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5-Aminolevulinic Acid Hydrochloride–Guided Surgical Resection of High-Grade Gliomas

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Key Messages

- One health technology assessment, 4 systematic reviews (1 with network meta-analysis and 1 with meta-analysis), and 2 non-randomized studies were identified regarding the clinical effectiveness of 5-aminolevulinic acid hydrochloride–guided surgical resection for adults with suspected high-grade gliomas.
- One systematic review was identified regarding the cost-effectiveness of 5-aminolevulinic acid hydrochloride–guided surgical resection for adults with suspected high-grade gliomas.

Research Questions

1. What is the clinical effectiveness of 5-aminolevulinic acid hydrochloride–guided surgical resection for adults with suspected high-grade gliomas?
2. What is the cost-effectiveness of 5-aminolevulinic acid hydrochloride–guided surgical resection for adults with suspected high-grade gliomas?

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, the Cochrane Database of Systematic Reviews, the international HTA database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were 5-aminolevulinic acid hydrochloride–guided surgery and gliomas. No filters were applied to limit the retrieval by study type. Comments, newspaper articles, editorials, and letters were excluded. Where possible, retrieval was limited to the human population. The search was also limited to English-language documents published between January 1, 2019 and June 30, 2021. Internet links were provided, where available.

Selection Criteria

One reviewer screened literature search results (titles and abstracts) and selected publications according to the inclusion criteria presented in Table 1. Full texts of study publications were not reviewed.

Results

One health technology assessment,[1] 4 systematic reviews[2,4-6] (1 with network meta-analysis[2] and 1 with meta-analysis[5]) and 2 non-randomized studies[7,8] were identified regarding the clinical effectiveness of 5-aminolevulinic acid hydrochloride–guided surgical resection for

Table 1: Selection Criteria

Criteria	Description
Population	Adults with suspected high-grade gliomas (defined as WHO grade III or grade IV tumours)
Intervention	5-aminolevulinic acid hydrochloride–guided surgical resection
Comparator	Standard surgical care or surgery guided by alternative intraoperative imaging technologies (e.g., white-light microscopy, neuronavigation, MRI, ultrasound)
Outcomes	Q1: Clinical effectiveness (e.g., extent of tumour resection, overall survival, progression-free survival, quality of life, neurologic function, safety [e.g., adverse events]) Q2: Cost-effectiveness (e.g., cost per quality-adjusted life-year gained)
Study designs	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies, economic evaluations

Q = question.

adults with suspected high-grade gliomas. One systematic review[3] was identified regarding the cost-effectiveness of 5-aminolevulinic acid hydrochloride–guided surgical resection for adults with suspected high-grade gliomas. No relevant randomized controlled trials or economic evaluations were identified.

Additional references of potential interest that did not meet the inclusion criteria are provided in Appendix 1.

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References

Health Technology Assessments

1. Ontario Health (Quality). 5-aminolevulinic acid hydrochloride (5-ALA)-guided surgical resection of high-grade gliomas: a health technology assessment. *Ont Health Technol Assess Ser*. 2020;20(9):1-92. PubMed

Systematic Reviews and Meta-analyses

2. Golub D, Hyde J, Dogra S, et al. Intraoperative MRI versus 5-ALA in high-grade glioma resection: a network meta-analysis. *J Neurosurg*. 2020 Feb 21:1-15. PubMed

3. Warsi NM, Zewude R, Karmur B, Pirouzmand N, Hachem L, Mansouri A. The cost-effectiveness of 5-ALA in high-grade glioma surgery: a quality-based systematic review. *Can J Neurol Sci*. 2020 11;47(6):793-799. PubMed

4. Coburger J, Wirtz CR. Fluorescence guided surgery by 5-ALA and intraoperative MRI in high grade glioma: a systematic review. *J Neurooncol*. 2019 Feb;141(3):533-546. PubMed

5. Gandhi S, Tayebi Meybodi A, Belykh E, et al. Survival outcomes among patients with high-grade glioma treated with 5-aminolevulinic acid-guided surgery: a systematic review and meta-analysis. *Front Oncol*. 2019;9:620. PubMed

6. Suero Molina E, Schipmann S, Stummer W. Maximizing safe resections: the roles of 5-aminolevulinic acid and intraoperative MR imaging in glioma surgery-review of the literature. *Neurosurg Rev*. 2019 Jun;42(2):197-208. PubMed

Randomized Controlled Trials

No literature identified.

Non-Randomized Studies

7. Baig Mirza A, Christodoulides I, Lavrador JP, et al. 5-Aminolevulinic acid-guided resection improves the overall survival of patients with glioblastoma-a comparative cohort study of 343 patients. *Neurooncol Adv*. 2021 Mar;3(1):vdab047. PubMed

8. Hansen RW, Pedersen CB, Halle B, et al. Comparison of 5-aminolevulinic acid and sodium fluorescein for intraoperative tumor visualization in patients with high-grade gliomas: a single-center retrospective study. *J Neurosurg*. 2019 Oct 04:1-8. PubMed

Economic Evaluations

No literature identified.

Appendix 1: References of Potential Interest

Systematic Reviews and Meta-analyses

Unclear Population (Grade of Glioma Not Specified)

9. Fountain DM, Bryant A, Barone DG, et al. Intraoperative imaging technology to maximise extent of resection for glioma: a network meta-analysis. *Cochrane Database Syst Rev*. 2021 Jan 04;1(1):CD013630. PubMed

10. Ye D, Yu T, Shi J, Piao H. Comparison of intraoperative magnetic resonance imaging, ultrasound, 5-aminolevulinic acid, and neuronavigation for guidance in glioma resection: A network meta-analysis. *Glioma*. 2020;3(1):3-12. https://www.jglioma.com/article.asp?issn=2589-6113;year=2020;volume=3;issue=1;spage=3;epage=12;aulast=Ye. Accessed 2021 Jul 6.

Unclear Comparator

11. Haider SA, Lim S, Kalkanis SN, Lee IY. The impact of 5-aminolevulinic acid on extent of resection in newly diagnosed high grade gliomas: a systematic review and single institutional experience. *J Neurooncol*. 2019 Feb;141(3):507-515. PubMed

12. Picart T, Berhouma M, Dumot C, et al. Optimization of high-grade glioma resection using 5-ALA fluorescence-guided surgery: A literature review and practical recommendations from the neuro-oncology club of the French society of neurosurgery. *Neurochirurgie*. 2019 Aug;65(4):164-177. PubMed

Non-Randomized Studies — Mixed Intervention

13. Della Pepa GM, Ius T, La Rocca G, et al. 5-aminolevulinic acid and contrast-enhanced ultrasound: the combination of the two techniques to optimize the extent of resection in glioblastoma surgery. *Neurosurgery*. 2020 06 01;86(6):E529-E540. PubMed

14. Bassaganyas-Vancells C, Roldan P, Gonzalez JJ, et al. Combined use of 5-aminolevulinic acid and intraoperative low-field magnetic resonance imaging in high-grade glioma surgery. *World Neurosurg*. 2019 Oct;130:e206-e212. PubMed

Review Articles

15. Yamamoto J, Kitagawa T, Miyaoka R, et al. 5-aminolevulinic acid: pitfalls of fluorescence-guided resection for malignant gliomas and application for malignant glioma therapy. *J UOEH*. 2020;42(1):27-34. PubMed

16. Navarro-Bonnet J, Suarez-Meade P, Brown DA, Chaichana KL, Quinones-Hinojosa A. Following the light in glioma surgery: a comparison of sodium fluorescein and 5-aminolevulinic acid as surgical adjuncts in glioma resection. *J Neurosurg Sci*. 2019 Dec;63(6):633-647. PubMed