REVIEW

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Stereotactic radiosurgery for the management of cavernous sinus meningiomas: A narrative review

Kavernöz sinüs menenjiyomlarının yönetiminde stereotaktik radyocerrahi: Bir derleme

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ABSTRACT

Cavernous sinus meningiomas (CSMs) are a challenging subgroup of intracranial meningiomas because of their close relationship with vital neurovascular structures. This systematic review evaluates the effectiveness and safety of stereotactic radiosurgery (SRS) for both primary and adjuvant treatment of CSMs. We analyzed data from 24 studies involving 2,302 patients treated with SRS using various platforms, such as Gamma Knife, LINAC-based systems, and CyberKnife. The median marginal doses ranged from 11 to 19 Gy, with the most recent series using 12 to 14 Gy. Long-term tumor control was excellent, with 5-year progression-free survival rates between 86% and 99%, and 10-year rates from 69% to 97%. Neurological improvement was seen in 20% to 46% of symptomatic patients, especially in cranial nerve function, notably abducens nerve palsy. Radiation-related complications were rare (0-12%) and usually temporary, with permanent deficits occurring in less than 7% of patients. Comparative analysis showed better neurological outcomes with primary SRS compared to adjuvant SRS after microsurgical resection, suggesting that early intervention with SRS may be preferable to watchful waiting or aggressive surgery for carefully selected patients. This review provides Class III, including retrospective comparative studies, and case series evidence that SRS has an excellent risk-benefit profile for CSMs, achieving durable tumor control with minimal morbidity. We recommend a treatment approach favoring primary SRS for small to medium-sized, asymptomatic, or minimally symptomatic CSMs, while advocating for surgical decompression followed by adjuvant SRS in larger lesions with significant mass effect or worsening neurological deficits.

Keywords: Cavernous sinus meningioma, stereotactic radiosurgery, Gamma Knife, cranial nerve function, primary radiosurgery

ÖZ

Kavernöz sinüs menenjiyomları (KSM'ler), hayati nörovasküler yapılarla yakın ilişkileri nedeniyle intrakraniyal menenjiyomların zorlu bir alt grubunu oluşturmaktadır. Bu sistematik derleme, KSM'lerin hem primer hem de adjuvan tedavisinde stereotaktik radyocerrahinin (SRC) etkinliğini ve güvenliğini değerlendirmektedir. Gamma Knife, LINAC tabanlı sistemler ve CyberKnife gibi çeşitli platformlar kullanılarak SRC ile tedavi edilen 2.302 hastayı içeren 24 çalışmadan elde edilen verileri analiz ettik. Medyan marjinal dozlar 11 ile 19 Gy arasında değişmekte olup, en son serilerde 12 ile 14 Gy kullanılmıştır. Uzun dönem tümör kontrolü mükemmel olup, 5 yıllık progresyonsuz sağkalım oranları %86 ile %99 arasında ve 10 yıllık oranlar %69 ile %97 arasında bulunmuştur. Semptomatik hastaların %20 ile %46'sında, özellikle kraniyal sinir fonksiyonlarında, bilhassa abdusens sinir felcinde nörolojik iyileşme gözlenmiştir. Radyasyonla ilişkili komplikasyonlar nadir (%0-12) ve genellikle geçici olup, kalıcı defisitler hastaların %7'sinden azında görülmüştür. Karşılaştırmalı analiz, mikrocerrahi rezeksiyon sonrası adjuvan SRC'ye kıyasla primer SRC ile daha iyi nörolojik sonuçlar göstermiş olup, bu durum dikkatli seçilmiş hastalar için SRC ile erken müdahalenin bekle-gör yaklaşımına veya agresif cerrahiye tercih edilebileceğini düşündürmektedir. Bu derleme, SRC'nin KSM'ler için mükemmel bir risk-fayda profiline sahip olduğuna, minimal morbidite ile kalıcı tümör kontrolü sağladığına dair Sınıf III kanıt sunmaktadır. Küçük-orta boyutlu, asemptomatik veya minimal semptomatik KSM'ler için primer SRC'yi tercih eden bir tedavi yaklaşımı önerirken, belirgin kitle etkisi veya kötüleşen nörolojik defisitleri olan daha büyük lezyonlarda cerrahi dekompresyon ardından adjuvan SRC'yi savunuyoruz.

Anahtar Kelimeler: Kavernöz sinüs menenjiyomu, stereotaktik radyocerrahi, Gamma Knife, kraniyal sinir fonksiyonu, primer radyocerrahi

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Highlights

- Stereotactic radiosurgery provides excellent tumor control with 5-year progression-free survival rates of 86-99% for cavernous sinus meningiomas.
- Neurological improvement was observed in 20-46% of symptomatic patients, particularly in abducens nerve palsy.
- Permanent radiation-related complications occur in less than 7% of patients, demonstrating a favorable safety profile.
- Primary stereotactic radiosurgery offers superior neurological outcomes compared to adjuvant treatment after microsurgical resection.
- Primary stereotactic radiosurgery is recommended for small to medium-sized, asymptomatic or minimally symptomatic cavernous sinus meningiomas.

INTRODUCTION

Cavernous sinus meningiomas (CSM) account for 1-2% of all intracranial meningiomas and represent a clinical challenge in terms of treatment strategy and management of initial treatment outcomes. The CSM is a parasellar structure that harbours critical neurovascular structures, including the cranial nerves (CN) II, IV, V1, V2, and VI, as well as the cavernous segment of the carotids bilaterally. These anatomical properties make the surgical resection a high-risk approach due to the imminent danger to these structures inherent in the surgery.

Historically, microsurgical resection was considered the primary treatment approach that could offer subtotal resection in the majority of cases (1–5).

Stereotactic radiosurgery (SRS) offers a non-invasive treatment approach with comparable tumor control rates and excellent neurologic outcomes. However, with or more aggressive and larger tumors, initial resection is inevitable, which makes SRS also a good candidate for adjuvant therapy to residual disease.

This review synthesized the current evidence regarding SRS to cavernous sinus meningiomas with a focus on tumor control and neurologic outcomes. This review aims to provide an overview of major studies from the literature and guide surgeons on choosing the optimal initial treatment paradigm.

Tumor Control

Across multiple studies, stereotactic radiosurgery for cavernous sinus meningiomas has consistently shown good tumor control outcomes in both primary and adjuvant approaches. The 5- and 10-year progression-free survival rates reported in the literature range from 92% to 99% and 84% to 94%, respectively (6–13) (Table 2).

In Park et al.'s. study, the authors found that progressive tumors following surgery had significantly worse outcomes (8) (Hazard Ratio: 4.1, p=0.009). Furthermore, Kano et al. in their study, comparing patients with or without previous surgery who underwent SRS for their cavernous sinus meningiomas, they reported 94% PFS at 5 years and 86% at 10 years, with a median follow-up of 62 months (7). The authors found that prior microsurgery was not linked to either improvement or worsening of PFS. In one of the larger studies, Park et al. reported 90% PFS at 5 years and 88% at 10 years, with a median follow-up of 101 months (2). They reported a tumor progression rate of 11.7% over a median of 48.9 months, a lower rate of progression compared to our results (17.4%). Santacroce et al. conducted a multicenter study including 945 cavernous sinus meningiomas demonstrated 96.7% 5-year PFS and 90.1% 10-year PFS (6). Lastly, Wei et al reported a 5-year 92.1% PFS for the entire cohort for meningiomas located anywhere intracranially (14). They have demonstrated superior control rates for unresected meningiomas, 94.0% vs 90.8% for resected meningiomas at 5 years. Nicolato et al., in their multicenter analysis of 122 patients, achieved 97% tumor control, with tumor regression in 63% of the cases at a 48.3 months median follow-up (12). Pollock et al. and Hasegawa et al. reported 99% and 87%, 93% and 73% 5- and 10-year PFS rates, at 89 and 62 months median follow-ups, respectively (13,15). Lastly, Spiegelmann et al. reported 98% tumor control at 5 years, with a LINAC-based treatment strategy in 67 months of median follow-up. Furthermore, these results can be attributable to many factors, one of which may have changed tumor biology following surgery due to surgical trauma and damage to the vascular supply of the tumor, or altered skull base anatomy, causing less conformal treatment plans, which may be a factor for decreased radiosurgical efficacy. Primary SRS consistently shows superior tumor control in the literature. However, it must be noted that for patients with compressive symptoms, especially to the optic nerve, pituitary, and internal carotid, surgical debulking is inevitable. These factors can affect tumor control regardless of treatment strategy. For asymptomatic patients

Table 1: Characteristics of Major Studies on Stereotactic Radiosurgery for Cavernous Sinus Meningiomas

Author, Year	Study Design	Patients (n)	SRS Platform	Primary/ Adjuvant SRS n / n (% / %)	Mean Tumor Volume (cm³)	Median Margin Dose (Gy)	Median Follow-up (months)
Pikis et al., 2022 (16)	Multi-institutional	37	Gamma Knife	37 / 0 (100 / 0)	5.73	12.27	72
Rueß et al., 2020 (13)	Single-center	116	LINAC/CyberKnife	75 / 41 (65 / 35)	5.7	12.6	55
Pollock et al., 2013 (7)	Single-center	115	Gamma Knife	69 / 46 (60 / 40)	9.3	16	89
Hasegawa et al., 2007 (15)	Single-center	115	Gamma Knife	49 / 66 (43 / 57)	14	13	62

CSM: Cavernous Sinus Meningioma, **LINAC:** Linear Accelerator, **SRS:** Stereotactic Radiosurgery

Table 2: Treatment Outcomes After Stereotactic Radiosurgery for Cavernous Sinus Meningiomas

Author, Year	5-year Tumor Control Rate (%)	10-year Tumor Control Rate (%)	Improved Symptoms (%)	Worsened Symptoms (%)	Radiation-Related Complications (%)
Pikis et al., 2022 (16)	100	N/A	N/A	0	5.4
Pollock et al., 2013 (13)	99	93	36	N/A	12 permanent
Kano et al., 2013 (7)	94	86	39	11	N/A
Hasegawa et al., 2007 (15)	94	92	46	4	N/A

NA: Not Available

or those with minimal symptoms, our findings support early treatment. Pikis et al. have reported on the management of these lesions in asymptomatic patients (16). The authors have reported 100.0% tumor control in 72-month median follow-up. In selected patients, primary SRS can provide excellent tumor control without the risks of surgery.

The analysis of dose parameters showed that tumor control can be achieved at a wide range of margin doses. The current literature has failed to find a dose-response relationship. Pollock et al. used a median dose of 16 Gy (12-20Gy); however, they couldn't associate the margin dose with tumor control (13). Hasegawa et al. reported good tumor control with lower marginal doses, including 34 patients with a 12 Gy or less dose, and 15 patients 10 Gy or less dose (15). They achieved 93% and 88% tumor control, respectively. Lastly, Spiegelmann et al. used a mean margin dose of 13.5 Gy, normalized to an 80% isodose line, achieving 98% tumor control with less than 10 Gy dose to the optic apparatus (17). They attributed their results to the introduction of minimultileaf collimators and multiple dynamic arcs that enable single isocenter treatment with high conformality.

Neurological Outcomes

The current literature reports outcomes on skull base meningiomas, and reported improvement in neurologic deficits ranged from 26%-58% in several series looking at cerebellopontine angle and petroclival meningiomas following primary SRS (18–21) (Table 2). Furthermore, Pollock et al. also reported increased CN deficit improvement with primary SRS patients compared to patients who had surgery first (41% vs 20%, p<0.01) (13).

Similar findings were found in Faramand et al.'s multicenter study, including 245 patients (22). 46.5% of primary SRS patients showed improved cranial nerve deficits in a median follow-up of 58 months, compared to 19% of 15o adjuvant SRS patients. One interesting finding of their study is that patients with subtotal resection were found to have better tumor control than gross total resection, strengthening our hypothesis that extensive tumor scarring diminishes the efficacy of SRS. In their volumetric analysis, Cohen-Inbar et al. reported 39.2% overall neurologic improvement and underscored that 90.7% of new or worsening deficits were attributable to tumor progression rather than radiation effects (23). Lastly, Spiegelmann et al. also demonstrated that 43% of patients with primary SRS had neurologic deficit improvements compared to 19% of patients with prior resection (17). Furthermore, the authors stated that patients treated with only SRS within 1 year of deficit onset had higher improvement rates compared to patients with surgery and then adjuvant SRS (58% vs 25%, p=0.052).

Hasegawa et al. reported similar results: 28% of patients with CN VI deficits improved, showing higher improvement rates in the primary group (15). Hafez et al. also documented CN VI improvements in their primary SRS group (24). The authors reported that early onset deficits, less than 1 year before SRS, had significantly higher improvement rates compared to deficits older than 1 year, 49% vs 19%, respectively (p<0.03). These significant improvement rates unique to CN VI can be attributable to several anatomical and pathological properties. Firstly, CN VI runs freely across the cavernous sinus, unlike CN III, CN IV, and CN V1 and V2. These nerves run between two dural layers along the lateral wall of the cavernous sinus. So when the meningioma progression begins, these nerves are trapped without room to expand and vulnerable to tumor infiltration, whereas CN VI has room to expand, which protects it from tumor infiltration. This makes the compression from the reversible tumor progression the major source of the reversible deficit. Furthermore, the abducens nerve has a small caliber and lacks a myelin sheet in its intracavernous segment, which makes it susceptible to ischemic injury. However, early alleviation of this reversible compression increases improvement rates. Pollock et al. have reported 36% improvement rates in trigeminal dysfunction (13). While Faramand et al., results showed that tumor location affected improvement rates (22). Trigeminal dysfunction improvement rates were significantly higher in the petroclival meningiomas compared to their cavernous counterparts (27% vs 10%, p=0.02). It must be noted that surgery plays a vital part in neurologic deficits, showing surgery as a major contributor.

Adverse Radiation Effects, Malignant Transformation, and Death Related to Tumor Progression

Giotta Lucifero et al., in their report on 436 patients with grade I meningiomas, report 49% malignant transformation following postoperative radiation therapy compared to 20% malignant transformation in surgery alone (25). Their overall mortality rates were 26% in the irradiated group vs 4% in the non-irradiated group. Historical data from previous studies support their results (26–30). However, a clear distinction should be made between primary SRS to intact meningiomas and postoperative radiotherapy. Gioatta Lucifero et al. have reported predominantly postoperative residual disease with fractionated radiation therapy, where 54% of patients have progressed at the time of radiation therapy (25). Their findings suggest a progressive disease more aggressive than the initial presentation. These findings also support the hypothesis that surgically scarred tumors have less response to radiation due to the alteration of the blood supply to the tumor with hypoxic niches, making tumor cells more susceptible to mutagenesis. In contrast, primary SRS treats undifferentiated tumors with high conformality and delivers an ablative radiation dose (12-16 Gy) in a single session. This treatment paradigm overwhelms the tumor cells' repair mechanisms rather than accumulating carcinogenic mutations.

Comparison with Microsurgical Series

The current surgical literature provides valuable insight into the role of SRS in the management of CSM. DeMonte et al. shared their significant experience with aggressive microsurgical resection in 41 patients, achieving gross total resection in 76%, but 59% experienced new or worsened cranial nerve deficits (1). Al-Mefty and Smith outlined their surgical method for tumors invading the cavernous sinus, highlighting the technical difficulties in removing the tumor completely while maintaining neurovascular integrity (31). Goel et al. shared their experience with extradural techniques for treating cavernous sinus lesions, detailing the anatomical factors and surgical pathways for tumor removal (32). Pamir et al. compared radical resection, conservative surgery, and adjuvant radiosurgery at a single institution, finding that extracavernous resection followed by Gamma Knife radiosurgery achieved comparable tumor control but fewer cranial nerve complications than radical surgery (33). Couldwell's group presented long-term results for 50 patients who had decompressive surgery, with a 52% improvement in preoperative cranial neuropathies. Only 2% experienced permanent deterioration. However, 50% of patients required further radiation therapy (34). Nanda et al. analyzed 65 microsurgically treated patients and found a complete resection in only 41.5% of cases. They noted that cranial nerve recovery was independent of the extent of tumor removal and that adjuvant SRS significantly reduced recurrence rates (35). Sindou et al. reported their experience with 100 consecutive patients treated with surgery alone, achieving stable tumor Sindou et al. documented their experience with 100 consecutive patients who underwent surgery alone, maintaining stable tumor control in about 60% over the long term. However, they observed significant rates of new cranial nerve deficits and tumor control in approximately 60% at long-term follow-up, but with substantial rates of new cranial nerve deficits (36). These surgical series collectively show that although microsurgery is crucial for cases with significant mass effect needing decompression, combining limited surgery with adjuvant SRS or using primary SRS alone provides better neurological preservation while achieving similar tumor control in carefully selected patients.

Conclusion

Stereotactic radiosurgery represents a safe and highly effective treatment modality for cavernous sinus meningiomas, with consistent tumor control rates exceeding 90% at 5 years across multiple large studies. The literature demonstrates excellent long-term outcomes with minimal morbidity, regardless of the specific radiosurgical platform employed. Based on this evidence, we recommend primary SRS as the preferred initial treatment for small to medium-sized, asymptomatic or minimally symptomatic CSMs. For larger tumors with significant mass effect or progressive neurological deterioration, surgical decompression followed by adjuvant SRS for residual tumor remains appropriate. This individualized treatment approach optimizes the balance between effective tumor control and preservation of neurological function. Future prospective studies should further delineate the optimal timing of intervention and identify biological markers predictive of treatment response to further refine management strategies for this challenging skull base pathology.

Author Contributions

Study conception and design: **Mehmet Denizhan Yurtluk,** data collection: **Mehmet Denizhan Yurtluk,** analysis and interpretation of results: **Mehmet Denizhan Yurtluk,** draft manuscript preparation: **Mehmet Denizhan Yurtluk.** The author reviewed the results and approved the final version of the article.

Conflicts of Interest

The author have no confict of interest to declare.

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