

STANDARD TREATMENT WORKFLOW (STW)

IMAGE GUIDED THERAPIES FOR PRIMARY LIVER TUMORS

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CITATION

Sharma S, Mukund A, Khera PS, Rajagopal R, Banode P, Kumar NS, Kumar S, Shaw M, Hatimota P, Pandey N. IMAGE GUIDED THERAPIES FOR PRIMARY LIVER TUMORS. Journal of the Epidemiology Foundation of India. 2024;2(2Suppl):S268-S270.

DOI: <https://doi.org/10.56450/JEFI.2024.v2i2Suppl.008>

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2024/AFRC



Department of Health Research
Ministry of Health and Family Welfare, Government of India



Standard Treatment Workflow (STW) IMAGE GUIDED THERAPIES FOR PRIMARY LIVER TUMORS ICD-10-C22.8

PRIMARY LIVER TUMORS	DIAGNOSTIC WORK-UP
<ul style="list-style-type: none">Primary liver tumors majorly consists of Hepatocellular carcinoma (HCC), Intrahepatic cholangiocarcinoma (IHCC) and combined hepatocellular cholangiocarcinoma (cHCC-CC) HCC being is the most commonThere are no specific signs or symptoms for primary liver tumorsRadiological and lab investigations are the main tool for the diagnosis <p>In patients with underlying cirrhosis new onset of ascites, jaundice and/or variceal haemorrhage should prompt investigations to look for HCC</p> <ul style="list-style-type: none">Patients with pre-existing cirrhosis; are at high risk of developing HCC and should be under surveillance for development <ul style="list-style-type: none">Risk Factors<ul style="list-style-type: none">Hepatitis B (33%)Alcoholic liver disease(30%)Hepatitis C (21%)NASHOther causes of cirrhosisSerum Alpha fetoprotein: elevated AFP value should prompt imaging work up	<ul style="list-style-type: none">LI-RADS classification system should be used for diagnosisMultiphasic CT/MRI or contrast enhanced ultrasound is needed for diagnosisIn patients at risk, if a lesion of size > 2cm with arterial phase hyperenhancement and washout on subsequent phase is diagnostic of HCCBiopsy is needed if<ul style="list-style-type: none">Equivocal imaging findingsNon-cirrhotic liver
INVESTIGATIONS	PATIENT MANAGEMENT
<p>Essential</p> <p>Lab investigations</p> <ul style="list-style-type: none">Liver function testsKidney function testsCBCPT/INR	<p>Multiphasic contrast-enhanced CT/MRI</p> <ul style="list-style-type: none">Tumor characterization staging and presence of extrahepatic disease <p>IR therapies based on size and number of lesions</p> <ul style="list-style-type: none">< 3 lesions of < 3 cm: consider ablationLesion > 3cm & < 5cm may consider combination of TACE & AblationLesion > 5 & < 8 cm consider TACELesion > 8 cm consider TACE



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IMAGE GUIDED THERAPIES
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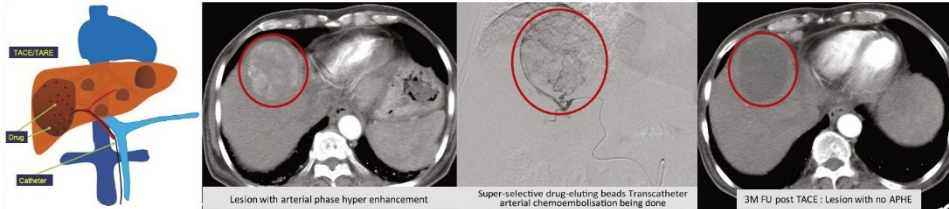
PRIMARY LIVER TUMORS		DIAGNOSTIC WORK-UP	
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INVESTIGATIONS	PATIENT MANAGEMENT		
<p>Essential</p> <p>Lab investigations</p> <ul style="list-style-type: none"> Liver function tests Kidney function tests CBC PT/INR Alpha fetoprotein (AFP) <p>Imaging</p> <ul style="list-style-type: none"> Recent contrast enhanced multiphasic CT/MRI <p>Desirable</p> <ul style="list-style-type: none"> PIVKA II <p>Optional</p> <ul style="list-style-type: none"> FDG PET CECT 	<p>Multiphasic contrast-enhanced CT/MRI</p> <ul style="list-style-type: none"> Tumor characterization staging and presence of extrahepatic disease <p>IR therapies based on size and number of lesions</p> <ul style="list-style-type: none"> < 3 lesions of < 3 cm: consider ablation Lesion > 3cm & < 5cm may consider combination of TACE & Ablation Lesion > 5 & < 8 cm consider TACE Lesion > 8 cm consider TARE <p>Portal vein status:</p> <ul style="list-style-type: none"> Portal vein tumoral thrombus: consider TARE/SBRT, TACE may be considered for segmental/sub-segmental branch tumoral thrombus <p>Location of the tumor:</p> <ul style="list-style-type: none"> Tumors at critical location like Perivascular/pericholedochal/exophytic/subdiaphragmatic lesion <ul style="list-style-type: none"> Consider TACE Combination of TACE & ablation / MWA in experienced centres <p>Performance status (ECOG)^{ref} PS 0, 1 suitable for IR therapies, PS 2 may consider TARE</p> <p>Liver function tests: Serum bilirubin >3 mg/dl & AST > five times the upper limit of normal contraindication for TACE</p> <p>Child-Pugh class: IR therapies should be considered for Child-Pugh class^{ref} < B8</p>		
ABLATIVE THERAPIES	THERMAL ABLATION: INDICATIONS	CONTRAINDICATION	
<p>Chemical ablation</p> <ul style="list-style-type: none"> Ethanol Acetic acid <p>Thermal ablation</p> <ul style="list-style-type: none"> Radiofrequency Ablation Microwave ablation Cryoablation <p>Non chemical-non thermal ablation</p> <ul style="list-style-type: none"> Irreversible electroporation 	<ul style="list-style-type: none"> Very early (single lesion <2 cm) and early HCC single lesion or upto three lesions each less than 3cm Ablation may be considered for all primary liver lesions amenable for ablation in following situation <ul style="list-style-type: none"> Bridging therapy for liver transplantation Residual and recurrent HCC Combination therapy with TACE Repeat ablation should be considered for focal residual lesion < 3 cm along the periphery or within the ablation zone 	<ul style="list-style-type: none"> Ascites Sepsis and uncorrectable coagulopathy Intrahepatic biliary dilatation Intravascular invasion or extrahepatic metastatic disease Arrhythmias (for IRE) Poor PS (>2) Severely deranged liver function (CTP class C) 	
IMAGE GUIDANCE			
<ul style="list-style-type: none"> USG (contrast optional) CT (contrast optional) Both CT & USG 	<p>POST PROCEDURE COMPLICATIONS</p> <ul style="list-style-type: none"> Immediate Post procedure: Bleed/hemoperitoneum <p>Post procedure appearance of perihepatic hematoma/fluid/ascites suggestive of bleed/hemoperitoneum If continuous increase in size/volume of hematoma/fluid plan CT angiogram to localize bleeding vessels</p> <p>If active contrast extravasation noted on CT angiogram plan urgent angio-embolization of the bleeding vessel</p> <ul style="list-style-type: none"> Post embolization syndrome: Fever may persist for 2-3 days and pain may persist for 5-7 days <ul style="list-style-type: none"> Severe/excruciating pain at any point of time should be evaluated with USG and if needed CECT to look for the cause Visceral/diaphragmatic/lung/GB injury: Rare complications but may be looked for if severe/excruciating pain persists 		
TRANSARTERIAL CHEMOEMBOLIZATION (TACE)	TACE INDICATIONS	TACE CONTRAINDICATIONS	
<ul style="list-style-type: none"> TACE: Intra-arterial infusion of cytotoxic agent followed by embolisation of the tumor-feeding blood vessels TACE performed in 2 ways <ul style="list-style-type: none"> cTACE: Emulsion of Lipiodol & chemotherapeutic agent is injected into the arteries supplying the tumor DEB TACE: Chemotherapy loaded microspheres are selectively injected into the arteries supplying the tumor The use of drug-eluting beads has shown similar benefit to conventional TACE (cTACE; gelfoam-Lipiodol particles) and either of the two can be utilized TACE is suitable for patients with well-defined nodules and preserved portal flow TACE should be performed in a super-selective manner and avoid all possible non-target embolization 	<ul style="list-style-type: none"> Multinodular or single nodule HCC of size > 5 cm with preserved portal flow, preserved liver function and PS=0 (INASL-BCLC/BCLC-2022 stage B) In small HCC where ablation is not possible 	<ul style="list-style-type: none"> Decompensated cirrhosis (Child-Pugh B ≥8, including jaundice with Serum Bilirubin > 3.0 mg/dl, hepatic encephalopathy, refractory ascites and hepatorenal syndrome) Portal vein tumoral thrombus Extensive tumor involving both liver lobes Untreatable arteriovenous fistula Renal insufficiency, including creatinine ≥2 mg/dL or creatinine clearance <30 mL/min 	
POST TACE COMPLICATIONS			
<ul style="list-style-type: none"> Immediate post procedure: <ul style="list-style-type: none"> Arterial injury/dissection (small vessel and minor injury may be left as it is and major vessel injury may require measures like angioplasty and/or stenting) Tumor rupture (Rare) presents as hemoperitoneum/ascites/hemodynamic shock and may be seen in few hours to 24 hours post TACE Post embolization syndrome: Pain, fever, Nausea/Vomiting – these symptoms are mostly self limiting resolves in 2-3 days and needs symptomatic care (Paracetamol and/or antiemetics) <p>If there is deterioration on clinical condition of the patient after TACE (3-7 days) with severe post embolization syndrome then lab investigations (LFT, KFT, CBC and PT/INR) and USG should be done to look for post TACE liver failure</p> <ul style="list-style-type: none"> Post TACE Liver failure <ul style="list-style-type: none"> > 10 times elevation of baseline AST/ALT > 3 times elevation of baseline serum Bilirubin Post procedure hepatic encephalopathy INR elevation > 2.5 of baseline 			



Standard Treatment Workflow (STW) IMAGE GUIDED THERAPIES FOR PRIMARY LIVER TUMORS (Continued)

IMAGE GUIDANCE FOR TACE/TARE

- DSA (Cone beam CT optional)



TRANSARTERIAL RADIOEMBOLISATION

- TARE is infusion of radioactive substances or microspheres into the arteries supplying the tumor. It mostly contains yttrium-90 (Y90)
- TARE may be performed in a lobar, sectorial, or segmental approach based on tumor burden and location
- Pre-procedure assessment
 - Assessment of anatomic variant, collateral vessels [prophylactic coil embolisation of gastroduodenal artery, right gastric artery left gastric artery, left gastric artery (optional)]
 - Assessment of degree of shunting to lung.
 - T99m Tc MAA - Macro aggregated albumin- is used for pre-procedure assessment as it has diameter and distribution similar to Y90 microspheres
 - Tc99 (2-5 mCi) microspheres is used in preprocedure assessment - In case of rhenium-188 isotope

TARE INDICATIONS

- Palliation for unresectable HCC with or without PVTT
- Bridge to transplantation
- Neoadjuvant therapy for resection
- Definitive ablative radiotherapy for smaller lesions

TARE CONTRAINDICATIONS

- Lung shunting > 20% or radiation doses to lungs > 30 Gy in single treatment or cumulative dose of 50 Gy
- Severe liver dysfunction (Child - Pugh C), total bilirubin >3mg/dl
- Significant immediate life threatening extrahepatic disease
- Patients with ECOG PS >2

POST TARE COMPLICATIONS

• Immediate post procedure

- Arterial injury/dissection (small vessel and minor injury may be left as it is and major vessel injury may require measures like angioplasty and/or stenting)

• Post embolization syndrome: Mild and self limiting resolve in 2-3 days and need symptomatic care (Paracetamol and/or antiemetics)

- Radioembolization-induced liver disease (REILD)
 - It is a rare complications which occurs due to liver injury caused by 90Y microspheres.
 - It develops in 4-8 weeks after treatment and manifests as jaundice and ascites without biliary obstruction or tumor progression.
 - It may be mild or severe

• Gastrointestinal complications: Gastroduodenal ulcers and pancreatitis is a rare complication due to non-target reflux of 90Y particles

• Radiation Pneumonitis: Rare complication, occurs due to excessive arterio-venous shunting and is seen after 1-6 months of treatment

FOLLOW-UP (Common for all IR therapies)

- Lab investigations (LFT, KFT, CBC) may be repeated after 1-2 weeks of IR therapies to assess infection/liver & kidney dysfunction
 - USG abdomen may be done if there is prolonged pain/fever and/or abdominal distension
 - Response to evaluation and follow up consists of clinical, biochemical and imaging at 1 month
 - Clinical - General condition, performance status
 - Biochemical - LFT, KFT, CBC, PT/INR, AFP
 - Multiphasic contrast enhanced CT/MRI
 - To assess treatment response as per (mRECIST) criteria at 1 month for Ablation/TACE and 6 or 12 weeks (12 weeks preferable) for TARE
- Treatment response should be assessed using mRECIST criteria and should be reported as complete response (CR), partial response (PR), Stable disease (SD) and progressive disease (PD)

OUTCOME MEASURES AND LONG TERM FOLLOW UP

- Treatment response should be assessed using mRECIST criteria and should be reported as complete response (CR), partial response (PR), Stable disease (SD) and progressive disease (PD)
- If complete response achieved, then periodic follow-up at 3, 6, 9, 12 months and 6-12 months thereafter same as above
- Partial response at 1 month: plan repeat session consisting of same or different modality
- Progressive disease at one month: change treatment plan based on advanced HCC as per INASL-BCLC/BCLC-2022 classification

ABBREVIATIONS

AFP: Alpha Fetoprotein	MRI: Magnetic Resonance Imaging
CBC: Complete Blood Count	MWA: Microwave Ablation
CT: Computed Tomography	PET: Positron Emitting Tomography
DSA: Digital subtraction angiography	PIVKA II: Protein Induced by Vitamin K Absence-II
ECOG: Eastern Cooperative Oncology Group	PS: Performance Status
HCC: Hepatocellular Carcinoma	PT: Prothrombin Time
IHCC: Intrahepatic Cholangiocarcinoma	PVTT: Portal Vein Tumor Thrombus
INR: International Normalized Ratio	mRECIST: modified Response Evaluation Criteria in Solid Tumors
IRE: Irreversible Electroporation	SBRT: Stereotactic Body Radiotherapy
KFT: Kidney Function Test	TACE: Transarterial Chemoembolization
LFT: Liver Function Test	TARE: Transarterial Radioembolization
LI-RADS: Liver Imaging Reporting & Data System	USG: Ultrasonography

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➔ HCC: EARLY DETECTION AND TREATMENT IS ASSOCIATED WITH BEST OUTCOME

This STW has been prepared by national experts of India with feasibility considerations for various levels of healthcare system in the country. These broad guidelines are advisory, and are based on expert opinions and available scientific evidence. There may be variations in the management of an individual patient based on his/her specific condition, as decided by the treating physician. There will be no indemnity for direct or indirect consequences. Kindly visit the website of ICMR for more information: icmr.gov.in for more information. ©Indian Council of Medical Research, Ministry of Health & Family Welfare, Government of India.