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Comparison of operative outcomes of eloquent glioma resection performed under awake versus general anesthesia: A systematic review and meta-analysis

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ABSTRACT

Surgical resection of eloquent glioma can be achieved under general anesthesia (GA) or awake anesthesia (AA). The appeal of AA is that it facilitates intraoperative identification and avoidance of eloquent areas, which has the potential to minimize functional compromise. The aim of this meta-analysis was to compare the operative outcomes of eloquent glioma resection performed under GA compared to AA to assist in optimizing the decision algorithm between the two approaches. Searches of seven electronic databases from inception to December 2017 were conducted following Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines. There were 1037 articles identified for screening. Data were extracted and analyzed using meta-analysis of proportions. A total of 9 comparative studies were included for analysis. Resection of glioma involving eloquent areas achieved under AA is mostly comparable in terms of operative and functional outcomes to that of GA. AA did demonstrate significantly lower incidence of postoperative nausea and vomiting (PONV, OR, 0.17; $p < 0.001$) and shorter length of stay (LOS, MD, -1.76 days; $p = 0.02$) when compared to GA. Future studies that are larger, prospective, randomized, and include long term quality of life metrics will assist in elucidating the true clinical benefit of AA in resecting glioma involving eloquent areas. This will assist in further developing management protocol of these glioma.

1. Introduction

Traditionally, the use of general anesthesia (GA) has allowed surgeons to capably attempt maximal safe resection of intracranial glioma. The emergence of awake anesthesia (AA) approach has proved to be a viable alternate option. The key feature of AA is that the patient is responsive during surgery [1]. With the use of cortical or subcortical direct electrical stimulation, surgeons are able to identify functional, eloquent areas intraoperatively [2]. The advantage of this is two-fold [3]. Firstly, the surgeon is able to pursue greater resection of non-functional tissue with glioma invasion. Secondly, the surgeon is also able to avoid functional tissue which makes these areas eloquent. This avoids otherwise functional compromise postoperatively should these areas be interrupted. Ultimately, AA with or without cortical mapping has permitted surgeons to safely approach tumors historically deemed suboptimal for resection due to proximity to eloquent brain [4].

Despite the pragmatic appeal of AA as an anesthetic option in the management of eloquent glioma, there is a paucity of literature comparing the operative outcomes of performed under AA versus GA. While the concept of AA is not completely novel, a greater familiarity of resection under GA has the possible ability to influence a surgeon's decision algorithm in the absence of evidence of superior outcomes otherwise. Furthermore, patient wellbeing, doctor aptitude, the required support staff, as well as the potential for intraoperative pain during AA may limit its applicability to eloquent glioma resection [5]. Should there be distinct operative gains achieved under one approach, then these findings should be incorporated more into the decision algorithm of managing eloquent glioma in the future. The aim of this meta-analysis was to collate and compare operative outcomes of eloquent glioma resections performed either under AA or GA based on all available comparative studies to date.

2. Methods

2.1. Search strategy

The strategy was designed around the PICO question format - Do patients with intracranial glioma presenting in eloquent areas

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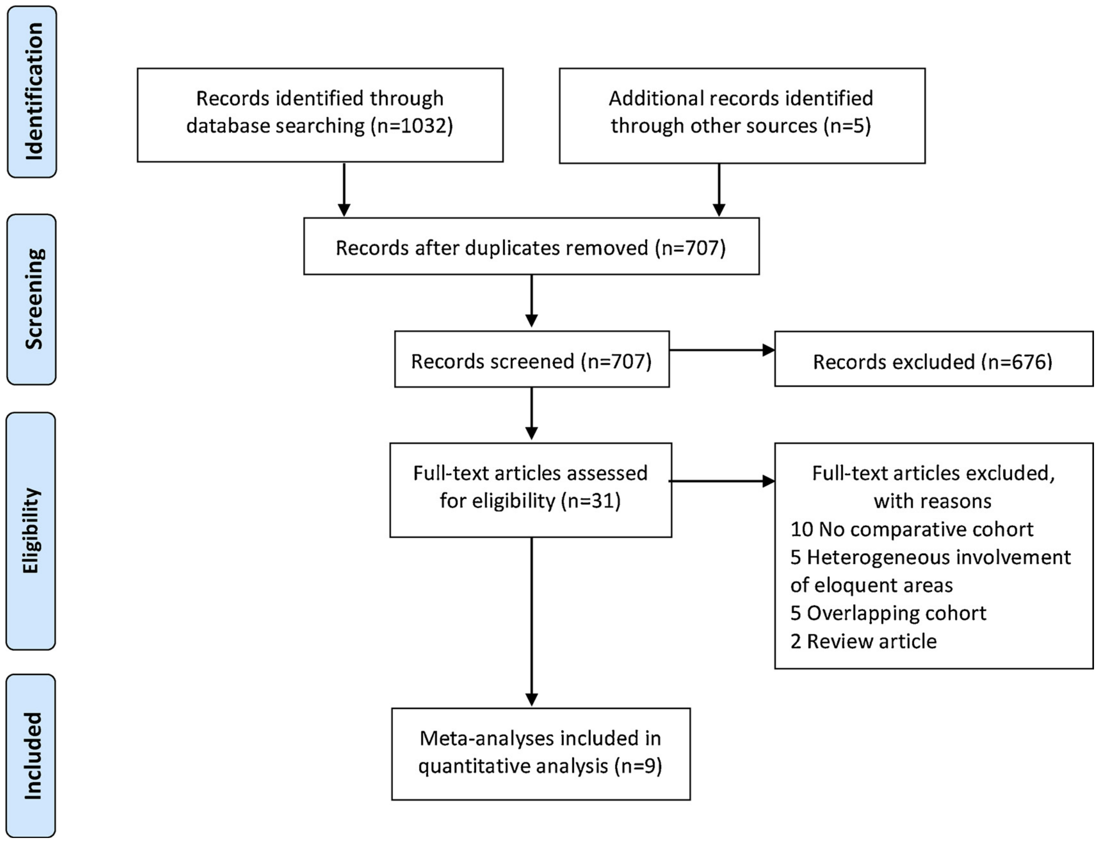

Fig. 1. Search strategy results.

(Population) surgically treated by resection under AA (Intervention) compared to those treated under GA (Comparator) differ in operative outcomes (Outcome)? The present review was conducted according to PRISMA guidelines and recommendations [6]. Electronic searches were performed using Ovid Embase, PubMed, SCOPUS, Cochrane Central Register of Controlled Trials (CCTR), Cochrane Database of Systematic Reviews (CDSR), American College of Physicians (ACP) Journal Club and Database of Abstracts of Review of Effectiveness (DARE) from their dates of inception to December 2017. The literature involving all comparative studies were searched by using the following MeSH terms in all logical permutations: 'awake craniotomy', 'awake anesthesia', 'direct electrical stimulation', 'surgery', 'tumor', and 'glioma'. The reference lists of all retrieved articles were reviewed independently by two investigators (V.M.L. and K.P.) for further identification of potentially relevant studies. All identified articles were then systematically assessed against the inclusion and exclusion criteria.

2.2. Selection criteria

The inclusion criteria used to screen all identified articles were 1) reported clinical outcomes of separate AA and GA cohorts, 2) surgical resection for histologically confirmed glioma, with or without neuronavigation 3) located in an eloquent area, and in 4) patients > 18 years. The exclusion criteria applied to all identified articles were 1) mixed cohorts with indiscernible pediatric cases, 2) treatment for extracranial glioma, and 3) intraoperative imaging, e.g. ultrasound. When institutions published duplicate studies with accumulating numbers of patients or increased lengths of follow-up, and when studies reported multiple time courses of the same treated cohort, only the most complete reports were included for quantitative assessment at each time interval. All publications were limited to those involving human subjects and in the English language. Reviews, abstracts, case reports, conference presentations, editorials and expert opinions were excluded to minimize potential publication bias and duplication of results.

2.3. Data extraction and critical appraisal

All data were extracted from article texts, tables and figures with any estimates made based on the presented data and figures. This includes variance estimations based on established statistical methodologies when appropriate [7–9]. Clinical outcomes of interest were; operative outcomes – blood loss, operation time, intraoperative seizures; resection outcomes – extent of resection (EOR), gross total resection (GTR); postoperative outcomes – complications, postoperative nausea and vomiting (PONV), length of stay (LOS), follow-up Karnofsky Performance Score (KPS); and functional outcomes– immediate and follow-up neurological status, transient and permanent motor and languages deficits. Two investigators (V.M.L. and K.P.) independently reviewed each included article with any discrepancy resolved by discussion to reach consensus. All attempts were made to contact study authors for any clarification of data if needed. Because quality scoring is controversial in meta-analyses of observational studies, each article included in our analysis was appraised according to the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) criteria [10].

2.4. Meta-analysis

The mean difference (MD) and odds ratio (OR) were used as the summary statistics for each relevant outcome. Each outcome was presented as a forest plot; the weighted MD or OR, the 95% Confidence Interval (CI) and the relative weightings were represented by the middle of the square, the horizontal line, and the relative size of the square respectively. The dotted line represents the pooled mean of the statistic. The I^2 statistic was used to estimate the percentage of total variation across studies, owing to heterogeneity rather than chance, with values greater than 50% considered as substantial heterogeneity