Very Early and Early HCC

Treatment options?

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Introduction

• Staging of HCC is different from any other tumor

• Underlying liver disease.
  • Impact on prognosis beyond the tumor burden

• BCLC (Plan treatment option and predict clinical outcomes)
  • Endorsed
    • EASL
    • AASLD
BCLC classification

**Prognostic stage**

- **Very early stage (0)**
  - Single <2 cm
  - Preserved liver function
  - PS 0

- **Early stage (A)**
  - Single or 2-3 nodules <3 cm
  - Preserved liver function
  - PS 0

- **Intermediate stage (B)**
  - Multinodular, unresectable
  - Preserved liver function
  - PS 0

- **Advanced stage (C)**
  - Portal invasion/extrahepatic spread
  - Preserved liver function
  - PS 1-2

- **Terminal stage (D)**
  - Not transplantable HCC
  - End-stage liver function
  - PS 3-4

**Treatment**

- Ablation
- Resection
- Transplant
- Chemoembolization
- Systemic therapy
- BSC

**Survival**

- >5 years
- >2.5 years
- ≥10 months
- 3 months
• Decision of treatment of HCC (BCLC, rigidity) is performed in a multidisciplinary tumor board.

• Individual treatment plan (variables).

• Ablation therapies and surgery.
RFA, n = 8211; surgical resection, n = 10,085

- Only first-line HCC treatments were reported
- 10 year-period (2004, 2014)
- The majority of cases in the NCDB followed international guidelines, such as BCLC…
Subgroup analyses:

- **Overall survival was comparable for patients >65 yo and those with HCC less than 15mm.**

- Subgroups (HCC<50mm, HCC<30mm, single HCC>50mm, multiple HCC>30mm…)

- Short-term overall survival benefit for RFA

- Long-term OS was superior for surgical resection
Ablation vs Surgery
Very early and early HCC

✓ RFA:
  - Shorter duration of hospital stay
  - Better post operative outcomes
  - Lower readmission rate
  - Better short time morbi-mortality (no death 30-90d)

✓ Surgery: longer overall survival
• Single HCC or less than 2 HCCs less than 4-5cm
• 2-year overall survival 82.1-82.3%
Disease recurrence is common, and in some patients will occur outside transplant criteria.

Incidence and risk factors for recurrence beyond Milan criteria in potentially transplantable patients treated with RFA as first-line therapy.

Results: 28% despite close follow-up

• Early HCC (unresectable)
  • RFA could not be feasible (high risk location)
  
• Role of TACE
  • (TACE is often performed in early HCC)

• Inconspicuous nodule
  • Anatomic location:
    • Close to the hilum
    • Close to hepatic vein
    • Subcapsular
    • Colon, stomach…

Teratani T et al. RFA for HCC in so-called high risk locations. Hepatol. Baltim Md 2006; 43:1101-1108
TACE in early HCC

- Supraselective TACE (first line trt in early unresectable patient)
- Retrospective. 287 pts. Single HCC ≤ 2 cm
  - Mean follow-up period (66.1±25.7 months)
  - TACE was associated with an earlier time to progression TTP
  - Mean survival times in the RFA and TACE groups were 80.0±2.3 months 72.1±3.2 months

TACE vs LR in Early HCC

- BCLC staging system
  - Solitary HCC = Early stage (irrespective size)
- HR vs TACE in large HCC (solitary) 5-year survival was respectively 65% vs 17% (Jin YJ)
- Lee et al. 159 pts. HR vs TACE 5-year survival (TTP longer in the surgical group) 66% vs 50%


Pathology: Complete necrosis?

- TACE vs RFA
  - Safety margin
  - Tumor necrosis.
  - Satellite lesions.
  - Allard et al. TACE: benefit OS when it induces >90% tumor necrosis (specimens LT, or liver resection).
  - Seror et al. RFA can achieve complete necrosis in more than 90% case. (no touch multibipolar technique.)

Seror O et al. HCC with Milan criteria: No touch multipolar RFA for treatment-long term results. Radiology 2016 280;2:611-621
LR vs TACE

Liver Resection for Multiple Hepatocellular Carcinomas
A Japanese Nationwide Survey

Annals of Surg. 2019

- Liver resection in multiple HCC (Japanese data)
- LR (n=1944), TACE (N=1302)
- LR showed a survival benefit over TACE at 5 years (60% vs 41.6%)
- Subgroup analyses:
  - Tm size of < 30 mm OS after LR 70.7% at 5 years.
Early HCC TACE + RFA

- Patient with unresectable HCC that is a candidate for RFA.

- Combined therapy TACE + RFA
  
  • Metanalysis early stage HCC (TACE, RFA, PEI and combinations) 21 RCT1, 3, and 5-year survival.

- Rank 1: TACE + RFA. (no difference compared with HR alone)

  - Lan T et al. Comparative efficacy of interventional therapies for early stage HCC. A PRISMA-compliant systematic review. Medicine 2016. vol 95:15; 1-10
TACE prior liver resection or liver transplant

- Patient with resectable HCC going for surgical resection.
- Preoperative TACE prior liver resection or LT (373 pts)

**Hypothesis:** the pathologic response to TACE may impact survival as the prognostic value of PR to chemo has been previously demonstrated in other malignancies.

**CPR (complete pathologic response):**
- 59 pts (32%) LR group
- 37 pts (20%) LT group.

TACE prior liver resection or liver transplant

- The mean pathology response to tumor size
- Best PR was observed in nodules 21-50mm (PR mean of 67%)
- PR 55% in nodules < 20mm
- PR 53% in nodules >50 mm.

✔ **Impact on survival after resection:**

Improved 3 and 5-year survival with CPR compared those without 84% and 84% compared to 72% and 65%
CONCLUSION

• Ablation therapies and surgery (liver resection or transplantation).
• Combined therapies.
• TACE (if ablation or surgical resection not suitable).