Clinical and experimental studies on portal vein embolization / Diagnosis of hepatocellular adenoma and focal nodular hyperplasia
van den Esschert, J.W.

Citation for published version (APA):
Part I

Introduction and outline of the thesis

Clinical and experimental studies on preoperative portal vein embolization
Introduction

Liver resection remains the main curative treatment for patients with liver malignancies. Although for single tumors, non-anatomical resections can be performed, for larger or multiple tumors anatomical liver resections are usually undertaken following the so called Couinaud segments (Figure 1). Unfortunately not all patients are suitable for liver surgery, because of the extent of the resection necessary to completely remove all tumor or the quality of the liver parenchyma which may be affected by pre-existing disease or induction chemotherapy. The part of the liver that remains after surgery must be sufficient in terms of volume and function to meet the metabolic needs of the body, otherwise postoperative liver failure occurs. The current method for determining the size of the liver that remains after liver resection is preoperative volumetry using computed tomography (CT). Liver volume is used as an indirect measure of liver function. The minimally required amount of remnant liver volume is under debate, but in general, 25-30% of the initial total liver volume is thought to be sufficient in patients with otherwise normal liver parenchyma. In patients with a compromised liver function (e.g. cirrhosis, cholestasis, steatosis) however, a remnant liver volume at least 40% is considered to be safe.

Figure 1. Liver segments according to Couinaud.
Fortunately, the hepatocellular mass of the liver has the unique possibility to regenerate. This phenomenon can be used to preoperatively treat patients who are at risk of developing postoperative liver failure because of a small for size liver remnant. Since the first publication of the clinical use of portal vein embolization (PVE) in 1990, the procedure has become a widely used method to preoperatively increase the future remnant liver. After occlusion of the portal vein to the part of the liver that has to be resected, atrophy of this part occurs while inducing a compensatory hyperplasia and hypertrophy of the contralateral liver segments.

Although PVE is largely applied worldwide, many issues concerning PVE and its consequences have emerged. Many questions still need to be elucidated, such as; What is the trigger for liver regeneration following portal vein occlusion? What is the underlying mechanism of liver regeneration after PVE? Which technique of portal vein occlusion results in the greatest hypertrophy response? What is the effect of PVE on tumor growth? These issues form the basis of the studies discussed in the first part of this thesis.

**Outline of the thesis**

The observation that portal vein occlusion leads to hypertrophy of the contralateral liver segments goes back much earlier than the 1980s. Chapter 1 gives an overview of how the concept of preoperative portal vein occlusion was defined.

Since its first clinical application, PVE has developed into a widely accepted, preoperative intervention to increase the future remnant liver. In Chapter 2, a systematic review is performed of all studies on PVE published in the last 20 years (1990-2011). The review discusses in particular, the effect of different embolization materials, prior treatment with chemotherapy, and the consequence of preexisting liver cirrhosis for the extent of hypertrophy response of the future remnant liver.

Preoperative PVE might hamper postresectional liver regeneration because a supposed trigger of liver regeneration, i.e. the instant increase of portal blood flow to the remnant liver, is largely unchanged after hemihepatectomy and previous PVE. A retrospective case-control study is described in Chapter 3 assessing the effect of preoperative PVE on liver volume and function, 3 months after major liver resection.

Unfortunately, PVE also has its drawbacks. The aim of Chapter 4 is to point out and discuss current controversies in the application of PVE. Chapter 5 reviews the clinical and experimental evidence regarding the effect of PVE on tumor growth in both the embolized and non-embolized liver lobes, as well as potential strategies to control tumor progression after PVE.
In an attempt to unravel some underlying mechanisms of liver regeneration after PVE and in order to optimize the technique for preoperative induction of liver regeneration, a standardized animal model is desired. In Chapter 6, a standardized rabbit model is described for PVE in experimental studies.

Clinical and experimental studies show opposite results regarding the issue if ligation or embolization of the portal vein leads to a greater regenerative response. The aim of Chapter 7 is to compare the hypertrophy response of the liver after ligation or embolization of the portal vein using this standardized rabbit model.

Many embolization materials have been used for PVE in the clinical setting. In Chapter 8, the hypertrophy response after the use of absorbable or permanent embolization materials is compared in the same rabbit model.

In order to further optimize the hypertrophy response, the effect of hepatic vein embolization on liver regeneration in addition to PVE is assessed in Chapter 9.
References