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Radiosurgery for intracranial meningiomas: A systematic review and meta-analysis

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ABSTRACT

Background: Radiosurgery(RS), both in single and multiple sessions, have been performed for intracranial meningiomas. Different aspects are still controversial on this field. The aim of this systematic review is to summarize the current literature on long-term efficacy and safety of RS for meningiomas.

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Methods: Online databases were searched for studies published until April 2015. The primary outcomes were disease control and progression-free-survival(PFS). The secondary outcomes were symptom control and radiation-induced toxicity.
Results: The estimate of disease control rate ranged from 87.0% to 100.0% at 5 years and from 67.0% to 100.0% at 10 years. The PFS rate ranged 78.0%–98.9% and 53.1%–97.2% at 5 and 10 years, respectively. The overall symptom control was 92.3%, the overall toxicity was 8.1%.
Conclusions: RS can be considered a safe and effective treatment. Efforts are needed in standardizing the definition of local and symptom control and toxicity in order to properly compare different treatment schedules.

1. Introduction

Meningiomas are the most common primary intracranial tumors among adults. The prognosis depends on different factors, such as tumor grading according to World Health Organization (WHO) Classification System (Thurnher, 2009), type of surgery according to Simpson criteria (Simpson, 1957) molecular markers (Jensen and Lee, 2012; Lee et al., 2010) and genetic syndromes (Barbera et al., 2013; Linsler et al., 2014). Indeed, different authors have attempted to better define both histology and genetic profiles, as the current WHO classification does not completely take into account prognostic factors. Moreover, the relevance of the Simpson grade as a predictor of recurrence has also been questioned (Sughrue et al., 2010).

A maximum safe surgical resection is still considered the treatment of choice for meningiomas. However, since meningiomas often develop close to the critical neural or vascular structures, complete resection is not always achievable. For these reasons, radiosurgery (RS), both in single session and staged approach, as well as hypo-fractionated stereotactic radiotherapy (HFSRT), have been used in primary and adjuvant settings (Aichholzer et al., 2000; Feigl et al., 2007; Hakim and Alexander, 1998; Kim et al., 2005; Malik et al., 2005; Selch et al., 2004; Stafford et al., 2001). Elderly and frail patients with intracranial meningioma who underwent RS increased the chances for quality of life preservation, thus avoiding surgery-related risks (Fokas et al., 2014). Although these treatments play a crucial role in meningioma patient management (Kondziolka et al., 2008), controversy remains regarding timing, prescription doses and fractionation of delivery (Marcus et al., 2008). So far, data on treatment-related symptom control and toxicity are not yet conclusive (Kim et al., 2005; Malik et al., 2005; Rowe et al., 2004; Shrieve et al., 2004).

From this perspective, the aim of this systematic review was to evaluate the role of both single session and staged RS, summarizing available data on long-term efficacy and safety.

2. Methods

In order to avoid the bias induced by *post hoc* decisions, the eligibility criteria and methods of analysis were specified in advance and then summarized with a final protocol as described below.

2.1. Eligibility criteria

2.1.1. Type of studies and patients

We included experimental and observational studies, such as case series, retrospective and prospective analyses, focused on adult patients with radiological and/or pathological diagnosis of intracranial grade I–II meningioma. In case of heterogeneous population, as for the studies including both benign and malignant meningiomas, we have considered eligible only those that reported results, separately for subgroups, (e.g. histo-pathological subtype).

Studies enrolling a number of patients inferior to five for each arm (for comparative studies) or overall (for non-comparative studies) were excluded. Studies including patients with malignant meningioma (WHO grade III), radiation-induced meningioma or patients who had previously undergone brain radiation therapy were excluded from our review.

2.1.2. Type of interventions

The analyzed treatment was RS (high total dose of radiation delivered in 1 to few large fractions with dedicated device) (Barnett et al., 2007) in both first-line and post-operative settings. The latter included both adjuvant (up to 6 months from surgery) and salvage (at progression) approaches. The eligible treatment schedules were those delivering a number of fractions from 1 to 5 with a dose of at least 4 Gy.

2.1.3. Outcome measures

The primary outcomes were disease control rate, expressed as the rate of patients free from relapse at fixed time points, and progression free survival (PFS) rate, defined as the rate of freedom from progression or death at fixed time points. The studies were considered eligible if at least one of our primary end-points was assessed with a minimum follow-up of 3 years, or if actuarial disease control rate or actuarial PFS rate were reported at 3 years at least.

The secondary outcomes were symptom control and radiation-induced toxicity. Symptom control was expressed as frequency of patients with stable or improved neurological deficits, compared to pre-treatment neurological symptoms. Toxicity was expressed as frequency of patients with new neurological signs or symptoms, compared to pre-treatment neurological signs and symptoms. We classified the reported toxicities in 8 groups: cranial nerve, neurocognitive and optic pathway deficits, neurological and movement disorders, cerebral signs, skin effects and uncategorized signs and symptoms (any toxicity type not specified in the article).

2.2. Search strategy

The Medline and Embase databases were searched for English abstracts and keywords of relevant studies published until 28 April 2015. The details and words of search are listed in Supplementary Table S1.

We used a two-step process to select the eligible papers. In the first step two reviewers independently checked the titles, abstracts and key words of identified studies. In the second step other two independent reviewers evaluated the full text of included abstract by matching all of the inclusion criteria. Dissentions were solved by consensus.

We also searched the reference lists of identified studies, reviews and meta-analysis for other relevant articles.

Reasons for excluding studies have been recorded.