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REVIEW

Outcome of regional and local ablative therapies for hepatocellular carcinoma: a collective review

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Abstract *Background*. Transcatheter arterial (chemo) embolization (TACE), cryoablation (CA) and percutaneous ethanol injection (PEI) were the first regional and local ablative techniques that came into use for irresectable HCC. Radiofrequency ablation (RFA) and interstitial laser coagulation (ILC) followed and have now evolved rapidly. It would not be ethical to compare resection with ablation in patients well enough to undergo major surgery. Therefore, hepatic resection and hepatic transplantation remain the only curative treatment options for HCC.

Methods. On the basis of a Medline literature search and the authors' experiences, the principles, current status and prospects of TACE and local ablative techniques in HCC are reviewed.

Results. Complete tumour necrosis can be achieved in 60–100% of patients treated with PEI (70–100%), cryoablation (60–85%), RFA (80–90%) or ILC (70–97%). After TACE significant tumour response is achieved in 17–61.9% but complete tumour response is rare (0–4.8%) as viable tumour cells remain after TACE. Five-year survival rates are available for TACE (1–8%), PEI (0–70%) and cryoablation (40%). Only PEI and RFA were compared in one RCT. RFA was associated with fewer treatment sessions and a higher complete necrosis rate. Furthermore, all techniques are associated with low morbidity and mortality, but cryoablation seems to be associated with a higher morbidity rate.

Conclusion. TACE has shown to be a valuable therapy with survival benefits in strictly selected patients with unresectable HCC. RFA and PEI are now considered as the local ablative techniques of choice for the treatment of, preferably small, HCC. When tumours are located close to bile ducts or large vessels, PEI remains a valuable therapy. Completeness of ablation can be more easily monitored during cryoablation and another advantage of cryoablation is the possibility of edge freezing. The results

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of ILC are comparable to RFA with only few side effects and high tumour response rates.

Introduction

Primary hepatocellular carcinoma (HCC) is the most prevalent type of liver carcinoma in the world. Hepatitis B virus (HBV), hepatitis C virus (HCV) and alcohol related cirrhosis is the leading causes associated with HCC carcinogenesis. The prognosis is poor while surgery remains the best curative therapy. Two surgical procedures are available; partial liver resection (PHx) and liver transplantation (LTx). Although liver transplantation is a curative treatment with good survival rates, its usage is restricted by the shortage of donor organs.[1] Surgical resection can result in a significant long-term survival benefit. However, only 9–27% of the patients that present with HCC are surgical candidates, because of multifocal intrahepatic disease, extrahepatic disease, inadequate functional hepatic reserve, inability to obtain an optimal tumour free margin, or involvement of the portal vein.[2,3] Surgical resection is restricted to patients with child A and possibly child B cirrhosis because of the high operative risk associated with the poor general status, reduced functional hepatic capacity and impairment of liver regeneration in patients with cirrhosis.[4] Surgical resection is associated with 5-year survival of over 30% and in the best surgical candidates even up to 70%.[5–7] Post-operative mortality and morbidity is considerable and is mainly caused by failure of the remnant liver, intraabdominal haemorrhage, hepatorenal or cardorespiratory failure or sepsis.[8–11]

In light of these surgical limitations and because of the severe shortage of donor livers, local ablative techniques have emerged as alternative therapies for unresectable HCCs. The use of these local ablative techniques has changed our approach of HCCs. Intraoperative ablative therapy has extended the limits of surgical treatment as patients with multiple HCCs can now be treated with curative intent in combination with partial liver resection. Which one of the local ablative methods is used, is often a matter of local preference and experience. Local ablative techniques can be applied in a variety of settings (at laparotomy, during laparoscopy or percutaneously). At laparotomy, organs surrounding the liver such as stomach or colon can be protected when necessary, and the liver can be mobilized allowing access to lesions otherwise difficult to reach by a percutaneous route. Therefore, knowledge of the principles and results of these local therapies is essential for all surgeons dealing with liver tumours.

In the absence of controlled randomized trials comparing each ablative technique, our aim was to review the various therapies currently available for the treatment of unresectable HCC. This review intends to expose the field of regional and local ablative techniques in the treatment of HCC, with special emphasis on outcome and survival.

Transcatheter arterial chemoembolization (TACE)

Mechanism of action and practical aspects

Transcatheter arterial chemoembolization (TACE) is a regional therapy for HCC in which targeted chemotherapy and arterial embolization is combined. The therapy has both selective ischemic and chemotherapeutic effects on HCC. Cytotoxic agents such as doxorubicin, cisplatin or mitomycin C are mixed with lipiodol and administered to the feeding artery of the tumour, followed by transarterial embolization with gelatin sponge particles or polyvinyl alcohol particles (PVA) blocking blood flow to the supplying artery. As the blood supply of HCC is predominantly derived from the hepatic artery, arterial embolization will enhance the effects of lipiodol and cytotoxic agents.

Indications and contraindications

Patients eligible for TACE should be strictly selected to optimize tumour response, decrease complication rate and hence, increase survival rates. Ischemia of unaffected liver tissue is prevented by selective catheterization of the arterial branches feeding the tumour and preservation of portal venous blood flow. Main portal vein thrombosis is therefore, a contraindication to TACE therapy, together with insufficient liver reserve (child C), extrahepatic metastases, severe clotting abnormalities and severe arteriovenous shunting to the portal/hepatic vein.[12]