Clinical Neurology and Neurosurgery 136 (2015) 20–24

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

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

Association of pituitary stalk management with endocrine outcomes and recurrence in microsurgery of craniopharyngiomas: A meta-analysis

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ARTICLE INFO

Article history:
Received 14 March 2015
Received in revised form 11 May 2015
Accepted 13 May 2015
Available online 27 May 2015

Keywords:
Craniopharyngioma
Pituitary stalk
Microsurgery
Recurrence
Endocrine function
Meta-analysis

ABSTRACT

Objective: A craniopharyngioma (CP) is a benign tumor commonly considered to originate from the pituitary stalk. However, it is still controversial as to whether the pituitary stalk should be maintained after microsurgery to resect the tumor despite its own physiological function of the pituitary stalk. In this study, meta-analysis was conducted to evaluate the influence of the pituitary stalk resection on endocrine function and tumor recurrence rate.
Methods: The relevant publications were identified by searching databases including Pubmed, Embase, Medline, and Web of Science. The extracted data were used as the basis for the meta-analysis by the RevMan 5.2 software program.
Results: Seven articles were selected, including 420 clinical cases. The meta-analysis showed that retaining the pituitary stalk might reduce the occurrence rate of diabetes insipidus (OR = 0.21, 95%CI = 0.10, 0.46, $P = 0.0001$) and the risk of potential impairment of anterior pituitary function (OR = 0.04, 95%CI = 0.01, 0.13, $P < 0.0001$). However, there was no significant relationship between craniopharyngioma recurrence and pituitary stalk treatment (i.e., preservation or resection) (OR = 1.40, 95%CI = 0.59, 3.34, $P = 0.45$).
Conclusion: The maintenance of the pituitary stalk may reduce the alterations in endocrine function and the occurrence of diabetes insipidus. However, it is not likely to enhance the recurrence rate of craniopharyngiomas.

1. Introduction

Craniopharyngioma is a benign congenital tumor originating from the residual tissue of cranialpharyngeal duct in the embryonic stage.[1] Approximately 4% of intracranial tumors are craniopharyngiomas [2–4]. However, it is the most common congenital and saddle region tumor in the children [5]. The primary treatment choice of craniopharyngioma is radical excision due to its benign nature [6,7]. Nevertheless, several critical tissues, such as optic nerve, optic chiasma, pituitary stalk, hypothalamus, the third ventricle, internal carotid artery and its branch vessels, might be injured during the microsurgery. It was reported that the epithelial squamous cell nest of the pars tuberalis of the adenohypophysis is the major source of craniopharyngioma [8]. Therefore, the handling of the pituitary stalk during surgery is important but controversial [5–7,9–16]. Although several investigations showed that maintenance of the pituitary stalk could reduce the risk of altered endocrine function complication after surgery [6,9–11], it was also frequently reported that the pituitary stalk might have lost its function due to the invasion of the craniopharyngioma [16–18]. Hence, the maintenance of the pituitary stalk might not protect the function of hypothalamus and could be a hidden danger of craniopharyngioma recurrence. This meta-analysis investigated the relevant publications to evaluate whether the preservation of the pituitary stalk in craniopharyngioma microsurgery could affect the endocrine function of the hypothalamus as well as tumor recurrence.

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http://dx.doi.org/10.1016/j.clineuro.2015.05.019
0303-8467/

2. Materials and methods

2.1. Article selection

2.1.1. Search strategy

Articles were identified via search in Pubmed, Embase, Medline, Web of Science using the key phrases "craniopharyngioma" alone and in combination of "craniopharyngioma" with "pituitary stalk", "endocrine", "recurrence" (the last search update was 28 Jan 2015). In addition, the references of all retrieved articles were checked for additional potential studies.

2.2. Inclusion/exclusion criteria

Inclusion criteria were listed as follows: (1) studies had compared the effects of pituitary stalk preservation and non-preservation on patients with craniopharyngioma, (2) studies had assessed the outcome including anterior pituitary function, diabetes insipidus or recurrence rates, (3) all the patients had available follow-up data. Studies were excluded if: (1) there were no control groups defined as patients receiving pituitary stalk non-preservation during surgery, (2) the data about anterior pituitary function, diabetes insipidus or recurrence rates were unavailable, (3) article types were reviews, meta-analysis, editorial comments and guidelines.

2.3. Data extraction and quality assessment

The following data was extracted independently from each study by two of the authors using a standardized data extraction form: study design, patient eligibility criteria, authors, date of publication, patient number, average age, gender, intraoperative handling of the pituitary stalk, extent of resection, dysfunction of anterior pituitary after surgery, occurrence rate of diabetes insipidus, and rate of tumor recurrence. Disagreements were resolved by consulting with a third author.

2.4. Outcome

We assessed the following outcomes to explore the correlation between the resection (partial resection was also considered as resection) of the pituitary stalk in craniopharyngioma microsurgery and the endocrine function change or craniopharyngioma recurrence. (The cases in which the pituitary stalk could not be identified were excluded.) The evaluation on endocrine function included the anterior pituitary function and the diabetes insipidus occurrence. Anterior pituitary function impairment was defined as dysfunction of any anterior pituitary hormone or the case in which patients received partial or total hormone replacement therapy (HRT). Diabetes insipidus occurrence was defined as the occurrence during the follow-up period, regardless that the diabetes insipidus were resolved partially or completely after a period of time, which happened in some cases [10]. The recurrence of the tumor was determined by imaging examination after surgery [5]. Pooled analysis of the association between management of the pituitary stalk and outcome adjusted by other variables were not carried out due to the unavailable data for individual subjects.

2.5. Statistical analysis

Specified outcomes were calculated by odds ratios (ORs). Moreover, the significance of the pooled OR was determined by the *Z*-test, with a *P*-value less than 0.05 being considered statistically significant. The heterogeneity between studies was assessed by the chi-square based *Q* test and I^2 test [19], and heterogeneity was considered significant when a *P*-value was less than 0.05. A random-effects (DerSimonian-Laird) model was used for pooled estimates when the heterogeneity was significant, otherwise, a fixed-effects (Mantel-Haenszel) model was applied [20]. Publication bias was investigated using visual evaluation of funnel plots and the Egger regression asymmetry test [21]. All statistical analysis was performed using Review Manager (RevMan) (Version 5.2) or STATA (version 12) software.

3. Results

3.1. Search results and study characteristics

A diagram summarizing the process of study selection is shown in Fig. 1. Our searches yielded 468 articles, of which 457 were excluded by review of titles and abstracts, because they did not meet the inclusion/exclusion criteria as they were reviews, case reports, letters to editor, comments, or duplicate studies. Further, full texts of the remaining 11 articles were reviewed and analyzed in detail. In these studies, four articles lacked control groups and were excluded. Eventually, seven studies met our criteria, with a total of 563 patients. Of these patients, 46 were dropped from the analysis since there were no follow-up data [7]. Other patients were excluded, including 5 patients who received immediate radiotherapy after surgery [5,15], two patients undergoing both transcranial surgery and gamma knife surgery before the second operation, one patient having transcranial surgery three times [16], 10 cases without ambiguous statistics [10], 16 patients with stereotactically guided cyst puncture, and/or biopsy and/or cerebrospinal fluid shunt placement [11], and 64 patients without pituitary stalk identification [11,12]. There were total 420 patients making up the study population, including 185 patients who had their pituitary stalk maintained and 235 patients who had their pituitary stalk removed. The main characteristics of the studies included in this meta-analysis are summarized in Table 1.

3.2. Anterior pituitary function

Six of the seven studies included in the meta-analysis accounted for 280 patients with anterior pituitary function data after surgery. The statistical results were obtained via a fixed-effect model and showed homogeneity ($P = 0.76$, $I^2 = 0\%$). According to the meta-analysis, the preservation of the pituitary stalk significantly

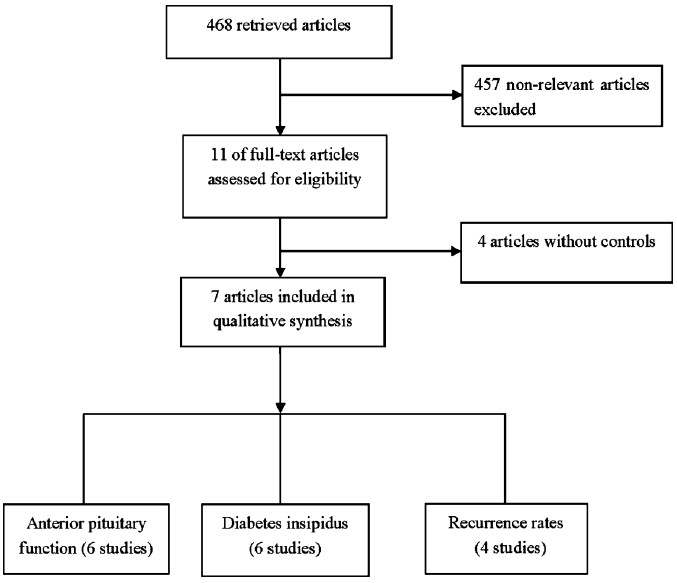

Fig. 1. Study selection procedures for the present meta-analysis.