Carcinoma hepatocelular
Terapêuticas loco-regionais

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EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma

HCC in cirrhotic liver

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 1^2-2

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

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

Treatment

Ablation

Resection

Transplant

Ablation

Chemoembolization

Systemic therapy

BSC

Survival

>5 years

>2.5 years

≥10 months

3 months
RMD

- Age
- Child-Pugh
- α-fetoprotein (prognosis and follow-up)
- Performance status
- Comorbidities
- Tumor – size and location
- Tumor – number
- Tumor - Vascular invasion
- Ascites
- Extra-hepatic disease

Candidato TX

Não

Sim

Terapêuticas loco-regionais (TLR)

Intra-arterial

percutânea

RH/TLR

Sorafenib/BSC

Ponte ou Downstaging - TLR
Studies have shown that response to locoregional treatment is an important factors for prognosis. Thus, as proposed by Mazzaferro, future selection criteria may be based on response to locoregional treatments. In other words, all patients with HCC on a waiting list for Ltx should be treated with locoregional treatments followed by a suitable observation period regardless of tumor size and number. Transplant priority should be given to patients based not only on conventional criteria, but also on the response to locoregional treatment. The results of the present paper support this notion.
Liver-Directed Therapy for Hepatocellular Carcinoma: An Overview of Techniques, Outcomes, and Posttreatment Imaging Findings

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Shahid M. Hussain²

OBJECTIVE. The purposes of this article are to describe the indications, techniques, and results of arterially directed therapies and ablation and to review the imaging assessment of response and complications.

CONCLUSION. Most patients with hepatocellular carcinoma are not eligible for surgery, and systemic treatments are suboptimal. Therefore, locoregional therapy plays a large role in this disease. Locoregional therapies include arterially directed therapies, ablation, and radiation therapy.
Terapêuticas Intra-arteriais
TAE  TACE  TARE

TAE - Transarterial embolization is defined as blockade of hepatic arterial flow with a vascular occlusive agent, such as gelatin sponge, polyvinyl alcohol, or calibrated microspheres.

TACE – Transarterial chemoembolization is defined as infusion chemotherapeutic agents and embolic material.

cTACE ou DEB TACE
Contraindications

- Decompensated liver cirrhosis (Child-Pugh B, score ≥ 8)
- Br > 2 mg/dL
- Kidney failure (creatinine ≥ 2 mg/dL or creatinine clearance < 30 ml/min)
- > 60% tumoral invasion in both lobes
- Extra-hepatic disease
- Severe allergic reaction to iodinated contrast medium

Contra-indicação Relativa:
- Biliary obstruction/manipulation
- Esophageal varices at high risk of bleeding
- Severe comorbidities

Portal vein occlusion was once considered a contraindication to ADT. The current practice of TAE, TACE, and radioembolization has shown efficacy without an increase in complications in selected cases.
Conclusions
Chemoembolization with PEG embolic agents for HCC is safe and effective, achieving an objective response rate of 85.5%.
TARE - Radioembolization
Y90 ou Ho166

• The aim of SIRT is the delivery of a high-energy beta emitter (90Y) to the tumor bed on a glass (TheraSphere, BTG) or resin (SIR-Sphere, Sirtex) bead.

• QuiremSpheres® is based on Holmium-166 microspheres, which were developed in the clinic as an alternative to Yttrium-90 microspheres for treating unresectable liver tumors with selective internal radiation therapy (SIRT).

• these beads are not intended to embolize the target vessels.

Conclusions: There was insufficient evidence to assess the beneficial and harmful effects of yttrium-90 microsphere radioembolisation for people with unresectable hepatocellular carcinoma. Further randomised clinical trials are mandatory.
Complications of arterially directed therapies

- non target embolization
- liver failure
- vessel injury
- Post embolization syndrome. Post embolization syndrome consists of pain, fever, nausea, or a combination of these symptoms, that can last for several days.

**Conclusion:** The dose of doxorubicin, the size of the largest nodule treated and female gender are potential risk factors for the development of postembolization syndrome after hepatic transarterial chemoembolization for hepatocellular carcinoma.
Ablação CHC

- PEI - alcoolização
- RFA - Radiofrequência
- MWA – Microondas
- Laser, CRIO,HIFU,IRE
Percutaneous ethanol injection - PEI

- Absolute alcohol 95%
- fine needle (22G)
- Coagulative necrosis: cellular dehydration, protein denaturation and chemical occlusion of small tumor vessels
- Ethanol diffusion is blocked by the intratumoral fibrotic septa and/or tumor capsule
- PEI is cheap, well tolerated, simple to perform, and does not require a general anaesthetic. Severe complications are infrequent at 0–2%, including seeding
- Complete necrosis: 90% of tumors <2 cm
- Since 1983
Radiofrequency ablation - RFA

- High-frequency alternating currents causing heat due to ionic agitation, resulting in coagulation necrosis

- Temperatures higher than 60 °C

- A limitation of RFA is the “heat sink” effect, which is related to the decrease in temperature from ablation in proximity to blood vessels
PEI vs RFA

In Conclusion: Our study results show that RF thermal ablation is more effective than PEI in the treatment of small HCC in patients with cirrhosis. Therefore, RF ablation should be considered the percutaneous treatment of choice for patients who are not candidates for resection or transplantation.

Clinical outcomes of radiofrequency ablation, percutaneous alcohol and acetic acid injection for hepatocellular carcinoma: A meta-analysis

Giacomo Germani¹, Maria Pleguezuelo¹, Kurinchi Gurusamy², Tim Meyer³, Graziella Isgrò¹, Andrew Kenneth Burroughs¹,

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In conclusion:
RFA seems to be better than PEI in patients with HCC, especially for nodules >2 cm diameter.
Microwave ablation - MWA

• High-frequency waves causing oscillation of H2O molecules, creating friction, tissue heating, and destruction by coagulation necrosis

• MWA energy achieves higher temperatures than RFA (up to 180 °C). MWA ablation also seems less affected by “heat sink” effect

• the short total time

• MWA is superior to RFA in treating larger tumors
CHC Termoablação - MWA
In conclusion: RF and MW ablation therapy showed no significant difference in the treatment of HCC regarding the complete response, rates of residual foci of untreated disease, recurrence rate, and survival indices.

MWA having a more advantageous profile in terms of ablation volume, procedural time and simultaneous treatment of multiple lesions. However, with respect to clinical end-points, there is no solid proof as yet to support the advantage of one over the other.
## Ablação

1. O número de lesões a tratar, normalmente ≤ 3 tumores
2. A dimensão do tumor: até 3 cm para RFA / ≤ até 4 cm para MWA (margem 5mm)
3. A localização do tumor: proximidade com os grandes vasos, os ductos biliares, muito periférico

<table>
<thead>
<tr>
<th></th>
<th>Alcoolização</th>
<th>RF</th>
<th>MW</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dimensão</strong></td>
<td>&lt; 1,5cm</td>
<td>Até 3cm</td>
<td>Até 4cm</td>
</tr>
<tr>
<td><strong>Localização</strong></td>
<td>Não depende</td>
<td>Depende Cl: Junto a G Vasos; Vesícula biliar; Sub-capsulares; Estruturas digestivas</td>
<td>Depende Cl: Estruturas digestivas; ductos biliares ectasiados</td>
</tr>
<tr>
<td><strong>Anestesia</strong></td>
<td>Sem sedação</td>
<td>Sedação</td>
<td>Sedação</td>
</tr>
</tbody>
</table>
Contraindications

Contraindications for RFA are as follows:

1. tumour located <1 cm from the main biliary duct (due to risk of delayed stenosis of the main biliary tract);
2. intrahepatic bile duct dilation;
3. anterior exophytic location of the tumour (due to the risk of tumour seeding);
4. bilioenteric anastomosis; and
5. treatable/unmanageable coagulopathy.
Termoablação - complicações

- Imediatas: mais comum é o derrame pleural e a hemorragia
- Tardias: raras (≤ 2.4%) abcesso, biloma, fistula biliar, estenose canal biliar, fistula arterio-venosa, hernia diafragmática, perfuração gástrica ou do colon

Mortalidade peri procedimento baixa < 0.01%,
Dimensão / localização
Localização vs dimensão
Conclusão

Terapêuticas loco-regionais

• Importante arma no tratamento do carcinoma hepanoacelular
• Diferentes opções
• Variar ou combinar as terapêuticas segundo o caso e a sua evolução

• Sempre em contexto multidisciplinar
• Sempre em centros de referência
• Disponibilidade de todas as opções: RI; CIRURGIA; HEPATOLOGIA; ONCOLOGIA