Anthem

Medical Policy

Subject: Catheter-based Embolization Procedures for Malignant Lesions Outside the Liver
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Description/Scope

This document addresses the use of transcatheter arterial chemoembolization (TACE) and transcatheter arterial embolization (TAE) for malignant lesions outside the liver. These catheter-based embolization procedures are proposed as adjunct therapeutic interventions prior to operative resection or for palliation of symptoms.

Note:

- This document does not address malignant lesions of the central nervous system (intracranial and spinal).
- This document does not address TACE or TAE as therapeutic interventions for actively *bleeding* malignant or non-malignant lesions, or for services addressed in any of the documents noted below.
- This document does not address benign tumors.

Note: For additional information please refer to the following related documents:

- CG-SURG-28 Transcatheter Uterine Artery Embolization
- CG-SURG-61 Cryosurgical, Radiofrequency, Microwave or Laser Ablation to Treat Solid Tumors Outside the Liver
- CG-SURG-78 Locoregional Techniques for Treating Primary and Metastatic Liver Malignancies

Position Statement

Investigational and Not Medically Necessary:

Transcatheter arterial chemoembolization and transcatheter arterial embolization are considered **investigational and not medically necessary** for malignant lesions outside the liver.

Rationale

TACE and TAE are catheter-based embolization procedures performed with or without chemotherapeutic agents. TACE involves the regional injection of a form of chemotherapeutic or antitumor agent immediately followed by injection of an embolizing agent into the arterial vasculature supplying a tumor. TAE involves injecting an embolizing agent without a chemotherapeutic agent into the arterial vasculature. Both procedures have a tumoricidal effect on the targeted malignant tumor(s) and have been proposed for tumor destruction, preoperative tumor bulk reduction and palliative treatment. While there are data in the peer-reviewed literature to support TACE and TAE for hepatic (liver) indications, there is limited evidence supporting their use for non-hepatic malignant indications.

TAE for Malignant Carotid Body Tumors

Bercin and colleagues (2015) conducted a small retrospective case series to determine the efficiency of preoperative embolization on vascular rupture rates during surgery in individuals with malignant carotid body tumors. A total of 13 records were included in the analysis that compared preoperative carotid body tumor embolization (n=7 cases) to no tumor embolization (n=6 cases). Data was collected on demographics, preoperative anatomical presentation of the carotid artery (including blood flow), tumor size, and complications of embolization (blood loss, other injury). The mean age of participants was 48 years (range, 22-70 years); 12 of 13 participants had stage II tumors with a mean diameter of 4.42 centimeters. Relative rates of blood flow reduction during embolization were greater than 50% in 4 participants and 25%-50% in 3 participants. Carotid artery injury was recorded in 4 embolized participants (57%) and 1 non-embolized participant. There were no significant differences between carotid artery rupture and embolization, blood loss, tumor size, and supplying artery. The authors concluded that the benefit of embolization before surgical excision of carotid body tumor is “controversial” and “does not appear to be an advantage in reducing intraoperative blood loss, ease of dissection, and reducing the duration of the operative procedure following embolization.”

The National Comprehensive Cancer Network® (NCCN) Clinical Practice Guideline (CPG) in Oncology® for head and neck cancer (2024) does not address TACE or TAE for carotid body tumors.

TACE and TAE for Malignant Kidney Cancer

Renal artery embolization (RAE) has been used as an adjunct procedure prior to resection of locally advanced malignant renal tumors, but its role remains controversial given the lack of randomized prospective trials demonstrating a clinical benefit. Initially it was hypothesized that preoperative TAE may lead to improved survival in individuals with renal cell carcinoma (RCC) through immunomodulation, where TAE-induced tumor necrosis promoted tumor-specific natural killer cells (Bakke, 1982).

Liu and colleagues (2008) conducted a randomized, prospective trial in China investigating TACE followed by tumor resection in children diagnosed with Wilms’ tumor. A cohort of 44 children (ages 6 months to 12 years) were randomized to treatment with preoperative TACE (n=24) or tumor resection alone (n=20, control group). The 2-year tumor-free survival rate was 83.3% in the TACE group compared to 10% in the control group ($p<0.001$). The rate of tumor recurrence and death within 1 year was 16.6% (4 of 24) in the TACE group compared to 60% (12 of 20) in the control group ($p<0.001$). While the results of this small study suggest that children with Wilms’ tumor may benefit from preoperative TACE, randomized comparative trials of larger sample size are needed to confirm these preliminary findings.

Zielinski and colleagues (2000) retrospectively compared the survival benefit of preoperative RAE followed by radical nephrectomy (n=118) to radical nephrectomy alone (n=116) in a matched group analysis of participant selected from a series of 474 individuals with RCC. Individuals were selected for embolization based on preference of the urologist responsible for their care. As a result of this selection process, criteria for preoperative embolization was difficult to define; however, embolized participants were expected to have T2-T3 tumors, tumors > 6 cms (as demonstrated on preoperative imaging studies), M0 disease, and good performance status. The timing of embolization prior to surgery ranged from 1 to 3 days (66 participants, 56%), 4 days (22 participants, 19%), and 5 to 13 days

(30 participants, 25%). Embolization was performed most frequently with a gelatin sponge product or wire coil device. The overall 5- and 10-year survival for the 118 participants embolized before nephrectomy was 62% and 47%, respectively, and 35% and 23%, respectively for the matched group of 116 participants treated with surgery alone (p=0.01). The reported favorable survival benefit associated with preoperative TAE for RCC needs to be interpreted with caution, as the data was derived from a nonrandomized, single-institution clinical trial.

TAE has been proposed to facilitate dissection secondary to resultant tissue plane edema, reduce blood loss, and decrease the extent of tumor thrombus in the preoperative management of RCC. These benefits have been evaluated in small case series and uncontrolled studies and have not been established in large, randomized, prospective trials. May and colleagues (2009) conducted a matched-pair retrospective study of individuals treated with RAE prior to nephrectomy (Group 1; n=189) or nephrectomy alone (Group 2; n=189) for RCC. Pairing of participants was based on age, gender, clinical tumor size, grading, staging histology and microvascular invasion. Cancer specific survival and overall survival were defined as the primary endpoints. Cancer specific survival at 1, 5, and 8 years for Group 1 was 95%, 79%, and 70%; and, for Group 2, 93%, 83%, and 79% (p=0.085), respectively. Overall survival at 1, 5, and 8 years for Group 1 was 93%, 73%, and 62%; and, for Group 2, 91%, 75%, and 67%, respectively (p=0.677). Based on this data, the authors concluded that RAE prior to nephrectomy did not improve clinical outcomes or demonstrate a survival benefit for individuals with RCC.

The National Comprehensive Cancer Network® (NCCN) Clinical Practice Guideline (CPG) in Oncology® for kidney cancer (2024) does not include a recommendation for the use of TACE or TAE for the treatment of RCC.

TACE and TAE for Malignant Bone Cancer

Only uncontrolled observational studies were identified evaluating TACE and TAE for the treatment of malignant bone cancer. Yang and colleagues (2011) conducted a retrospective review of 60 individuals with sacral tumors to determine the value of preoperative TAE. The authors evaluated intraoperative blood loss, need for transfusion, treatment, local recurrence and surgical complications. There were no symptomatic complications associated with TAE. All tumors were resected without intraoperative shock or death. Participants having surgery 1 day post-TAE had lower blood loss than those having surgery 2 to 3 days post-TAE, but the difference was not statistically significant (p=0.073 and p=0.086, respectively). With regard to surgical technique, participants having a wide excisional margin (n=8) had no local recurrence or evidence of disease. Participants having a marginal excision had local recurrence (6 of 34) and those having an intralesional excision had local recurrence (13 of 18). The average follow-up period was 75.2 months (range, 15 to 180 months), with 22 participants presenting with varying degrees of neurological dysfunction in the form of motor weakness or loss of bowel/bladder control. Based on these findings, the authors concluded that preoperative TAE may significantly reduce intraoperative hemorrhage. Limitations of this study include lack of an active comparator control group and the retrospective design.

Koike and colleagues (2010) conducted a single center retrospective study evaluating both TACE and TAE as palliative treatments for symptomatic bone metastases. A total of 24 hypervascular lesions in 18 participants were treated with either TACE or TAE. Devascularization of targeted lesions was obtained in 75% (18 of 24) of the lesions without serious complication. Pain relief was obtained in 20 lesions (83%) with a significant decrease in the visual analog scale (VAS) for pain score (5.08 pre-procedure VAS vs. 1.3 post-procedure; p<0.001). Mean time to pain relief was 1.6 days. Primary lesions included hepatocellular, colorectal, renal, ovarian, thyroid and cervical cancers. Symptomatic lesions treated were thoracic/lumbar spine, pelvis, rib and femur. The treatment effect of TACE and TAE was difficult to evaluate since participants received a variety of adjuvant therapies including radiation therapy, bisphosphonates and steroids during their clinical course limiting comparison; in addition, the mean follow-up period was limited to 7.5 months (range, 1 to 29 months).

The NCCN CPG for bone cancer (V1.2024) includes a recommendation for the use of selective serial embolizations in the treatment of localized resectable giant cell tumor (GCT) of the bone (with unacceptable morbidity) and/or unresectable axial lesions. Neither TACE nor TAE were specifically mentioned. The category 2A recommendation is based on two single case reports, one case involving presurgical embolization of a proximal humerus tumor with cortical bone destruction extending to the shoulder joint (Emori, 2012) and a case involving embolization of a sacral tumor (Onishi, 2010). In addition, the NCCN cited two small retrospective case series (Hosalkar, 2007 [n=9]; Lin, 2002 [n=18]) that evaluated mid- to long-term outcomes of serial arterial embolization as primary treatment for large GCT of the sacrum. In the study by Lin and colleagues (2002), 14 of 18 participants responded favorably to embolization with improvement in pain and neurologic symptoms. A total of 9 of 18 participants also received intraarterial cisplatin as part of the treatment plan. There was 1 death that occurred 1 day after embolization. With long-term follow-up, 3 participants developed late disease recurrences within the sacrum. Randomized trials comparing embolization to other therapies (such as, radiation, denosumab, and interferon) for the treatment of GCT of the bone have not been reported.

TACE and TAE for Metastatic Thyroid Cancer

The NCCN CPG for thyroid carcinoma (2023) includes a recommendation to consider embolization as an option in the treatment of metastatic follicular, Hürthle cell, and papillary thyroid carcinoma when these tumors are not amenable to radioactive iodine (RAI) therapy. The therapeutic approach for metastatic disease depends on the site and number of tumor foci. Embolization (or other interventional procedures) of metastases may also be considered prior to surgical resection of bone metastases to reduce the risk of hemorrhage, or as an alternative to surgical resection, external beam radiation therapy, or intensity-modulated radiation therapy in select cases. Neither TACE nor TAE were specifically mentioned.

The category 2A recommendation was based on a single study of the effects of selective embolization in individuals with symptomatic bone metastases from differentiated thyroid carcinoma. A total of 41 embolizations were performed in 16 individuals who were followed-up (range, 2 months to 8.6 years) after the first embolization by evaluation of clinical symptoms and tumor dimensions. Success was defined as an improvement in clinical symptoms without tumor progression. Embolization was reported as successful in 24 of 41 occasions (59%). A total of 26 embolizations were preceded or followed-up by additional therapies, consisting of surgery (laminectomy), external irradiation, or radioiodine. The authors reported, however, that subgroup analysis revealed the additional therapies did not influence the success rate, but a potential effect on success duration may have been present. For embolizations without additional radioiodine or external irradiation therapy, the median success duration was 6.5 months; for embolizations combined with additional radioiodine or external irradiation, the median success was 15 months (p=0.0146). The eventual health outcomes of these participants were unfavorable, as 9 subjects died and 5 participants had progressive disease. Despite a rapid induction and relief of symptoms, the treatment effect was transient and lacked durability (Eustatia-Rutten, 2003). For follicular, Hürthle cell, and papillary thyroid carcinoma, randomized comparative trials with other therapies, such as surgical palliation, radioiodine treatment, and/or external beam radiation, intravenous bisphosphonate, denusomab, and small molecular kinase inhibitors or systemic therapy have not been reported.

The NCCN CPG on thyroid carcinoma (2023) includes a recommendation for treatment of recurrent or persistent medullary thyroid carcinoma with symptomatic distant metastases (for example, those in the bone). There are a number of recommended treatment options and these include palliative resection such as radiofrequency ablation or embolization.

Other Considerations

The current NCCN CPGs do not include recommendations for TACE or TAE for the treatment of malignant lesions outside the liver for other cancers (except bone and metastatic thyroid cancer, as discussed above), including, colon, gastric, head and neck (such as, carotid body tumors), rectal, pancreatic, and prostate cancer.

Further study is needed to establish a clinical outcome benefit of TACE and TAE in the management of primary or metastatic tumors outside of the liver. Evidence published to date is limited to retrospective case series and single or small case reports. Prospective, randomized controlled trials are needed to better define the role of TACE and TAE in the management of these conditions.

Background/Overview

TACE and TAE have been proposed as alternatives to conventional systemic or intra-arterial chemotherapy as well as various nonsurgical ablative techniques for the treatment of resectable and nonresectable tumors. TACE and TAE target the arterial blood supply to tumors utilizing selective catheter-based infusion of particles, with or without chemotherapeutic agents. TAE involves the infusion of lipiodol (without a chemotherapeutic agent) and TACE involves the delivery of chemotherapeutic agents, either alone or in combination, mixed with a viscous embolic material, such as lipiodol. TAE may also involve the use of coils and balloons for embolization. Both TAE and TACE are followed by infusion of embolic agents, such as liquid embolitics (absolute alcohol), gelatin sponge particles, polyvinyl alcohol particles (PVA), or hydrophilic, polyacrylamide microporous beads (microspheres). The rationale for use of TACE is that infusion of viscous material containing one or more antineoplastic agents may exert synergistic effects on the tumor while minimizing systemic toxicities associated with oral or intravenous chemotherapy.

Definitions

Adenocarcinoma: A type of cancer that develops in cells lining glandular types of internal organs, such as the lungs, breasts, colon, prostate, stomach, pancreas, and cervix.

Malignant Lesion: An abnormal new growth of cells (neoplasm) which has the ability to invade surrounding tissues and metastasize (spread to other organs). In contrast, non-malignant (benign) neoplasms are usually localized and do not spread to other parts of the body (although some can grow large and impinge on adjacent tissue/organs).

Palliative treatment: Treatment given for relief of symptoms and pain rather than effecting a cure.

Tumoricidal: Any treatment that is destructive to cancer cells.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services are Investigational and Not Medically Necessary:
When the code describes a procedure indicated in the Position Statement section as investigational and not medically necessary.

CPT

37243	Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; for tumors, organ ischemia, or infarction

HCPCS

C9797	Vascular embolization or occlusion procedure with use of a pressure-generating catheter (e.g., one-way valve, intermittently occluding), inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; for tumors, organ ischemia, or infarction

ICD-10 Diagnosis

	For the following diagnoses **when the procedure is related to treatment or palliation of symptoms of malignant lesions outside the liver**:
C00.0-C21.8	Malignant neoplasm of lip, oral cavity and pharynx, esophagus, stomach, small intestine, colon, rectosigmoid junction, rectum, anus and anal canal
C23-C26.9	Malignant neoplasm of gallbladder, other parts of biliary tract, pancreas, other digestive organs
C30.0-C49.A9	Malignant neoplasm of respiratory and intrathoracic organs, bone and articular cartilage, skin, mesothelial and soft tissue
C50.011-C68.9	Malignant neoplasm of breast, female and male genital organs and urinary tract
C73-C76.8	Malignant neoplasm of thyroid and endocrine glands, neuroendocrine tumors
C77.0-C77.9	Secondary and unspecified malignant neoplasm of lymph nodes
C78.00-C78.6	Secondary malignant neoplasm of lung, respiratory organs, intestines, retroperitoneum and peritoneum
C78.80-C78.89	Secondary malignant neoplasm of other digestive organs
C79.00-C79.2	Secondary malignant neoplasm of kidney, bladder and other urinary organs, and skin
C79.51-C80.2	Secondary malignant neoplasm of other sites, and without specification of site
C81.00-C96.9	Malignant neoplasms of lymphoid, hematopoietic and related tissue
D00.00-D01.49	Carcinoma in situ of oral cavity, esophagus, stomach, colon, intestine
D01.7-D01.9	Carcinoma in situ of other digestive organs
D02.0-D09.9	Carcinoma in situ all other sites

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Peer Reviewed Publications:

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9. Lin PP, Guzel VB, Moura MF, et al. Long-term follow-up of patients with giant cell tumor of the sacrum treated with selective arterial embolization. Cancer. 2002; 95(6):1317-1325.
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11. May M, Brookman-Amissah S, Pflanz S, et al. Pre-operative renal arterial embolisation does not provide survival benefit in patients with radical nephrectomy for renal cell carcinoma. Br J Radiol. 2009; 82(981):724-731.
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13. Vogl TJ, Lehnert T, Zangos S, et al. Transpulmonary chemoembolization (TPCE) as a treatment for unresectable lung metastases. Eur Radiol. 2008; 18(11):2449-2455.
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15. Zielinski H, Szmigielski S, Petrovich Z. Comparison of preoperative embolization followed by radical nephrectomy with radical nephrectomy alone for renal cell carcinoma. Am J Clin Oncol. 2000; 23(1):6-12.

Government Agency, Medical Society, and Other Authoritative Publications:

1. NCCN Clinical Practice Guidelines in Oncology® (NCCN). © 2024 National Comprehensive Cancer Network, Inc. For additional information: http://www.nccn.org/index.asp. Accessed on December 21, 2023.
   - Bone Cancer (V1.2024). Revised August 7, 2023.
   - Head and Neck Cancer (V2.2024). Revised December 8, 2023.
   - Kidney Cancer (V1.2024). Revised June 21, 2023.
   - Pancreatic Adenocarcinoma (V1.2024). Revised December 13, 2023.
   - Thyroid Carcinoma (V4.2023). Revised August 16, 2023.

Websites for Additional Information

1. National Cancer Institute (NCI). Cancer Topics. Available at: https://www.cancer.gov/about-cancer. Accessed on December 21, 2023.

Document History

Status	Date	Action
Reviewed	02/15/2024	Medical Policy & Technology Assessment Committee (MPTAC) review. Revised Rationale, Definitions and References sections. Updated Coding section with 04/01/2024 HCPCS changes, added C9797.
Reviewed	02/16/2023	MPTAC review. Updated Rationale and References sections.
Reviewed	02/17/2022	MPTAC review. Updated Rationale, References and Websites sections.
Reviewed	02/11/2021	MPTAC review. Updated Rationale, References and Websites sections.
Reviewed	02/20/2020	MPTAC review. Title changed to “Catheter-based Embolization Procedures for Malignant Lesions Outside the Liver.” Description/Scope, Rationale, Definitions and References sections updated.
Reviewed	03/21/2019	MPTAC review.
Reviewed	03/20/2019	Hematology/Oncology Subcommittee review. Rationale and References sections updated.
Reviewed	05/03/2018	MPTAC review.
Reviewed	05/02/2018	Hematology/Oncology Subcommittee review. The document header wording updated from “Current Effective Date” to “Publish Date.” Updated Rationale, References, and Websites for Additional Information sections.
Revised	05/04/2017	MPTAC review.
Revised	05/03/2017	Hematology/Oncology Subcommittee review. Made minor typographical revision in the Position Statement section. Updated References section.
Reviewed	05/05/2016	MPTAC review.
Reviewed	05/04/2016	Hematology/Oncology Subcommittee review. Updated Rationale, References and Websites for Additional Information sections. Removed ICD-9 codes from Coding section.
Reviewed	05/07/2015	MPTAC review.
Reviewed	05/06/2015	Hematology/Oncology Subcommittee review. Updated Description, Rationale, and Websites for Additional Information sections.
Reviewed	05/15/2014	MPTAC review.
Reviewed	05/14/2014	Hematology/Oncology Subcommittee review. Updated Rationale, Background, Definitions, References, and Websites for Additional Information sections.
	01/01/2014	Updated Coding section with 01/01/2014 CPT changes; removed 37204 deleted 12/31/2013, and 75894.
Revised	05/09/2013	MPTAC review.
Revised	05/08/2013	Hematology/Oncology Subcommittee review. Minor format change/clarification to the Position Statement. Updated Rationale, Background, Definitions, and References. Added Websites for Additional Information. Removed Index.
Reviewed	05/10/2012	MPTAC review.

Reviewed	05/09/2012	Hematology/Oncology Subcommittee review. Title changed to exclude CNS and spinal cord lesions. Rationale and References updated.
Reviewed	05/19/2011	MPTAC review.
Reviewed	05/18/2011	Hematology/Oncology Subcommittee review. Description, Rationale and References updated.
New	02/17/2011	MPTAC review. Initial document development.

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