm had all clinical presentations but headache, dizziness and others being higher (38.5%), (15.4%) and (15.4%) respectively, and those with tumor volume (>4)cm had headache (45.7%) , seizure (23.9%) and Motor deficit (13%).

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**Table (6):** Clinical presentations by tumor volume

| | Tumor volume | | | | |
|---|---|---|---|---|---|
| | 1-2 cm | >4 cm | <4 cm | Total | |
| Clinical presentation | No. (%) | No. (%) | No. (%) | No. (%) | p |
| Headache | 6 (46.2) | 21 (45.7) | 5 (38.5) | 32 (44.4) | |
| Seizure | 6 (46.2) | 11 (23.9) | 1 (7.7) | 18 (25.0) | |
| Motor deficit | 0 (0.0) | 6 (13.0) | 1 (7.7) | 7 (9.7) | |
| Vomiting | 0 (0.0) | 4 (8.7) | 1 (7.7) | 5 (6.9) | |
| Dizziness | 0 (0.0) | 1 (2.2) | 2 (15.4) | 3 (4.2) | |
| Visual disturbance | 0 (0.0) | 1 (2.2) | 1 (7.7) | 2 (2.8) | |
| Others | 1 (7.7) | 2 (4.3) | 2 (15.4) | 5 (6.9) | 0.226* |
| Total | 13 (100.0) | 46 (100.0) | 13 (100.0) | 72 (100.0) | |

*By Fisher's exact test

Majority (80.6%) of the patients improved after surgery, 12.5% stayed in the same condition, and the rest (6.9%) deteriorated. As it is shown in the following figure

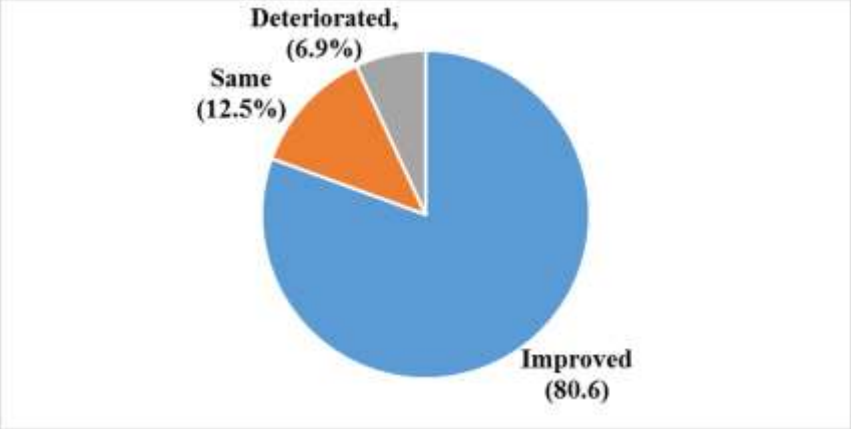


**Figure (1):** The outcome

## Discussion

Meningioma is one of the prevalent brain tumor type occurring at all ages with a peak prevalence above age of 60 years. Generally, meningiomas are histologically benign tumors that can be removed entirely in about three-quarters of the cases but tend to recur even after surgical removal. Many causative factors have been investigated, however, there is no consensus on the elements that cause tumor recurrence. In our study, the mean age at diagnosis of meningioma was 51.2 years, compared to Caucasians ranging from 57 to 59 years. Meanwhile, the African-origin population had a lower mean age at diagnosis of meningiomas, ranging from 39.9 to 45.7 years [9-13].

In addition to age distribution, the majority of studies have found a gender discrepancy in meningiomas, with male-to-female ratios ranging from (1:1.1) to (1:3) [14]. According to the findings of the survey, the female preponderance in the African-origin population is lower than in other ethnic groups [15]. Male-to-female ratio in the

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current study is (0.55:1) showing to be as same as previous studies in Caucasian populations [16, 17]. Surprisingly, a newly population-based study has concluded an absence of female predominance among patients with meningiomas undergoing surgery [17]. The differences are possibly can be explained by environmental, genetic differences, or other factors.

The location of the tumor is suggested to be an important determining factor in surgical prognosis and resectability. Meningiomas are usually found in the convexity, parasagittal, and sphenoid wing and falx regions [16, 18]. Meningiomas are less commonly include an olfactory groove, intraventicular and posterior fossa [16, 19]. A recent study conducted in Nigeria showed a different anatomical distribution of meningioma locations [15]. According to several reports and research, intracranial meningiomas can occur anywhere in the skull [20, 21]. The cerebral convexity, followed by the sphenoid ridge and the parasagittal area, was the most prevalent anatomical location of meningioma in our study. This finding is consistent with other researches showing that meningiomas typically develop in the cerebral convexity in adults. Because tumor location influences the extent of surgery, as it did in our patients, it is reasonable to predict that tumor location influences the likelihood of relapse. A greater propensity for recurrence was seen in meningiomas that were situated near the cranial base, which are more challenging to remove completely [22-25]. The recurrence rates were higher in patients with Foramen magnum and Optic nerve meningiomas observed in our study. We observed tumor recurrences less in patients with parasagittal and Convexity meningiomas, likely as a result of the shorter follow-up period compared to individuals with meningiomas in other regions.

Meningioma progression and recurrence are predicted using the Simpson grading system, which describes the extent of resection.

Completeness of excision was expressed by using Simpson grading system [26]. This system defines five grades. Grade one refer to excision that is macroscopically complete, with removal of the dural attachment of the tumor and any abnormal bone. Grade two means macroscopically complete removal of the tumor and its visible extensions, with coagulation of its dural attachment. Grade three refer to macroscopically complete removal of the intradural tumor without resection or coagulation of its dural attachment or extradural extensions. Grade four refer to subtotal tumor resection. Grade five means decompression with or without biopsy. Macroscopic complete excision with the removal of affected dura and bone cannot prevent the recurrence of benign meningioma subtype. However the exact etiology of tumor recurrence after Simpson Grade one resection has not been resolved until now [27, 28].

The overall recurrence rate was 23.6% in our series. Simpson grades four and five were substantially related with greater recurrence risk when compared to the other grades, according to invariable analysis, A point which should be highlighted is that Simpson grade V is associated with recurrence since it involve only taking biopsy without change in the actual size of tumor. On follow up we found that those tumors were highly vascular and deeply seated in brain and there was

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change in its actual size. Such outcome is consistent with earlier research on the association between Simpson grade and meningioma control [29-31].

The usefulness of radiation in reducing the growth of meningiomas remains debatable. Meningiomas were formerly thought to be radio-resistant [32].Despite that, radiation is still used today. Among our patients, a significantly high rate of recurrence was detected when the radiotherapy was not received compared with the patients who received radiotherapy. However, larger sample size is required to conduct further study to derive significant conclusions.

The majority of intracranial meningiomas are benign according to histopathological examination, however 5 to 10% of them show aggressive characteristics like high-grade (WHO grade II/III) behavior.2, 33. In our study, the distribution of tumor types was the same as other studies, showing that majority being benign meningiomas (81.8%). Meningiomas have a significant recurrence risk following surgery and an unsatisfactory clinical outcome despite being slow-growing and histologically benign tumors. When compared to benign tumors (grade I), atypical and malignant meningiomas have a greater incidence of recurrence [34,35]. However, benign meningiomas experience a disproportionately high rate of relapses of tumor. This study discovered that the most prominent symptoms in meningioma patients were headache and seizures which were more noticeable with tumor volume more than 4 cm.

This study demonstrated that cerebral edema had no effect on clinical presenting symptoms. there was no significant relationship between patient gender and age and recurrence. We found that majority of patients were improved [36].

## Conclusions

It was concluded from this study that Meningioma recurrence is well recognized and there are many factors including age, gender, extend of tumor resection, location, histological type of tumor and adjuvant therapy that would determine the pathological outcome and impact on patient's life.

## Recommendations

Firstly, we observed a higher prevalence of meningioma in females in comparison to male in addition tumor incidence increasing with age more focus should be added on in screening and follow up among these two entities, secondly, Short follow-up periods may cause underestimation of late tumor relapse that may happen three years following surgery, necessitating additional extension of follow-up periods. Lastly more detailed studies like investigating immunohistochemical markers and genetic factors, in addition larger scale of patients to be included in future studies to conclude more specific risk factors.

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**Conflict of interest:** Nil

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# تحليل رجوع الورم السحائي داخل الجمجمة بعد العلاج الجراحي

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## الملخص

**خلفية الدراسة:** الورم السحائي هو أحد أورام الدماغ الأولية المعروفة والتي تمثل أكثر من ٢٠٪ من الأورام داخل الجمجمة. تم التعرف على تكرار الورم السحائي داخل الجمجمة بعد الجراحة منذ فترة طويلة ، على الرغم من أن آلية رجوعها لا تزال غير واضحة.

**اهداف الدراسة:** لتحليل تأثير القياسات قبل الجراحة وقبل الجراحة فيما يتعلق بالنتائج المرضية.

**المرضى والطرائق:** تم تحليل المرضى الذين يعانون من الأورام السحائية الذين عولجوا جراحيًا وأعيدوا الجراحة مرة أخرى في مستشفى هولير التعليمي ومستشفى الطوارئ الغربية من يونيو ٢٠١٧ حتى يونيو ٢٠٢١ في محافظة أربيل في شمال العراق. تم تقييم الخصائص الديموغرافية والسريرية التي يحتمل أن تكون مرتبطة رجوع الورم ، بما في ذلك العمر والجنس والأعراض السريرية وبيانات علم الأمراض وموقع الورم والعلاج الإشعاعي ومعدل رجوع.

**النتائج:** تم تضمين ما مجموعه ٧٢ حالة مصابة بالورم السحائي في الدراسة ، حيث لوحظ رجوع ١٧ حالة ، و ٥٨ حالة حميدة (الدرجة الأولى) ، و ١٤ حالة غير نمطية / خبيثة (الدرجة الثانية / الثالثة). كان متوسط عمر المرضى ٥١,٢ سنة ومدة المتابعة ٤ سنوات. معدلات رجوع الإجمالية ٢٣,٦٪ مع نسبة الذكور إلى الإناث ١: ٠,٥٥. لا يمكن إثبات العمر والجنس كعامل ارتباط مهم في رجوع الورم. كانت العوامل المرتبطة بشكل كبير بانتكاس الورم في التحليل هي موقع الورم في الثقبة ماغنوم والعصب البصري ، وكلاهما (٥٠٪). كانت معدلات الرجوع عالية بشكل ملحوظ عندما كانت درجة الإزالة (حسب تصنيف سمبسون) من الدرجة الثالثة (٥٠٪) أو الدرجة الرابعة والخامسة (٧٠٪) ، مقارنة بـ ٦,٣٪ و ٨,٨٪ للصف الأول والثاني على التوالي. تم الكشف عن معدل رجوع مرتفع عند عدم تلقي العلاج الإشعاعي مقارنة بالمرضى الذين تلقوا العلاج الإشعاعي. كان لدى غالبية المرضى نتائج أفضل.

**الاستنتاجات:** : استنتج من هذه الدراسة أن رجوع الورم السحائي معروف جيدًا وأن هناك العديد من العوامل بما في ذلك العمر والجنس ومدى استئصال الورم والموقع والنوع النسيجي للورم والعلاج المساعد الذي سيحدد النتيجة المرضية والتأثير على حياة المريض.

**الكلمات المفتاحية:** الورم السحائي ، الرجوع ، تصنيف سمبسون ، العلاج الإشعاعي

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