



Evolution of Surgical Management and Outcomes of Neuroendocrine Tumor Liver Metastases

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There are more treatment options available to patients diagnosed today with neuroendocrine tumor liver metastases (NELM) than ever before. Over the past few decades, the increased use of somatostatin analogues, combination chemotherapy, liver-directed therapy, and PRRT has paralleled improvements in perioperative safety and surgical technique to revolutionize the care for patients with NETLM. There is still, however, much to be gained in oncologic outcomes and quality of life for our patients with NETLM. As systemic and liver-directed therapy continue to evolve, it will be increasingly important to quantify the outcomes of cytoreductive surgery and to identify optimal pathways for treatment sequencing. To answer these questions, it is helpful to gain a perspective of outcomes over time in the surgical management of this rare and heterogeneous group of diseases.

Such perspective is well represented in the recently published article by Gudmundsdottir et al., which analyzes outcomes over 21 years from one institution and 546 patients with NETLM from mostly small bowel and pancreas primary sites.¹ This large, retrospective cohort study includes patients who underwent cytoreductive hepatectomy between the years 2000 and 2020, spanning the publication of the PROMID, CLARINET, Radiant-4, and ECOG2211 trials

and the development of the Dotatate scan, each of which had a significant impact on the standard of care for NETLM. This article is best read side by side with a previous review from the same institution analyzing 170 cases of NETLM since the beginning of cytoreductive hepatectomy in 1977 and until 1998.² Compared with their previous cohort, the proportion of patients who underwent major hepatectomy decreased from 54%² to 27%.¹ This proportion further decreased within the second cohort. Whereas the first cohort discussed radiofrequency ablation as an alternative to cytoreductive hepatectomy, the second includes the increasingly frequent use of ablation as an intraoperative adjunct to cytoreduction. Despite these changes, the current study reported 96% effectiveness in achieving complete symptomatic relief for symptomatic patients, which is the same percentage as the success for symptomatic control in the previous cohort. The current study also reported significantly improved overall survival at 5 years of follow-up, up to 81% in its most recent 7-year period compared with 61% in the previous cohort.^{1,2} These changes over time reflect trends in surgical management for NETLM, emphasizing parenchymal-sparing cytoreduction and the use of adjuncts to achieve sustained symptomatic relief and prolong progression-free survival. The current study found a 6.2% incidence of posthepatectomy liver failure among patients who underwent major hepatectomy, highlighting the benefits of a parenchymal-sparing approach when feasible.¹

The art and science of medicine in managing patients with NETLM remains in the selection and sequencing among the several contemporary options available for systemic, liver-directed, and surgical management of these patients. Retrospective cohort studies, such as Gudmundsdottir et al.'s, are helpful to establish benchmarks for outcomes and safety. Other large cohorts, such as Fairweather et al.'s cohort of 649 patients, have compared cytoreductive hepatectomy to nonoperative management, finding superior outcomes for hepatectomy.³ These results are informative;

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however, their interpretation must keep in mind that multivariable analysis on observational studies will still have some residual confounding and does not fully account for selection bias. Certainly, more prospective research needs to focus on estimating the comparative effectiveness of different treatment options for specific patient populations, such as patients with large-volume disease and extrahepatic metastatic lesions. The same applies to patients with higher numbers of NETLMs, which had not been previously found to be correlated with worse overall and progression-free survival but were found to have worse outcomes in the present study.^{1,4} Additionally, the optimal management of disease progression remains to be clarified. Gudmundsdottir et al. included 41 patients who underwent second cytoreductive hepatectomy for disease progression.¹ The risks and benefits of repeat resection should be compared with PRRT and other adjuvant therapy in future studies to provide more information to clinicians and patients facing the likely outcome of disease progression after cytoreduction for NETLM. It is a good problem to have that the evolving options for managing patients with NETLM have produced an intricate field that is more difficult to navigate than previously. It is our responsibility to match the advances in diagnosis, surveillance, and treatment of NETLM with granular data on surgical outcomes to provide adequate information for individualized decision-making and maximize our patient's quality of life and oncologic outcomes.

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