STANDARD TREATMENT WORKFLOW (STW)

IMAGE GUIDED THERAPIES FOR PRIMARY LIVER TUMORS

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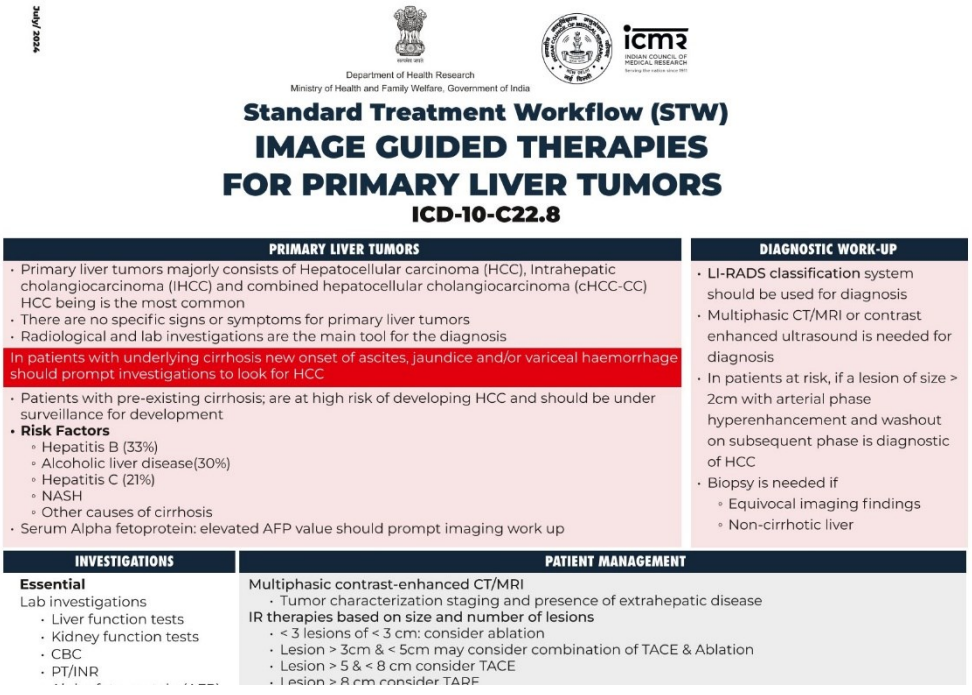

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Department of Health Research
Ministry of Health and Family Welfare, Government of India

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IMAGE GUIDED THERAPIES FOR PRIMARY LIVER TUMORS

ICD-10-C22.8

PRIMARY LIVER TUMORS

- Primary liver tumors majorly consists of Hepatocellular carcinoma (HCC), Intrahepatic cholangiocarcinoma (IHCC) and combined hepatocellular cholangiocarcinoma (cHCC-CC) HCC being is the most common
- There are no specific signs or symptoms for primary liver tumors
- Radiological and lab investigations are the main tool for the diagnosis

In patients with underlying cirrhosis new onset of ascites, jaundice and/or variceal haemorrhage should prompt investigations to look for HCC

- Patients with pre-existing cirrhosis; are at high risk of developing HCC and should be under surveillance for development
- **Risk Factors**
  - Hepatitis B (33%)
  - Alcoholic liver disease(30%)
  - Hepatitis C (21%)
  - NASH
  - Other causes of cirrhosis
- Serum Alpha fetoprotein: elevated AFP value should prompt imaging work up

DIAGNOSTIC WORK-UP

- **LI-RADS classification** system should be used for diagnosis
- Multiphasic CT/MRI or contrast enhanced ultrasound is needed for diagnosis
- In patients at risk, if a lesion of size > 2cm with arterial phase hyperenhancement and washout on subsequent phase is diagnostic of HCC
- Biopsy is needed if
  - Equivocal imaging findings
  - Non-cirrhotic liver

INVESTIGATIONS

Essential
Lab investigations
- Liver function tests
- Kidney function tests
- CBC
- PT/INR
- Alpha feto-protein (AFP)

Imaging
- Recent contrast enhanced multiphasic CT/MRI

Desirable
- PIVKA II

Optional
- FDG PET CECT

PATIENT MANAGEMENT

Multiphasic contrast-enhanced CT/MRI
- Tumor characterization staging and presence of extrahepatic disease

IR therapies based on size and number of lesions
- < 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

Portal vein status:
- Portal vein tumoral thrombus: consider TARE/SBRT,
- TACE may be considered for segmental/sub-segmental branch tumoral thrombus

Location of the tumor:
- Tumors at critical location like Perivascular/pericholedochal/exhophytic/subdiaphragmatic lesion
  - Consider TACE
  - Combination of TACE & ablation / MWA in experienced centres

Performance status (ECOG)[ref] PS 0, 1 suitable for IR therapies, PS 2 may consider TARE
Liver function tests: Serum bilirubin >3 mg/dl & AST > five times the upper limit of normal contraindication for TACE
Child-Pugh class: IR therapies should be considered for Child-Pugh class[ref] < B8

ABLATIVE THERAPIES

Chemical ablation
- Ethanol
- Acetic acid

Thermal ablation
- Radiofrequency Ablation
- Microwave ablation
- Cryoablation

Non chemical-non thermal ablation
- Irreversible electroporation

THERMAL ABLATION: INDICATIONS

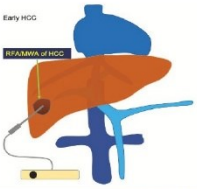
- Very early (single lesion <2 cm) and early HCC single lesion or upto three lesions each less than 3cm
- Ablation may be considered for all primary liver lesions amenable for ablation in following situation
  - Bridging therapy for liver transplantation
  - Residual and recurrent HCC
  - Combination therapy with TACE
  - Repeat ablation should be considered for focal residual lesion < 3 cm along the periphery or within the ablation zone

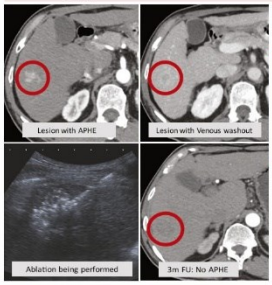
CONTRAINDICATION

- 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

- USG (contrast optional)
- CT (contrast optional)
- Both CT & USG





POST PROCEDURE COMPLICATIONS

- **Immediate Post procedure:** Bleed/hemoperitoneum

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
If active contrast extravasation noted on CT angiogram plan urgent angio-embolization of the bleeding vessel

- **Post embolization syndrome:** Fever may persist for 2-3 days and pain may persist for 5-7 days
  - 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: Intra-arterial infusion of cytotoxic agent followed by embolisation of the tumor-feeding blood vessels
- TACE performed in 2 ways
  - **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

TACE INDICATIONS

- 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

TACE CONTRAINDICATIONS

- 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

- 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)
  - 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)
- 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
- **Post TACE Liver failure**
  - > 10 times elevation of baseline AST/ALT
  - > 3 times elevation of baseline serum Bilirubin
  - Post procedure hepatic encephalopathy
  - INR elevation > 2.5 of baseline

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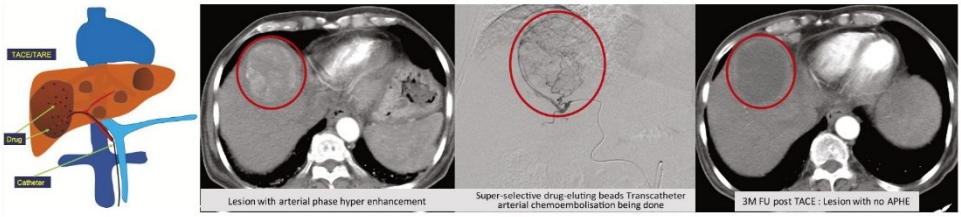
IMAGE GUIDED THERAPIES FOR PRIMARY LIVER TUMORS

(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 bilrubin >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 Tumoral 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