Updates in Transarterial Chemoembolization in Neuroendocrine Liver Metastases

The Ohio State University College of Medicine; Wexner Medical Center; Department of Radiology; Division of Interventional Radiology

Maria Lysandrou, BA, John Heyniger, BS, Mina S. Makary, MD

THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

Background

- Neuroendocrine tumors (NETs) are heterogeneous neoplasms arising in sites such as the gut, pancreas, and lung. Two-thirds of NETs occur in the gastroenteropancreatic (GEP) system, with an incidence that has increased six-fold since 1973.
- Up to 80% of GEP-NET patients develop liver metastases (NELMs), a clinically significant complication of neuroendocrine tumors, often representing the dominant site of disease progression and conferring poorer outcomes. While well-differentiated GEP-NETs may behave indolently, up to 80% of patients will develop NELM over their disease course, of which the liver is the most common site of metastasis, conferring significant clinical progression
- NELM management is complex and highly individualized. Systemic cytotoxic chemotherapy fails to control disease progression or improve overall survival (OS) in many patients, so it is generally not pursued.
- Given the limited efficacy of systemic cytotoxic chemotherapy and few patients being ideal candidates for surgical resection, liver-directed locoregional therapies (some examples are transarterial chemoembolization, transarterial embolization, and transarterial radioembolization) have emerged as a central tenet of disease management, offering symptomatic relief, cytoreduction, and in certain cases, improved survival.

Materials and Methods

- A comprehensive review of literature was conducted through PubMed and Google Scholar database. focusing on overall survival (OS), progression-free survival (PFS), tumor response, and symptom control to evaluate the clinical outcomes of conventional TACE (cTACE) and drug-eluting bead TACE (DEB-TACE) in patients with NELM. This included an analysis of clinical trials, retrospective studies, and meta-analyses between 2020 and 2025.
- We present some findings from recent studies and discuss potential future directions in this area

Purpose

- Transarterial chemoembolization (TACE) is a well-established locoregional therapy for neuroendocrine liver metastases (NELM), offering both ischemic and chemotoxic effects. The purpose of this educational exhibit is to present an evidence-based update on the efficacy, prognostic factors, and potential of TACE in the management of NELM.

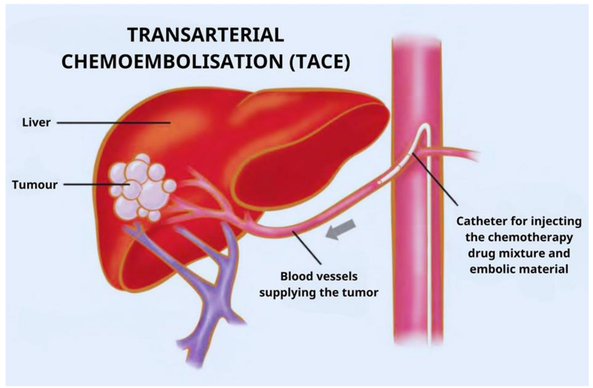

Figure 1: Illustration of the Transarterial Chemoembolization (TACE) liver procedure. Reference: https://tinyurl.com/mpvudazf

Results

- TACE is a well-established approach for symptom control with symptomatic improvement observed in approximately 80% of patients undergoing cTACE and 50% of those treated with DEB-TACE.
- Median OS varied across studies ranging from 30-44 months with some larger cohorts reporting survival beyond 5 years, with a 5 year OS for cTACE reporting between 28-36%.
- Tumor response assessed by the mRECIST criteria correlates with longer OS (80.5 months in responders vs 39.4 months in non-responders).
- Patients with pancreatic NET metastases have shorter OS (27.6 months) compared to non-pancreatic NETs (55 months), while PFS remains similar. Poor prognostic factors include extrahepatic disease, liver tumor burden ≥70%, impaired hepatic function, and elevated neutrophil-to-lymphocyte ratios.
- While cTACE may offer better symptom relief and OS in carcinoid syndrome, DEB-TACE is favored in patients with poor liver function due to fewer post-embolization effects.
- Although the recent RETNET trial raised safety concerns for DEB-TACE, recent studies suggest a tolerable safety profile. TACE and TAE demonstrate similar outcomes for OS, PFS, and symptom control.

Conclusions

- TACE remains a cornerstone therapy for NELM, with strong evidence for symptom control and prolonged survival. While cTACE is often preferred, DEB-TACE may still hold value for select patients, particularly those with compromised liver function, as emerging data challenges prior safety concerns.
- Direct comparisons between TAE and TACE are limited, but current evidence suggests similar efficacy, warranting individualized treatment selection based on patient comorbidities, liver function, and tumor characteristics.

Future Directions

Locoregional therapies continue to evolve offering promising directions for the management of NELM. Here are trials with these directions.

- **Peptide receptor radionuclide therapy (PRRT)** with ^{177}Lu-DOTATATE (Lutathera) is an emerging targeted treatment for well-differentiated GEP-NETs (grades 1–2).
- **NETTER-1 trial**:
  - Demonstrated significant improvement in PFS (28.4 vs. 8.5 months).
  - Showed longer mean OS (48 vs. 36.3 months), though not statistically significant.
  - Reported low toxicity with good tumor control.
  - Led to FDA approval for adults (2018) and children ≥12 years (2024).
- **NETTER-2 trial**:
  - Compared ^{177}Lu-DOTATATE + octreotide LAR vs. octreotide LAR alone in higher-grade NETs (G2–G3).
  - Showed median PFS extension of 14 months (22.8 vs. 8.5 months).
  - Results may shift the first-line treatment landscape for GEP-NETs.
- **LUTIA trial**:
  - Tested intra-arterial vs. intravenous administration of ^{177}Lu-DOTATATE.
  - No significant difference in tumor uptake between intra-arterial and IV groups.
  - Possible explanation: high vascularization of liver causing drug loss to urinary excretion.
  - Despite underwhelming results, provides foundation for further refinement of intra-arterial PRRT approaches.

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