

Veterans Health Administration

VA Collaborative Consensus on a Pathway for the Development of a Multidisciplinary Team to Manage Hepatocellular Carcinoma

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Introduction:

Hepatocellular carcinoma (HCC) has tripled in incidence in the US over the last three decades, and the HCC incidence rate among patients with cirrhosis has been shown to be 2%-4% per year.(1-3) HCC is the leading cause of death in patients with cirrhosis. In the West, over 80% of patients with HCC have concomitant cirrhosis. Veterans are an at-risk population for viral hepatitis, alcoholic liver disease and non-alcoholic fatty liver disease that can progress to cirrhosis and liver cancer. HCC is unique in that it is the only solid organ malignancy that can be diagnosed with imaging without tissue biopsy and the only solid organ malignancy for which liver transplantation offers a cure. However, HCC is a heterogeneous cancer with a phenotypic spectrum ranging from indolent to extremely aggressive. The complexity of the cancer and host requires careful consideration, including careful staging of both the cancer and the severity of liver disease to arrive at an optimal plan of care that will prolong survival.

Multidisciplinary care requires a dedicated team of professionals who understand the standard of care, are mindful of their center's capabilities and limitations, and seek to provide the best care for each patient. Multidisciplinary management of HCC has been shown to improve survival; however, resources and expertise for managing HCC are variable within the VA system, leading to disparities in access and delivery of care.(4) By setting best practices and standardizing HCC care across the nation, we will improve healthcare delivery to this vulnerable population.

The goal of this pathway is to set forth best practices in the VA for the multidisciplinary management of HCC regarding:

1. Diagnosis and staging of hepatocellular carcinoma (**Section I**)
2. Multidisciplinary tumor board: composition and requirements (**Section II**)
3. Defining key elements of tumor board documentation (**Section III**)
4. Surveillance intervals and duration after curative and palliative treatment (**Section IV**)

This document is not intended to establish guidelines to be enforced at VA medical centers. Rather, it is offered as a pathway to help guide the multidisciplinary management of patients with HCC. Multidisciplinary teams should always employ their best clinical judgement based on the latest medical evidence and local capabilities to provide care for Veteran patients.

Section I: Diagnosis and Staging of Hepatocellular Carcinoma

Recommendation 1.1

Liver cancer surveillance is recommended for all patients with Child-Turcotte-Pugh A and B cirrhosis and patients with Child-Turcotte-Pugh C cirrhosis listed for liver transplant who are eligible for curative or palliative (surgical, locoregional, or systemic) therapies for hepatocellular carcinoma (HCC).

Recommendation 1.2

Ultrasound surveillance every 6 months is the recommended surveillance modality with or without serological testing for alpha-fetoprotein (AFP) for patients with cirrhosis.(1)

Special circumstances:

- If a quality sonogram cannot be obtained due to limitation of local resources or as determined by the ultrasonographer/radiologist, contrast-enhanced imaging is advised, preferably MRI to limit radiation if readily available.
- If AFP is checked and significantly elevated at baseline or from a prior baseline, contrast enhanced imaging should be considered.

Quality Improvement Suggestions

- service agreements with radiology regarding:
 - designated orders for imaging
 - Imaging protocols should be standardized across the VISN. Contact your VISN Chief of Radiology to champion best imaging practices.
 - radiology reading templates for surveillance studies, including designated modalities for follow-up studies when liver masses are encountered

Recommendation 1.3

Non-invasive diagnosis of HCC using the AASLD diagnostic algorithm (Appendix A1) can be used in cirrhotic patients.(5)

Recommendation 1.4

In potential transplant/resection candidates, biopsy (if needed) *should not* be performed prior to discussion with transplant team or surgeon.(6)

Recommendation 1.5

This guidance document is not intended to address diagnosis of a mass in a non-cirrhotic patient or management of indeterminate nodules in patients with or without cirrhosis.

Recommendation 1.6

Non-contrast chest CT is advised when HCC is highly suspected or confirmed and *before* treatment is offered.(6)

Recommendation 1.7

Bone imaging is advised when there are specific skeletal complaints (NM vs. F18 PET). While not part of UNOS (7) or NCCN (6) guidelines, in patients with BCLC B and/or HCC >5 cm, the risk of metastasis is increased and bone imaging may be considered in such patients.(8)

Recommendation 1.8

PET scan may be considered for staging and prognostic evaluation, but it is neither a standard nor required modality. There are emerging data suggesting FDG avid HCCs are associated with poorly differentiated histologic grade.(9)

Section II: Multidisciplinary Liver Tumor Board: Composition and Requirements

Recommendation 2.1

A multidisciplinary liver tumor board (MDLTB) review of all liver cancer cases (incident and recurrent) is recommended.(5, 6, 10, 11)

Recommendation 2.2

The American College of Surgeons (ACOS) has issued Cancer Program Standards; these standards advise a 75% adherence rate with participation at tumor board among the required disciplines.(12) It is recommended that a MDLTB include the following disciplines (alphabetically); **only those marked in bold are required** (12):

- **Cancer care coordinators** (APRN/RN/PA)
- **Gastroenterology/Hepatology Clinicians**
- Infectious Diseases Clinicians
- **Interventional Radiology Provider**
- **Oncology Clinician**
- Palliative Care Team Representative
- **Pathologist (when tissue is to be reviewed)**
- Radiation Oncology Provider

- **Radiologist (with body imaging expertise)**
- Social Worker
- **Surgical team representative**
- Tumor registrar

Recommendation 2.3

The MDLTB operations should be reviewed annually by the Institutional Cancer Committee according to American College of Surgeons (ACOS) guidelines.(12)

Recommendation 2.4

Each center with a MDLTB should develop a policy and procedure for presentation and approval by the station's cancer committee.

Per the American College of Surgeons (ACOS) Cancer Program Standards, Cancer Conference Policy (ER3), elements to consider in the formation of MDLTB include:

- Frequency and format of cancer conference
- Composition of disciplines attending conference and the attendance rate of participants
- Consideration of stage, prognostic indicators, and treatment plan using national, evidence-based treatment guidelines
- Options for clinical trial participation
- Methods to address deficiencies when metrics established *a priori* are not met
- Regarding case content, ASCO sets forth specific criteria on the number of case presentations (a minimum of 15 percent of the annual analytic case load) and the prospective presentation rate (a minimum of 80 percent).
“Prospective cases include, but are not limited to, the following:
 - Newly diagnosed and treatment not yet initiated
 - Newly diagnosed and treatment initiated, but discussion of additional treatment is needed
 - Previously diagnosed, initial treatment completed, but discussion of adjuvant treatment or treatment for recurrence or progression is needed
 - Previously diagnosed, and discussion of supportive or palliative care is needed

Note that cases may be discussed more than once and counted each time as a prospective presentation as long as management issues are discussed.”(12)

Section III: Defining key elements of tumor board documentation

Recommendation 3.1

Initial case discussion for MDLTB should document:

1. Date of confirmed HCC diagnosis
 - a. For Tissue Diagnosis: date of pathology report
 - b. For Radiographic Diagnosis: date of MDTB consensus on HCC
2. Modality of diagnosis e.g. LIRAD radiological criteria (13) or histological
3. Staging completed to date:
 - a. Chest CT
 - b. Bone scan if indicated (see above)
4. Stage at diagnosis
 - a. BCLC (14) – preferred/required
 - b. Milan Criteria (15) – preferred/required
 - c. AJCC (16) – required for ACOS accreditation
 - d. UNOS/OPTN (7) – preferred/required for transplant centers
5. Number of definite HCCs (LIRAD 5)
6. Size of all LIRADS 5 and LIRAD 4 tumors
7. Total tumor diameter (cm) of all LIRAD 5 tumors
8. Presence or absence of macrovascular invasion
9. Presence or absence of nodal metastasis
10. Presence or absence of other metastasis
11. Presence of cirrhosis
 - a. CTP Score
 - b. MELD-Na Score
 - c. Absence/presence of portal hypertension as determined by platelet count <150K and fibroscan >20 kPa, imaging or endoscopic evidence of varices, the presence of ascites, or measurement of HVPG
12. Eastern Cooperative Oncology Group (ECOG) performance status (See Appendix B) (17)
13. Key labs (populated by CPRS): required: Plts, INR, Cr, Na, Alb, TBil, AFP; optional: WBC, Hgb, PT/PTT
14. Etiology of underlying liver disease and current status (e.g., active or treated viral hepatitis; alcohol use ongoing or in remission)
15. Relevant comorbidities (rate limiting for treatment)
16. Transplant eligibility where appropriate, noting absolute and relative contraindications
17. Plan of care with intent (curative or palliative)

18. The plan of care should contain a statement identifying the provider(s)/service responsible for completing next steps, i.e., communicating the plan to the patient and other providers and entering orders. Members who are unable to attend a given tumor board but are responsible for direct patient care should be added to the note as additional signers. Closed loop communication and clear identification of lines of responsibility are helpful to avoid confusion, misunderstanding, and losses to follow-up.
19. Goals of care discussion encouraged
20. Clinical trial availability, if patient will be referred for clinical trial, and name of clinical trial if referred
21. Alerting of referring and primary care providers

Recommendation 3.2

Subsequent/recurrent discussions at the MDLTB should include:

1. Prior treatment modality
2. Prior treatment results
3. Date of recurrence
4. Modality of diagnosis
5. Staging considerations (e.g. down staging)
6. Description of recurrence
 - a. Residual vs. recurrent vs. new
 - i. Definitions:
 1. Residual: Remaining viable tumor after incomplete treatment
 2. Recurrent: Regrowth of tumor within a prior treatment cavity/area
 3. New: A new focus of cancer at a new site within the liver
 - b. Number of new lesions or description of viability at prior treatment sites
 - c. Size of all LIRADS 5 and LIRADS 4 tumors
 - d. Interval development of macrovascular invasion/metastasis
7. Relevant changes in clinical status
8. Key labs (populated by CPRS): required: Plts, INR, Cr, Na, Alb, TBil, AFP; optional: WBC, Hgb, PT/PTT, Bil indirect
9. If cirrhotic:
 - a. Current CTP
 - b. Current MELD
 - c. Absence/presence of portal hypertension as determined by platelet count <150K and fibroscan >20 kPa, imaging or endoscopic evidence of varices, the presence of ascites, or measurement of HVPG
10. Plan of care with intent; goals of care encouraged to be revisited
11. Clinical trial availability, if patient will be referred for clinical trial, and name of clinical trial if referred

12. Alerting of referring and primary care provider

Section IV: Surveillance intervals and duration after curative and palliative treatments

Recommendation 4.1

The VA Collaborative Consensus on a Pathway for Imaging of Patients with Suspected or Confirmed Hepatocellular Carcinoma makes the following recommendations: “*After the surgical, ablative or catheter-based treatment of HCC,*

Recommendations:

- 1.1 *Follow up imaging should be performed after all the target tumors have been treated.*
- 1.2 *Multi-phase contrast enhanced MRI is the preferred modality utilizing protocol sequences outlined in **SECTION I** [of the VA Collaborative Consensus on a Pathway for Imaging of Patients with Suspected or Confirmed Hepatocellular Carcinoma]. Multi-phase contrast enhanced CT is an acceptable alternative. Ultrasound is inadequate.*

We offer the following recommendations with respect to imaging interval post treatment, understanding that follow-up may vary depending upon the specific treatment, lesion characteristics, treatment plan and practitioner experience:

- 1.3 **TACE/TAE:** *Initial scan at 6-12 weeks. If no residual disease present, follow-up at 3 months*
- 1.4 **Ablation:** *Initial scan at 6-12 weeks. If no residual disease present, follow-up at 3 months*
- 1.5 **Y90:** *Initial scan at 12 weeks. If no residual disease present, follow-up at 3 months*
- 1.6 **SBRT:** *Initial scan at 12 weeks. If no residual disease, follow-up at 3 months*
- 1.7 **Resection:** *Initial scan at 12 weeks. If no residual disease, follow-up at 3 months*
- 1.8 *Report residual disease per LI-RADS 2017 guidelines*
 - *LR-TR Nonviable (treated tumor probably or definitely not viable)*
 - *LR-TR Equivocal (treated tumor equivocally viable)*
 - *LR-TR Viable (treated tumor probably or definitely viable)*
- 1.9 *If no recurrence identified on first post treatment imaging, recommend contrast enhanced MRI-CT every 3 months until patient reaches 2-years recurrence free survival, then every 6-12 months thereafter, unless patient gets transplanted and is HCC-free after appropriate surveillance, or does not want additional surveillance.”*

Recommendation 4.2

After transplantation for liver cancer, surveillance imaging (contrast-enhanced MRI and/or CT) should be performed per local transplant center protocols. These protocols usually include repeat imaging of chest, abdomen and pelvis at 6-12 month intervals for 5 years.

Recommendation 4.3

For patients on systemic therapy, contrast-enhanced MRI/CT imaging should be considered to assess progression of disease. Patients on clinical trials should be imaged according to protocol. For immunotherapies, the phenomenon of pseudoprogression must be considered.

Once the patient transitions to end of life care, there is no further indication for imaging.

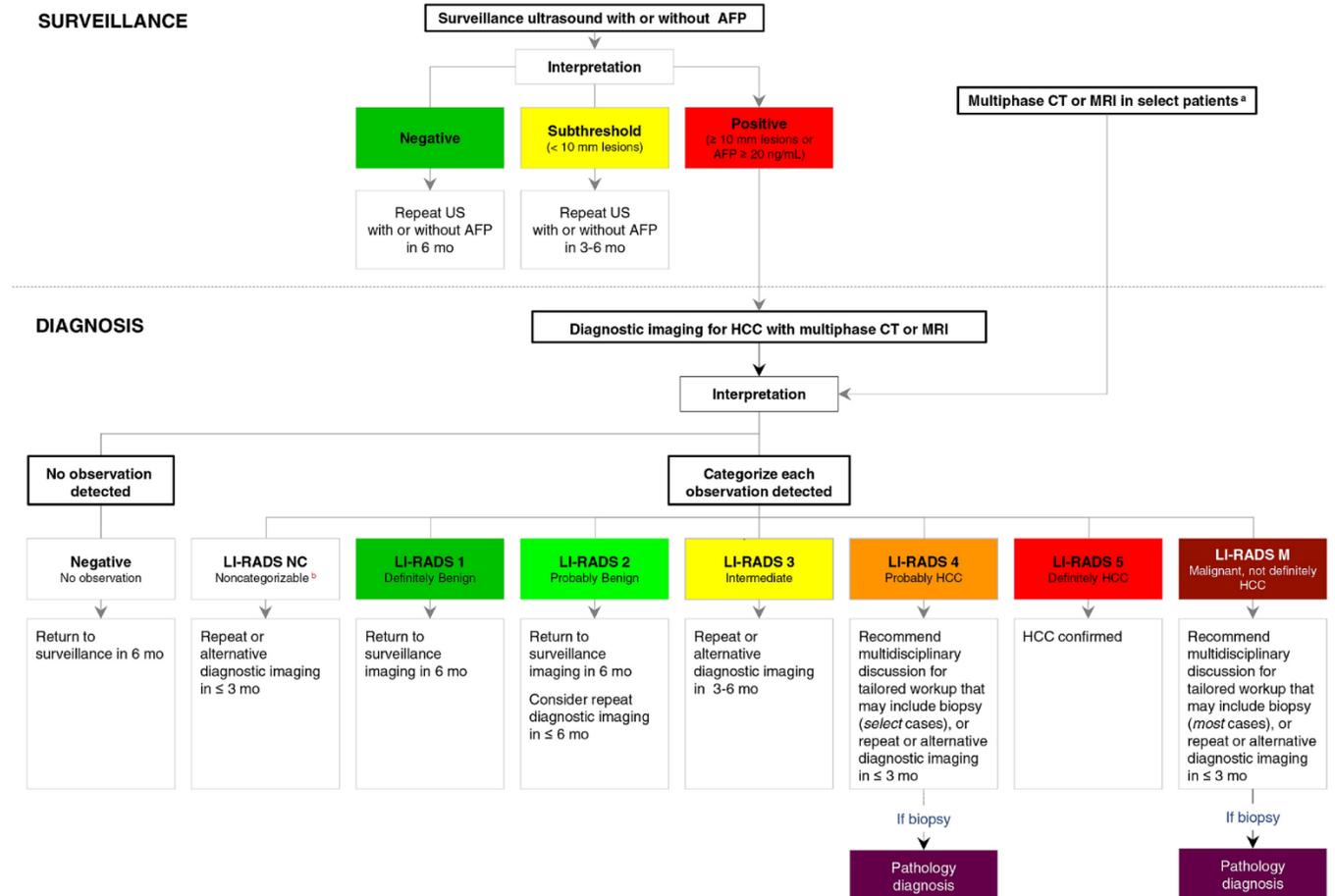
Recommendation 4.4

The provider(s)/service responsible for ordering and reviewing surveillance imaging should be agreed upon by the multidisciplinary team and any change in responsible provider(s)/service (for example, at the time of transitions of care between services) should be clearly communicated in the electronic medical record. Closed loop communication and clear identification of lines of responsibility are helpful to avoid confusion, misunderstanding, and losses to follow-up.

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Appendix A: AASLD Surveillance and Diagnostic Algorithm for Hepatocellular Carcinoma(5)



Footnotes

a. Multiphase CT or MRI in select patients Some high-risk patients may undergo multiphase CT or MRI for HCC surveillance (depending on patient body habitus, visibility of liver at ultrasound, being on the transplant waiting list and other factors).

b. Noncategorizable These are due to technical problem such as image omission or severe degradation

Appendix B: Eastern Cooperative Oncology Group Performance Status

GRADE	ECOG PERFORMANCE STATUS
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours
3	Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours
4	Completely disabled; cannot carry on any selfcare; totally confined to bed or chair
5	Dead

Developed by the Eastern Cooperative Oncology Group, Robert L. Comis, MD, Group Chair.(17)