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Surgical Management of G3 Gastroenteropancreatic Neuroendocrine Neoplasms: A Systematic Review and Meta-Analysis

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BACKGROUND

Grade 3 (G3) gastroenteropancreatic (GEP) neuroendocrine neoplasms (NENs) are rare, aggressive tumors with poor prognosis. The WHO 2017 classification further subdivided G3 NENs into G3 neuroendocrine tumors (NETs) and neuroendocrine carcinomas (NECs). Current guidelines favor medical management in most of these patients, and the role of surgical management is not well-defined. We performed a systematic literature review and meta-analysis of surgical management vs non-surgical management for G3 GEP NENs.

METHODS

A PRISMA-compliant systematic review of the MEDLINE, EMBASE, Scopus, and Cochrane Library databases (end-of-search date: July 16th, 2021) was conducted. Individual patient survival data were reconstructed, and random-effects meta-analyses were performed.

RESULTS

Fourteen studies comprising 1,810 surgical and 910 non-surgical patients were systematically reviewed. Publication bias adjusted meta-analysis of 12 studies (1,788 surgical and 857 non-surgical patients) showed increased overall survival (OS) after surgical compared with non-surgical management for G3 GEP NENs (HR: 0.40, 95%CI, 0.31-0.53). Subgroup meta-analyses showed increased OS after surgical management for both pancreatic and gastrointestinal primary tumor sites separately. In another subgroup meta-analysis of G3 GEP NETs (not NECs), surgical management was associated with increased OS compared with non-surgical management (HR: 0.26, 95%CI, 0.11-0.61) (Table).

Table. Comparison of Survival in GEPNENs treated Surgically or Non-Surgically.

Classification	Studies, n	Patients, n (surgery vs non-surgery)	Hazard Ratio (<1 favors surgery)	95% Confidence Interval
G3 GEP NEN (NET & NEC)	12	1,788 vs 857	0.40	0.31-0.53
G3 Pancreatic NEN (NET & NEC)	8	451 vs 370	0.31	0.24-0.40
G3 Gastrointestinal NEN (NET & NEC)	3	1,207 vs 379	0.42	0.34-0.52
G3 GEP NET (not NEC)	3	62 vs 25	0.26	0.11-0.61

CONCLUSIONS

Surgical management of G3 GEP NENs may provide a potential survival benefit in well-selected cases. Further research is needed to define which patients will benefit most from surgical vs non-surgical management. The current literature is limited by inconsistent reporting of survival outcomes in surgical vs non-surgical groups, tumor grade, differentiation, primary tumor site, and selection criteria for surgical and non-surgical management.

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