Management of Cirrhotic Complications in Hepatocellular Carcinoma

-portal hypertension, ascites, and varix-

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Terminal stage of HCC ??
- advanced HCC and deterioration of liver function
- HCC on decomp. cirrhosis (child C)
- non-response HCC by treatment

Best supportive care ??
- pain control...
- regulation of fluid retention with diuretics, abdominal paracentesis, and albumin infusion
- Intervention treatment of variceal bleeding
Prognosis of Cirrhosis

1. HRS (+sepsis)
2. Varix bleeding
3. HCC (~25%)
### Prognosis of Decomp-Cirrhosis

#### Meta-analysis of 72 studies predicting factors of mortality

<table>
<thead>
<tr>
<th>Parameters</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Follow-up periods (months)</td>
<td>21 months</td>
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<tr>
<td>Mortality</td>
<td>43%</td>
</tr>
<tr>
<td>Causes of death</td>
<td></td>
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<tr>
<td>Hepatocellular carcinoma</td>
<td>21%</td>
</tr>
<tr>
<td>Progression of liver disease</td>
<td>23%</td>
</tr>
<tr>
<td>Variceal bleeding</td>
<td>20%</td>
</tr>
<tr>
<td>Sepsis</td>
<td>7%</td>
</tr>
</tbody>
</table>

Tandon et al. Liver Int 2009;29:502-510
HCC and PHT

• HCC worsens portal hypertension (PHT).
  ➔ Portal vein thrombosis
  ➔ Tumor invasion
  ➔ Shunt formation around tumor
  ➔ Increase of VEGF
Tumor Growth and Angiogenesis

Matrix Metalloproteinases → Basal Membrane Degradation → TUMOR GROWTH

Central Tumor Hypoxia → HIF-1α → Upregulation of proangiogenic pathways → TUMOR GROWTH

Mutated Oncogenes or Tumorsuppressorgenes → TUMOR GROWTH

PDGF, bFGF, VEGF → Endothelium: Cell Survival, Proliferation, Migration → ANGIOGENESIS

Semela D et al. J Hepatol 2004;41:864-880
PHT and Angiogenesis

Fernandez M et al. Gastroenterology 2004;126:886-894
PHT and Complication

• Varix and bleeding

• Splenomegaly

• Portosystemic collaterals

• PHT-gastropathy (GAVE)

• Ascites
HCC and Variceal Bleeding

A

B


Chang GJ et al. J Gastroenterol 2012;47:531-539
HCC and Ascites

- Barcelona Clinic Liver Cancer (BCLC)
- Cancer of the Liver Italian Program (CLIP)
- Chinese University Prognostic Index (CUPI)
- Tokyo score
- Groupe d’Étude du Treatment du Carcinome H’épatocellulaire (GRETCH)

➡ Child-Pugh Classification
HCC and Cirrhosis

- HCC cirrhosis
- Tumor progression
- Deterioration
  - PHT
- Portosystemic collaterals
  - Variceal bleeding
  - Ascites
- Poor Prognosis
  - Death
Beneficial Effects of Sorafenib on Splanchnic, Intrahepatic, and Portocollateral Circulations in portal Hypertensive and Cirrhotic Rats

Sorafenib on PTH in cirrhosis and HCC – a pilot study

Hidaka H et al. J Gastroenterol 2012 (E-pub)
Ascites Control

- Worsening of Liver function
- Increase of portal pressure
- Lymphatic blockage from tumor growth

- Symptom
  ; abdominal distension and discomfort, dyspnea, nausea, vomiting, and pitting edema
HCC and Ascites

- Treatment
  - diuretics
  - large volume paracentesis and albumin infusion
- The rates of diuretics response (38~86%)
- The first-choice diuretic for patients with cirrhotic ascites is aldosterone antagonist. (A1)
- Loop diuretics can be used along with aldosterone antagonist. (B1)
- Repetitive large volume paracentesis is recommended in patients with refractory ascites. (A1)
- In the case of large volume paracentesis, 8-10 g/L (albumin/ascites) is recommended for the prevention of postparacentesis circulation dysfunction. (A1)

Suk KT et al. CMH 2012;18:1-21
HCC and Variceal Bleeding

• The mean survival after bleeding – 3~6 wks

• Recurrent bleeding ➔ uncontrolled hemorrhage, cachexia, decompensated hepatic function

• Endoscopy complication ➔ fever, infection, ulceration, aspiration

• Recurrent bleeding related factors ➔ liver function, PVT, and large varix
Variceal Bleeding Control

• It is recommended that patients with acute variceal bleeding initially be administered vasoconstrictor and antibiotic treatment. (A1)

• Endoscopic treatment is recommended for patients with acute variceal bleeding. (A1)

• TIPS can be recommended if drugs and endoscopic therapy have failed or endoscopic treatment is impossible. (B1)

Suk KT et al. CMH 2012;18:1-21
Summary and Conclusion

• Terminal stage of HCC 는 매우 다양한 양상의 증상을 보여준다. 특히 간암이 나빠짐에 따라 간기능이 떨어지고 혈관 침범 등으로 간문맥압 항진증이 악화되며, 복수, 위식도정맥류 그리고 출혈 등의 추가적인 합병증이 발생할 수 있고, 이는 간암의 예후를 더욱 악화시킬 수 있다.

• 이런 환자들에게 보전적인 치료로 간문맥압의 조절, 복수 조절, 그리고 위식도정맥류 출혈의 치료 등은 일시적인 증상의 완화를 가져다 줄 수 있지만, 질환의 예후를 호전 시키긴 힘들어 보인다.

• 위와 같은 환자에게 적극적인 증상완화를 위한 치료에 대해 고려해 볼 필요가 있었다.
Thank you for your attention