Clinical Neurology and Neurosurgery 166 (2018) 116–123

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Hypo-fractionated stereotactic radiotherapy of five fractions with linear accelerator for vestibular schwannomas: A systematic review and meta-analysis

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ARTICLE INFO

Keywords:
Vestibular schwannoma
Acoustic neuroma
Fractionated stereotactic radiosurgery
Radiotherapy

ABSTRACT

Vestibular schwannomas (VS) are benign tumors stemming from the eighth cranial nerve. Treatment options for VS include conservative management, microsurgery, stereotactic radiosurgery, and fractionated radiotherapy. Though microsurgery has been the standard of care for larger lesions, hypo-fractionated stereotactic radiotherapy (hypo-FSRT) is an emerging modality. However, its clinical efficacy and safety have yet to be established. We conducted a systematic review and meta-analysis of manuscripts indexed in PubMed, Scopus, Web of Science, Embase, and Cochrane databases reporting outcomes of VS cases treated with hypo-FSRT. Five studies representing a total of 228 patients were identified. Across studies, the pooled rates of tumor control, hearing, facial nerve, and trigeminal nerve preservation were 95%, 37%, 97%, and 98%. No instances of malignant induction were observed at median follow-up of 34.8 months. Complications included trigeminal neuropathy (n = 3), maxillary paresthesia (n = 1), neuralgia (n = 1), vestibular dysfunction (n = 1), radionecrosis (n = 1), and hydrocephalus (n = 1). Hypo-FSRT may be another useful approach to manage VS, but studies with extended follow-up times are required to establish long-term safety.

1. Introduction

Vestibular schwannomas (VS) are benign tumors stemming from Schwann cells of the eighth cranial nerve, and comprise 6% of intracranial tumors with an incidence rate of 2 tumors per 100,000 people each year [1–5]. Because VS growth impinges on surrounding cranial nerves, patients commonly present with sensorineural hearing loss, tinnitus, and vertigo and less often with Bell's palsy and facial sensation loss. Current management for patients with VS include: 1) observation, 2) surgical resection, or 3) stereotactic radiosurgery (SRS) or fractionated stereotactic radiotherapy (FSRT) with the appropriate modality dependent on size, location, previous treatment course, and tumor progression.

While small, non-progressing lesions can be managed through a conservative approach, microsurgery, SRS, and FSRT have been used to treat larger and symptomatic VS. However, because of significant surgery-associated risks, decreased hospital stays, and increased functional outcomes, SRS and FSRT can be attractive, non-invasive alternatives to microsurgery [6–11]. Whereas SRS delivers one high dose of radiation to the lesion, conventional FSRT involves smaller daily or weekly doses (eg. 20–30 fractions to total dose of 50–54 Gy). FSRT, in particular, provides an attractive management strategy, because the lower dose per fraction allows for the treatment of larger lesions. The temporally spaced treatment increases the probability of targeting tumor cells during periods of high radiosensitivity and cell division, as well as permitting better normal tissue sparing [12]. Furthermore, this lower dose per fraction is thought to minimize hearing loss and cranial nerve damage. Hypo-fractionated stereotactic radiotherapy (hypo-FSRT), given 5–20 fractions to a total dose of 20–35 Gy, has been favored over conventional FSRT, because of less frequent treatment visits,

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https://doi.org/10.1016/j.clineuro.2018.01.005
Received 29 November 2017; Received in revised form 31 December 2017; Accepted 7 January 2018
Available online 12 January 2018
0303-8467/

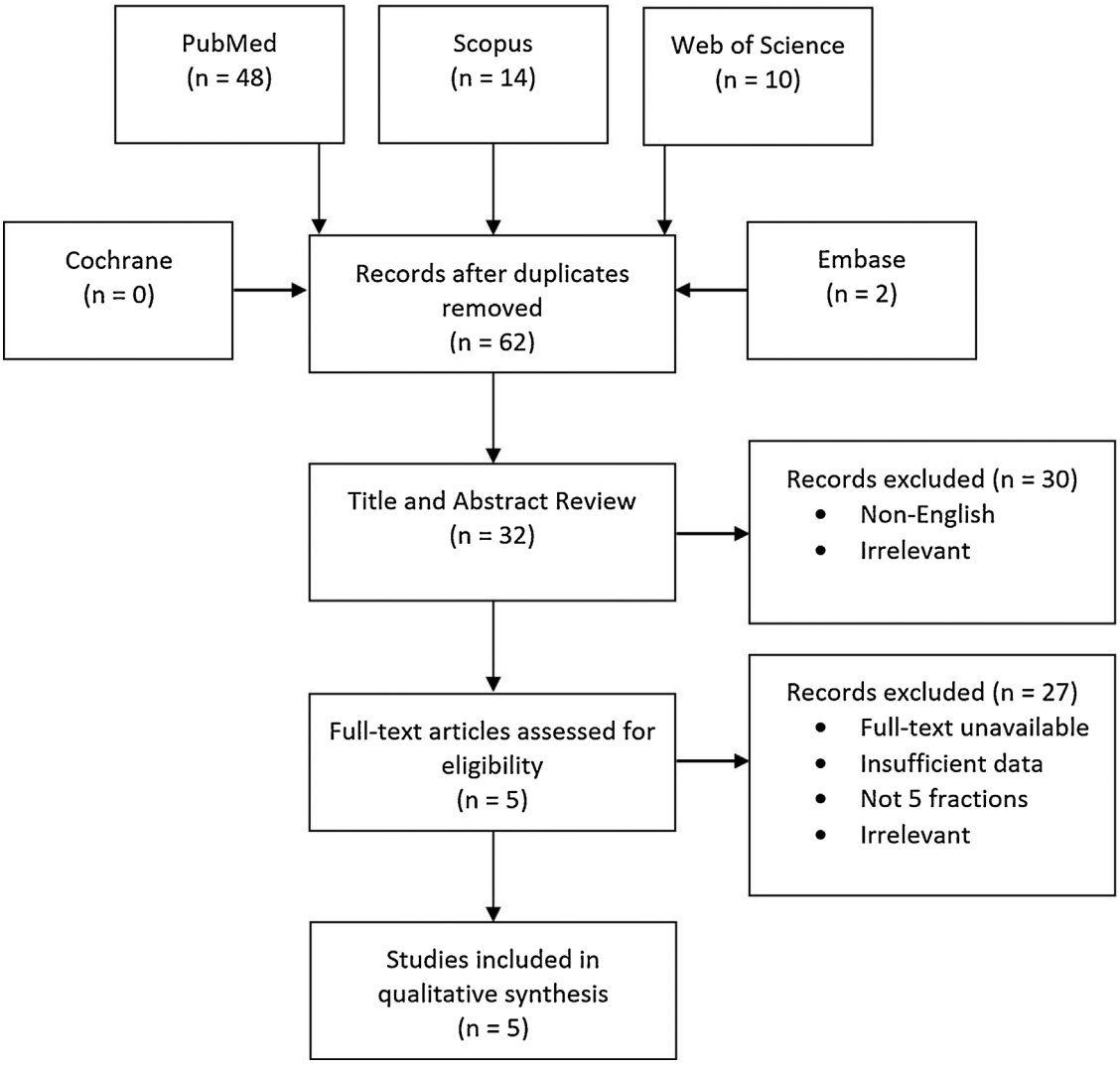

Fig. 1. Schematic diagram illustrating search strategy for hypo-fractionated stereotactic radiotherapy in five fractions for vestibular schwannomas.

comparable tumor control, and equally low complication risk to conventional FSRT (con-FSRT). Despite its recent use in treating larger VS, the clinical outcomes and safety of hypo-fractioned studies can be difficult to access between studies, because of varied dosing patterns and fractionation regimens among institutions [13–15]. Thus, there remains a need to evaluate hypo-FSRT outcomes based on a consistent singular fraction regimen. To discern the safety and efficacy of five-fraction hypo-FSRT treatments we performed a systematic review and meta-analysis with specific focus on tumor control rate, hearing preservation, and cranial nerve preservation.

2. Methods

2.1. Article selection and data collection

Adherence to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (www.prisma-statement.org) was maintained throughout this study. In this systematic review, PubMed, Scopus, Web of Science, Embase, and Cochrane databases were screened to identify relevant studies for five-fraction hypo-FSRT for patients with VS (Fig. 1). A strategic Boolean search, using the following terms: "acoustic neuroma," "vestibular schwannoma," "radiosurgery," "radiotherapy," "five fractions," "hearing," and "hypo-fractionated" was conducted. Full-text English articles that included patients with VS, treated with hypo-FSRT in exactly five fractions, were included. Papers which confounded differing fraction numbers were excluded. The bibliographies of the identified manuscripts were queried for additional relevant studies. Demographics (sex and age), radiotherapy parameters, and follow-up were extracted. Noted outcomes included rates of tumor control, hearing preservation, facial nerve preservation, and trigeminal nerve preservation. Preservation was defined as patients originally presenting with serviceable hearing, facial nerve or trigeminal nerve use, and maintained functional use post-radiotherapy. Patients with a Gardner-Robertson grade I or II before and after hypo-FSRT were scored to have preserved hearing. Patients with a House-Brackmann grade I or II pre- and post-treatment were scored to have facial nerve preservation.

2.2. Statistical analysis

Meta-analysis was performed to generate fixed and random effects estimates and confidence intervals for rates of tumor control, hearing, facial nerve, and trigeminal nerve preservation following hypo-FSRT. Heterogeneity analysis was conducted to quantify the magnitude of cross-study variability in outcome measures relative to within-study variance using τ^2, Cochran's Q, and I^2 statistics. Significance of study heterogeneity was quantified for each outcome measure based upon Cochran Q values, which are chi-square distributed. Aggregate estimates of outcome measures for which significant heterogeneity was observed were obtained using random effects analysis. If significant