

ABSTRACT

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Intraoperative 5-ALA fluorescence-guided resection of high-grade glioma leads to greater extent of resection with better outcomes: a systematic review.

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IMPORTANCE: High-grade gliomas (HGG) are the most aggressive and common malignant brain tumors in adults. They have a dismally fatal prognosis. Even if gross total resection of the enhancing tumor is achieved, inevitably, invading tumor cells that are indistinguishable to the un-aided eye are left behind, which eventually leads to tumor recurrence. 5-aminolevulinic acid (5-ALA) is an increasingly utilized intraoperative fluorescent imaging agent for patients with HGG. It enhances visualization of HGG tissue. Despite early promising randomized clinical trial data suggesting a survival benefit for 5-ALA-guided surgery, the growing body of literature must be analyzed to confirm efficacy on patient outcomes.

OBJECTIVE: To perform a systematic review of the literature to evaluate whether there is a beneficial effect upon survival and extent of resection due to the utilization of 5-ALA in HGG surgery.

EVIDENCE REVIEW: Literature regarding 5-ALA usage in HGG surgery was reviewed according to the PRISMA guidelines. Two databases, PubMed and SCOPUS, were searched for assorted combinations of the keywords "5-ALA," "high-grade glioma," "5-aminolevulinic acid," and "resection" in July 2020 for case reports and retrospective, prospective, and randomized clinical trials assessing and analyzing 5-ALA intraoperative use in patients with HGG. Entailed studies on PubMed and SCOPUS were found for screening using a snowball search technique upon the initially searched papers. Systematic reviews and meta-analyses were excluded from our PRISMA table.

FINDINGS: 3756 previously published studies were screened, 536 of which were further evaluated, and ultimately 45 were included in our systematic review. There were no date restrictions on the screened publications. Our literature search was finalized on July 16, 2020. We found an observed increase in the overall survival (OS) and progression-free survival (PFS) of the 5-ALA group compared to the white light group, as well as an observed increase in the OS and PFS of complete resections compared to incomplete resections. Of the studies that directly compared the use of 5-ALA to white light (13 of the total analyzed 45, or 28.9%), 5-ALA lead to a better PFS and OS in 88.4 and 67.5% of patients, respectively. When the studies that reported postoperative neurologic outcomes of surgeries using 5-ALA vs. white light were analyzed, 42.2% of subjects demonstrated 5-ALA use was associated with less post-op neurological deficits, whereas 34.5% demonstrated no difference between 5-ALA and without. 23.3% of studies showed that intraoperative 5-ALA guided surgeries lead to more post-op neurological deficits.

CONCLUSIONS AND RELEVANCE: Utilization of 5-ALA was found to be associated with a greater extent of resection in HGG surgeries, as well as longer OS and PFS. Postop neurologic deficit rates were mixed and inconclusive when comparing 5-ALA groups to white light groups. 5-ALA is a useful surgical adjunct for resection

of HGG when patient safety is preserved.

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