Challenges in diagnosis of hepatocellular carcinoma

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Liver nodule
Diagnosis of HCC: Typical imaging findings

- Increased enhancement on arterial phase
- Decreased enhancement (Washout) on delayed or equilibrium phase
AASLD 2010 Update

Liver nodule

- < 1 cm
  - Repeat US at 3 months
    - Growing/changing character
      - Investigate according to size
    - Stable

- > 1 cm
  - 4-phase MDCT/ dynamic contrast enhanced MRI
    - Arterial hypervascularity AND venous or delayed phase washout
      - Other contrast enhanced study (CT or MRI)
        - Yes
          - HCC
        - No
          - Biopsy
            - Yes
            - No

- Typical pattern (<2 cm)
  - → 61.7% sensitivity
  - 96.6% specificity

- HCC washout
  - → < 1 cm: 27%
  - 1 < 1.5 cm: 39%
  - >1.5, <2 cm: 50%
  - >2 cm: 82%

Bruix, Hepatology 2011
Forner, Hepatology 2008
Bruix and Sherman. Hepatology 2011
APASL guideline in 2010
(Asian Pacific Association for the Study of the Liver)

Nodule detected by US

Hypervascularity in the arterial phase on dynamic CT/MRI in chronic liver disease

+ or arterial hypervascularity

- or hypovascular

- Sonazoid/Levovist CEUS

Washout in the portal/venous phase

- or SPIO-MRI

- or Kupffer phase on Sonazoid/Levovist CEUS

Uptake (+)

Uptake (-)

HCC

Close follow-up
KLCSG guideline in 2009
(Korean Liver Cancer Study Group)

Liver nodule+ (Risk factor: HBV+, HCV+, Liver cirrhosis)

- AFP ≥ 200 ng/mL
  - One typical dynamic imaging technique

- AFP < 200 ng/mL
  - Two typical dynamic imaging techniques

- Liver biopsy

Treat as HCC

If liver cirrhosis patients have a tumor ≥ 2 cm, typical characteristic finding of HCC in either one of dynamic contrast enhancement CT or MRI, regardless of serum AFP level
Discordance among the guidelines

- Nodules <1cm showing typical CE pattern
  - AASLD, EASL: US F/U
  - APASL, JSH: regardless of size

- Hypervascularity
  - AASLD, EASL, Korean: CT, MRI
  - APASL, JSH: + CEUS (CTAP)
Discordance among the guidelines

• Hypervascular nodule /s WO
  – AASLD, EASL : Bx
  – APASL, JSH: further evaluation with CEUS, SPIO-MRI or EOB-MRI
    • some ICC, adenoma, FNH-like nodule

- Hypovascular nodule
  - AASLD, EASL, Korean: US F/U
  - APASL: defect on SPIO-MRI or CEUS → HCC
    - HGDN
  - JSH : defect on EOB-MRI & CEUS → HCC, one of them → Bx
Nodule (<1cm) showing hypervascularity /s WO
14m later, Dx of HCC & TACE
Nodule (<1cm) showing hypervascularity /s WO

AP → 4m later → AP
12m later, HCC with microvascular invasion
Hypervascular Small HCC (< 1cm) on Gd-EOB-DTPA MRI & DWI

TABLE 3: Results of Multivariate Analysis for Diagnosis of Hepatocellular Carcinoma 1 cm and Smaller

<table>
<thead>
<tr>
<th>MRI Finding</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperintensity on T2-weighted images</td>
<td>16.1</td>
<td>4.7–55.1</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Hyperintensity on diffusion-weighted images</td>
<td>5.7</td>
<td>1.6–20.5</td>
<td>0.0081</td>
</tr>
<tr>
<td>Hypointensity on hepatobiliary phase images</td>
<td>3.4</td>
<td>0.8–14.7</td>
<td>0.7537</td>
</tr>
<tr>
<td>Washout on portal venous or 3-minute late phase images</td>
<td>0.8</td>
<td>0.2–3.4</td>
<td>0.1063</td>
</tr>
</tbody>
</table>

TABLE 4: Sensitivity and Specificity for Diagnosis of Hepatocellular Carcinoma Measuring 1 cm or Smaller

<table>
<thead>
<tr>
<th>MRI Finding</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperintensity on T2-weighted images</td>
<td>90.7</td>
<td>78.8</td>
<td>55.1–91.8</td>
</tr>
<tr>
<td>Hyperintensity on diffusion-weighted images</td>
<td>73.2</td>
<td>84.9</td>
<td>61.7–95.1</td>
</tr>
<tr>
<td>Hyperintensity on T2-weighted images and diffusion-weighted images</td>
<td>67.6</td>
<td>87.9</td>
<td>65.2–96.6</td>
</tr>
</tbody>
</table>

Kim J, Kim SH. AJR 2011;196:W758
Hypovascular HCC
- On EOB-MRI, hypovascular hypointense nodule on HBP
Hypovascular HCC

• Among hypovascular hypointense nodule on HBP of EOB-MRI,
  → Recognition of HCC or high risk nodule

  – Size ≥ 15mm  
  – Hyperintensity on DWI

  – Hyperintensity on T2WI, growth rate

  – Fat within nodule, Hyperintensity on T1WI, growth rate
For early diagnosis of HCC

- Higher sensitivity using combination of contrast-enhanced MRI and DWI
Small Hepatocellular Carcinomas: Improved Sensitivity by Combining Gadoxetic Acid–enhanced and Diffusion-weighted MR Imaging Patterns

Consecutive patients with chronic liver disease underwent liver MR imaging between May 2009 and July 2010 (n=2530)

Excluded patients:
- Unavailable liver MR imaging, including gadoxetic acid-enhanced imaging and DWI (n=45)
- Previous treatment for HCC prior to MR examination (n=1760)

HCC (n=565)
- Excluded patients:
  - No surgery (n=262)
  - HCC > 2.0 cm in diameter (n=173)

Consecutive 130 patients enrolled with 179 HCCs

No HCC (n=160)

Consecutive 130 control patients matching the number of patients with HCC

<Dx criteria for HCC>

① Gadoxetic acid set :
  a. hypervascularity + WO + HBP low SI
② DWI set :
  DWI high SI + ADC value ≤ that of parenchyma
③ Combined set:
  a. hypervascularity + WO + HBP low SI
  a. hypervascularity + HBP iso- or low SI + DWI high SI
  faint or no a. hypervascularity + HBP low SI + DWI high SI
62/M,
HCC grade II

- Gadoxetic acid set: 4
- DWI set: 4
- Combined set: 4
66/M, HCC grade I

- Gadoxetic acid set: 1
- DWI set: 3 or 4
- Combined set: 3
55/M, HCC grade I > II

- Gadoxetic acid set: 3
- DWI set: 1
- Combined set: 3
The combination of gadoxetic acid–enhanced MRI and DWI yielded better sensitivity in the detection of small HCCs than each MR imaging technique alone.
Conclusions

- Increased detection of small HCC due to advanced imaging
- More studies necessary for indeterminate liver nodule
- Guidelines for HCC diagnosis; HBP (and DWI) MRI