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Review

The role of portal vein embolization in the surgical management of primary hepatobiliary cancers. A systematic review

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Abstract

Background: Primary liver and biliary cancers are very aggressive tumors. Surgical treatment is the main option for cure or long term survival. The main purpose of this systematic review is to underline the indications for portal vein embolization (PVE), in patients with inadequate future liver remnant (FLR) and to analyze other parameters such as resection rate, morbidity, mortality, survival after PVE and hepatectomy for primary hepatobiliary tumors. Also the role of trans-arterial chemoembolization (TACE) before PVE, is investigated.
Methods: A systematic search of the literature was performed in Pub Med and the Cochrane Library from 01.01.1990 to 30.09.2015.
Results: Forty articles were selected, including 2144 patients with a median age of 61 years. The median excision rate was 90% for hepatocellular carcinomas (HCCs) and 86% for hilar cholangiocarcinomas (HCs). The main indications for PVE in patients with HCC and presence of liver fibrosis or cirrhosis was FLR <40% when liver function was good (ICGR15 < 10%) and FLR < 50% when liver function was affected (ICGR15:10–20%). The combination of TACE and PVE increased hypertrophy rate and was associated with better overall survival and disease free survival and should be considered in advanced HCC tumors with inadequate FLR. In patients with HCs PVE was performed, after preoperative biliary drainage, when FLR was <40%, in the majority of studies, with very good post-operative outcome. However indications should be refined.
Conclusion: PVE before major hepatectomy allows resection in a patient group with advanced primary hepato-biliary tumors and inadequate FLR, with good long term survival.

Keywords: Portal vein embolization (PVE); Primary liver cancer; Biliary cancer; Liver resection; Hepatectomy; Hepatocellular carcinoma (HCC); Intrahepatic cholangiocarcinoma (IHC); Hilar cholangiocarcinoma (HC)

Introduction

Primary hepatobiliary tumors, which mainly include hepatocellular carcinoma (HCC), intrahepatic cholangiocarcinoma (IHC) and hilar cholangiocarcinoma (HC) are very aggressive tumors with mean survival less than one year if left untreated.[1–3]

HCC is the second leading cause of cancer-death worldwide. Surgical treatment (liver transplantation and hepatic

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resection) is the best way to achieve long term survival for HCC. Liver transplantation has limitations as the main indications are patients with cirrhosis who fulfill the Milan criteria (1 tumor < 5 cm, or 3 tumors < 3 cm in diameter each) and there is shortage in liver grafts.[4] Liver resection is the treatment of choice for large HCCs with preserved liver function. However, surgery is often prohibited by underlying chronic liver disease (CLD). Liver resection in presence of fibrosis and/or cirrhosis can have a dramatic impact on portal venous pressure and hepatic functional reserve, increasing the former and decreasing the latter. Consequently, this leads to an elevation of morbidity and mortality rates.[5–7]

IHCs are tumors with poor prognosis. Surgical resection is the only available method of treatment that can lead to long term survival. One recent multicenter study with 584 patients reported 5 year survival of 22% and disease-free survival of 11%.[8] The biggest limitation of surgical treatment is the tumor's location and size.

HC (Klatskin tumor) although it is a rare malignancy at the same time is the most, common bile duct cancer. Most of the patients present when the disease is in an advanced stage. Surgical treatment is the only option for long term survival. However it requires very complex surgery involving excision of the extrahepatic biliary tree, lymph nodes, major hepatic resection and reconstruction. It is a challenge for the hepatobiliary surgeon and requires excellent management in order to achieve low perioperative mortality and significant survival benefit.[3]

Like for all tumors, histologically negative resection margins (RO resection) is a major prognostic factor. The intent of portal vein embolization (PVE) is to induce atrophy in the embolized part of the liver which is going to be resected and compensatory hypertrophy in the future liver remnant (FLR). This allows safe surgical resection with negative surgical margins and low perioperative mortality in patients with inadequate FLR.[9–11]

Portal vein ligation was initially reported in humans in 1965 as part of a two-stage extended hepatectomy.[12] However pre-operative portal vein embolization was initially performed by Makuuchi et al in 1982[13,14] for patients with HC requiring extensive liver resection. The purpose was to reduce the postoperative liver failure after extensive liver resection for hilar bile duct carcinoma in a small number of patients. Kinoshita et al reported for the first time the use of preoperative PVE for patients with HCC.[15] Since its original description indications for PVE have expanded and include any primary or metastatic liver cancer requiring better FLR prior to hepatectomy. The aim is to make tumors resectable and with low perioperative mortality by increasing FLR. PVE induces hypertrophy on one side of the liver parenchyma in advance of a planned hepatic resection of the other side which becomes atrophic (atrophy-hypertrophy phenomenon). The procedure is frequently used in primary liver and biliary cancer (HCC, IHP and HC) and in liver metastases, mainly from colorectal origin.[16]

There are several techniques for portal vein occlusion: intraoperative portal branch ligation, transileocolic PVE, and the percutaneous transhepatic route which can be ipsilateral when the puncture in the portal vein occurs in the side of the tumor or contra-lateral. Nowadays, with the advances in interventional radiology, the percutaneous transhepatic approach is the standard of care for PVE.

Two systematic reviews have been previously published studying the role of preoperative PVE in patients undergoing major liver resection for primary and metastatic tumors. The first by Albulkhir et al was published in 2008[17] and it studied both techniques (percutaneous transhepatic and transileocolic). Its conclusion was that PVE is a safe and effective procedure in inducing liver hypertrophy to prevent post-resection liver failure due to insufficient liver remnant. The second one was published in 2013 by Lienden et al.[18] This review evaluated all publications between 01.1990 and 05.2011, on the effect of mainly percutaneous transhepatic PVE, in the surgical management of primary and metastatic liver tumors. It concluded that preoperative PVE has high technical and clinical success rate; liver cirrhosis has a negative effect on regeneration and the use of n-butyl cyanoacrylate may result in greater hypertrophy response.

In the present systematic review, we focused on the effect of preoperative percutaneous PVE in the surgical management of primary liver and biliary cancers with inadequate FLR. We highlighted the current indications, clinical success rates, postoperative morbidity and mortality and survival rates post-PVE and liver resection for patients with primary tumors with special emphasis on HCCs and HCs. Additionally sub-group analysis was performed in order to identify the role of other modalities such as trans-arterial chemo-embolization (TACE) prior to PVE.

Materials and methods

Search strategy and information sources

A systematic search of the published literature was performed in PubMed and the Cochrane Library from 01.01.1990 to 30.09.2015 using a predefined, pilot-tested search algorithm as follows: "portal vein AND (embolization OR chemoembolization) AND (hepatocellular cancer OR hepatocellular carcinoma OR cholangiocarcinoma OR liver cancer OR hepatobiliary malignancies). Two investigators independently screened (ET, SPB) the retrieved citations at the title and abstract level. Articles which included information about metastatic liver disease only, were excluded. The final selection of the articles was made in consensus by all authors.

Eligibility criteria

We included clinical studies on PVE and hepatobiliary tumors assessing the following clinical parameters: patient

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