Supplementary Appendix 1. Full questionnaire used in the KLCA survey

Title: Survey for Establishing Expert Consensus on the Need for Liver Biopsy in the Diagnosis of Hepatocellular Carcinoma and in Accurate Prognostic Assessment Before and After Non-surgical Treatment

1. What is your current professional position/practice setting?
   - Professor
   - Fellow
   - Employed physician (staff physician)
   - Resident
   - Private practitioner
   - Other

2. What is your specialty?
   - Internal medicine
   - Surgery
   - Radiology
   - Radiation oncology
   - Pathology
   - Other

3. How often do you perform liver biopsy when diagnosing hepatocellular carcinoma?
   - Do not perform liver biopsy.
   - Rarely, in fewer than 10% of cases.
   - In 10–30% of cases.
   - In 30–50% of cases.
   - In 50–80% of cases.
   - In >80% of cases.
   - I do not directly order liver biopsy (e.g., radiology, pathology, or radiation oncology).

3-1. If you rarely perform liver biopsy, what are the reasons? (Multiple responses allowed)
   - Concern about biopsy-related complications (e.g., bleeding, death, needle-track seeding).
   - I do not think liver biopsy is essential for the initial diagnosis of HCC.
   - Even when HCC has already been diagnosed radiologically, I do not think the information obtained from biopsy (diagnostic or prognostic) is very helpful.
   - I am concerned that treatment initiation may be delayed while waiting for biopsy results.
   - Patients are often reluctant to undergo an invasive diagnostic procedure.
   - The treatment strategy would not change.
   - Without clear treatment guidance based on biopsy results, biopsy has little practical value.
   - The in-hospital process for performing liver biopsy is not well established.
   - Other (please specify).

3-2. If liver biopsy confirms hepatocellular carcinoma, do you perform additional testing, such as genetic testing or immunohistochemical staining (e.g., PD-L1), for prognostic assessment or subtype classification?
   - Do not perform additional testing.
   - Rarely, in fewer than 10% of cases.

- In 10–30% of cases.
- In 30–50% of cases.
- In 50–80% of cases.
- In >80% of cases.
- I do not directly decide whether additional testing is performed (e.g., it depends on the pathologist's judgment).

4-1. Have you ever experienced a major complication (including death) after liver biopsy performed for the initial diagnosis of HCC?
- Yes
- No

4-2. Have you ever experienced a major complication (including death) after liver biopsy performed during treatment of HCC to assess biological changes or predict prognosis?
- Yes
- No

4-3. What types of complications have you experienced after liver biopsy? (Multiple responses allowed)
- Bleeding
- Infection
- Needle-track seeding
- Severe pain
- Death
- No such experience
- Other (please specify).

4-4. If a complication occurred after liver biopsy, how was it managed?
- Antibiotics
- Supportive treatment (e.g., intravenous fluids, transfusion, analgesics)
- Surgery
- Interventional procedure
- Other (please specify).

4-5. Have you ever experienced an insufficient or nondiagnostic biopsy result because of inadequate tissue, failure to target the tumor, or failure to obtain a definitive pathological diagnosis despite successful tumor targeting?
- Yes
- No

4-6. When biopsy results are insufficient, as described in Question 4-5, what decision do you usually make? (Multiple responses allowed)
- Repeat biopsy until sufficient tissue is obtained.
- Proceed with treatment after radiologic diagnosis without additional testing.
- If the tumor is small or located in a difficult-to-biopsy area, consider a laparoscopic approach.
- Other (please specify).

5-1. Do you agree that coagulation parameters (e.g., platelet count and prothrombin time) should be checked and corrected as needed to reduce bleeding risk after liver biopsy (e.g., platelet count ≤50,000/μL; PT INR ≥1.5)?
- Yes
- No

5-2. It is known that medications such as warfarin, clopidogrel, aspirin, and non-vitamin K antagonist oral anticoagulants (NOACs; e.g., dabigatran and rivaroxaban) are associated with bleeding risk after biopsy. Do you agree that medication history should be checked and that temporary discontinuation should be considered before liver biopsy?
- Yes
- No

5-3. Even when guidelines for transfusion and discontinuation of antiplatelet or anticoagulant agents are followed, there may still be a general concern about bleeding risk during liver biopsy. What is your opinion? (Multiple responses allowed)
- Even after corrective measures, I remain concerned about bleeding risk; therefore, biopsy should be performed only in strictly necessary cases.
- If pre-procedure medication management and correction of coagulation parameters are undertaken, bleeding risk may be somewhat reduced; therefore, biopsy can be considered cautiously.
- If pre-procedure medication management and correction of coagulation parameters are undertaken, bleeding risk is reduced sufficiently; therefore, biopsy can be performed more actively.
- Other (please specify).

6. What are your views on the role of liver biopsy in the initial diagnosis of HCC? (Multiple responses allowed)
- Liver biopsy is not essential for the initial diagnosis of HCC.
- Although it is not essential for initial diagnosis, biopsy may be performed intermittently for research purposes, such as biomarker development.
- Even when HCC is strongly suspected radiologically, biopsy may help predict prognosis for systemic therapy.
- Biopsy is needed for differential diagnosis from other malignancies, such as cholangiocarcinoma.
- Other (please specify).

7-1. Do you perform liver biopsy before starting systemic therapy for advanced HCC?
- Do not perform liver biopsy.
- Rarely, in fewer than 10% of cases.
- In 10–30% of cases.
- In 30–50% of cases.
- In 50–80% of cases.
- In >80% of cases.
- I do not directly order liver biopsy (e.g., radiology, pathology, or radiation oncology).

7-2. Do you perform liver biopsy when the tumor is refractory on response evaluation during systemic therapy for advanced HCC?
- Do not perform liver biopsy.
- Rarely, in fewer than 10% of cases.
- In 10–30% of cases.
- In 30–50% of cases.
- In 50–80% of cases.
- In >80% of cases.
- I do not directly order liver biopsy (e.g., radiology, pathology, or radiation oncology).

7-3. After an initial response to systemic therapy for advanced HCC, do you perform liver biopsy when the disease later progresses or recurs in order to identify biological changes (e.g., combined hepatocellular-cholangiocarcinoma or poorly differentiated carcinoma)?
- Do not perform liver biopsy.
- Rarely, in fewer than 10% of cases.
- In 10–30% of cases.
- In 30–50% of cases.
- In 50–80% of cases.
- In >80% of cases.
- I do not directly order liver biopsy (e.g., radiology, pathology, or radiation oncology).

8. Have you ever encountered a case that was strongly suspected to be HCC on imaging, but yielded a different pathological diagnosis on biopsy or surgical specimen?
   - Yes
   - No

8-1. If yes, please describe the pathological diagnosis.

9. For diagnostic and prognostic assessment, do you also perform biopsy of non-tumor liver tissue?
   - Do not perform liver biopsy.
   - Rarely, in fewer than 10% of cases.
   - In 10–50% of cases.
   - In 50–80% of cases.
   - In >80% of cases.
   - I do not directly order liver biopsy (e.g., radiology, pathology, or radiation oncology).

10. Do you agree with the opinion that liver biopsy may be considered for the diagnosis of HCC or for prognostic assessment before or after treatments other than surgery? (Multiple responses allowed)
   - No change to the current guideline is needed (i.e., biopsy-based diagnosis only when the patient is not in a high-risk group for HCC or when imaging-based diagnosis is difficult).
   - I agree that efforts are needed to improve awareness and acceptance of liver biopsy for the diagnosis of HCC.
   - I agree that efforts are needed to improve awareness and acceptance of liver biopsy for evaluation or prognostic prediction during HCC treatment.
   - With current guidelines maintained for diagnosis or treatment evaluation, the use of liver biopsy should be selectively expanded, provided that the patient agrees and patient safety can be ensured, to support future advances in HCC care.
   - Other (please specify).

11. How do you think the use of liver biopsy in HCC should change in the future?
   - The current use of liver biopsy should be increased.
   - The current level of liver biopsy use should be maintained.
   - The current use of liver biopsy should be reduced.
   - Not sure.

Abbreviations: HCC, hepatocellular carcinoma; KLCA, Korean Liver Cancer Association; NOAC, non-vitamin K antagonist oral anticoagulant; PD-L1, programmed death-ligand 1; PT INR, prothrombin time international normalized ratio.