

MALIGNANT TUMORS OF LIVER

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INTRODUCTION

- **Surgical resection is the first-line treatment for selected patients with hepatobiliary malignancies.**
- **With refinements in surgical techniques and perioperative patient care, the safety of liver resection has improved dramatically over the decades.**

MALIGNANT TUMORS IN LIVER

- **Secondary (most common):**
Metastases (mostly colorectal)
- **Primary:**
HCC, cholangiocarcinomas

LIVER METASTASES

- **Colo-rectal cancer**
- **GI (anywhere)**
- **Breast**
- **Others**
 - » **Neuro-endocrine tumours**
 - » **Renal**
 - » **Endocrine**
 - » **Genitourinary inc. prostate.**
 - » **Melanoma, sarcomas**
 - » **Anal**

CRC LM - EPIDEMIOLOGY

- **150.000 & 34.000 new cases of CRC each year in USA & UK, respectively.**
- **60% will develop metastatic disease, which is confined to the liver in half of them**
- **10-30% resectable**

CRC LM – DIAGNOSIS / STAGING

- **US** **solid/fluid differentiation**
- **CT** ***high sensitivity/specificity***
- **MRI** **further characterization in selected cases.**
- **FDG-PET** **if high clinical suspicion & negative imaging above.**

Invasive Assessment

- **Endoscopic Ultrasound (in selected cases)**
 - For lymph node assessment
 - For vascular involvement
- **Laparoscopy (intra-operatively before resection)**
 - For peritoneal deposits
 - For vascular involvement
- **Intraoperative US + bimanual palpation**
 - To help in assessing the tumor's location and depth during surgical resection

TUMOR MARKERS

- CEA false –ve in 30% of cases
- CA 19-9

CRC LM – SCORING SYSTEM for prognosis

| | |
|-----------------------------------|--|
| Number of lesions | > 3 |
| Size of largest lesion | > 5 cm |
| CEA level | > 200 ng/ml |
| Presentation | < 1 years from primary |
| Stage of primary | Positive nodal status |
| <u>Risk</u> | 0-2 low 3-5 high |
| 5 years actuarial survival | 0 points 60%, 1 point 50% 2 points 40%, 3 points 20% 5 points 14% |

Recommendation against hepatic resection if have 3 *Points or more*

Surgical Planning Based on the Anatomy

In general terms, all tumors should be assessed based on:

1) Couinaud's *(queeno's)* segments of the liver anatomy

And

2) proximity / involvement of major inflow pedicles & hepatic venous outflow.

Couinaud's Classification

The Couinaud classification of liver anatomy divides the liver into eight functionally independent segments.

Each segment has its own vascular inflow, outflow and biliary drainage. In the centre of each segment there is a branch of the portal vein, hepatic artery and bile duct.

Surgical Planning Based on the Anatomy

Preoperative evaluation may vary slightly based on tumor type:

For hepatocellular carcinoma (HCC), anatomic resection of the tumor-bearing portal region is recommended to reduce the risk of local recurrence and eradicate micrometastases scattered from the main lesion via portal veins.

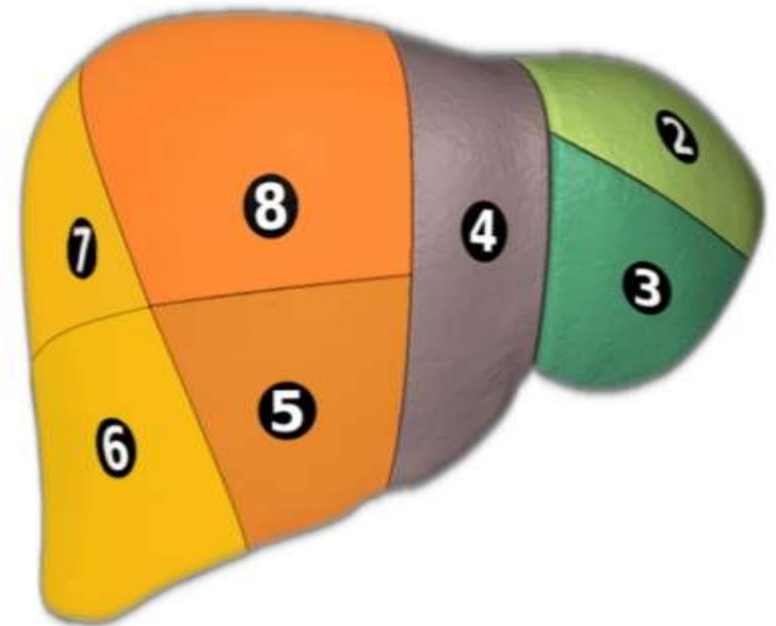
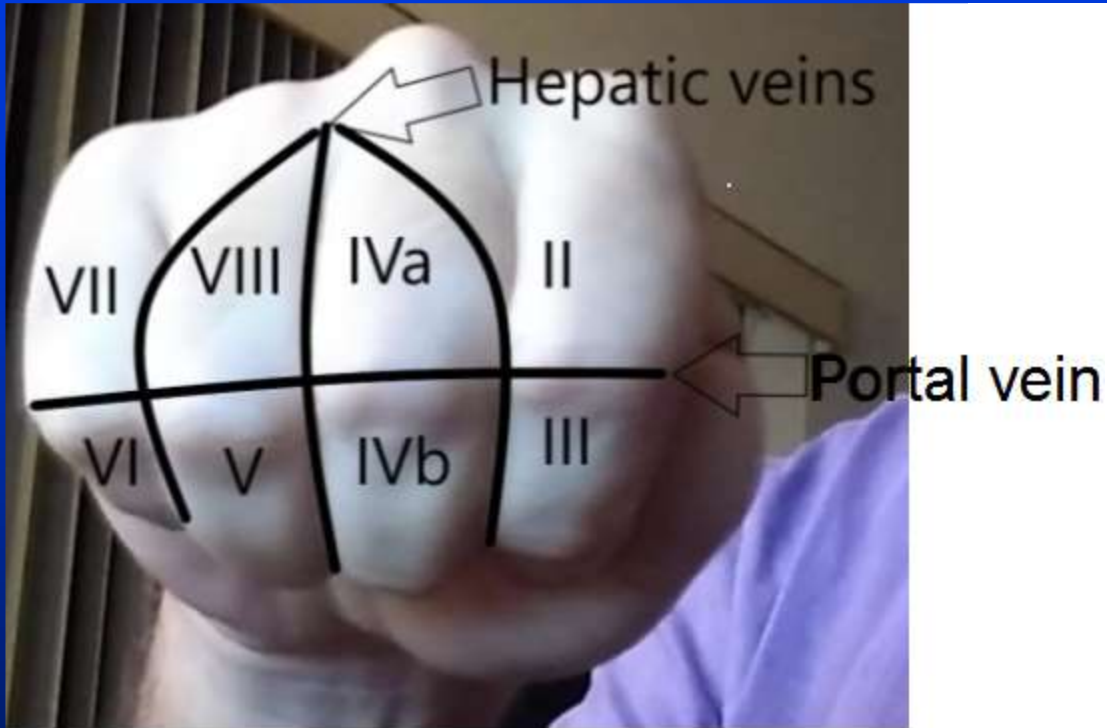
For colorectal liver metastases (CLMs), limited resection with adequate surgical margins and major hepatectomy have been used because a 2- to 4-mm surgical margin has been shown to be required in order to encompass micrometastases around CLM lesions in histopathologic studies.

Surgical Planning Based on the Anatomy

The relationship between the tumor and surrounding major vascular structures should be evaluated for each tumor. HCC usually grows in an expanding fashion (rather than in an invading fashion) with a thick capsule. Empirically, these tumors can be detached from the vessels without increasing the risk of local recurrence, even though huge HCC lesions will compress the inferior vena cava severely.

In contrast, concomitant resection of the vessels should be considered in adenocarcinomas such as CLM and intrahepatic cholangiocarcinoma when a tumor is inseparable from adjacent major vascular structures. Although histopathologic invasion of the vessel wall is relatively uncommon on histopathologic examinations, adenocarcinomas lack capsules and easily invade blood vessel walls. Because it is difficult to predict whether histopathologic invasion will occur even after good response to chemotherapy, en bloc resection of adjacent blood vessels with sufficient margins is recommended for adenocarcinomas.

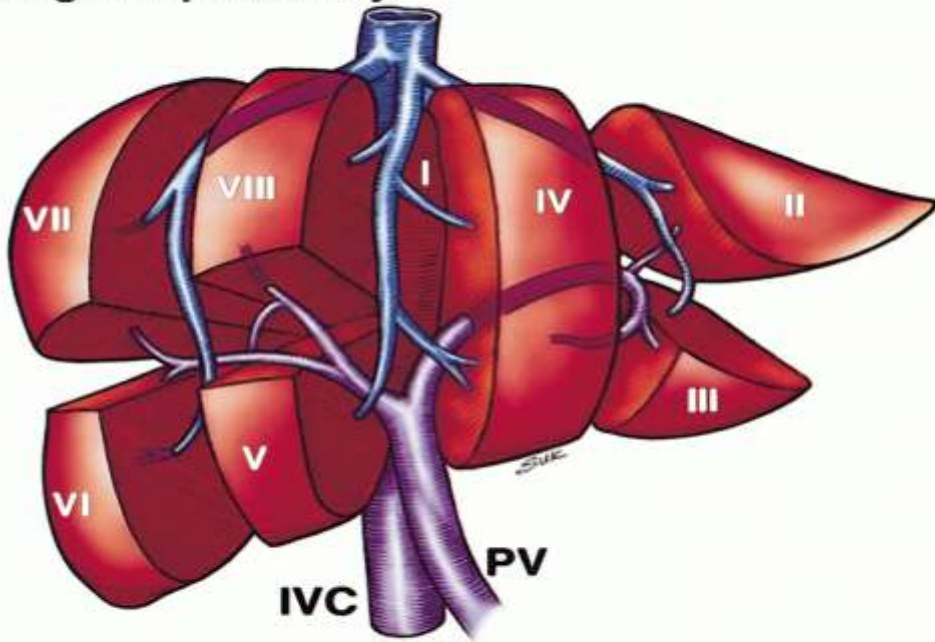
Liver anatomy



TYPE OF RESECTION

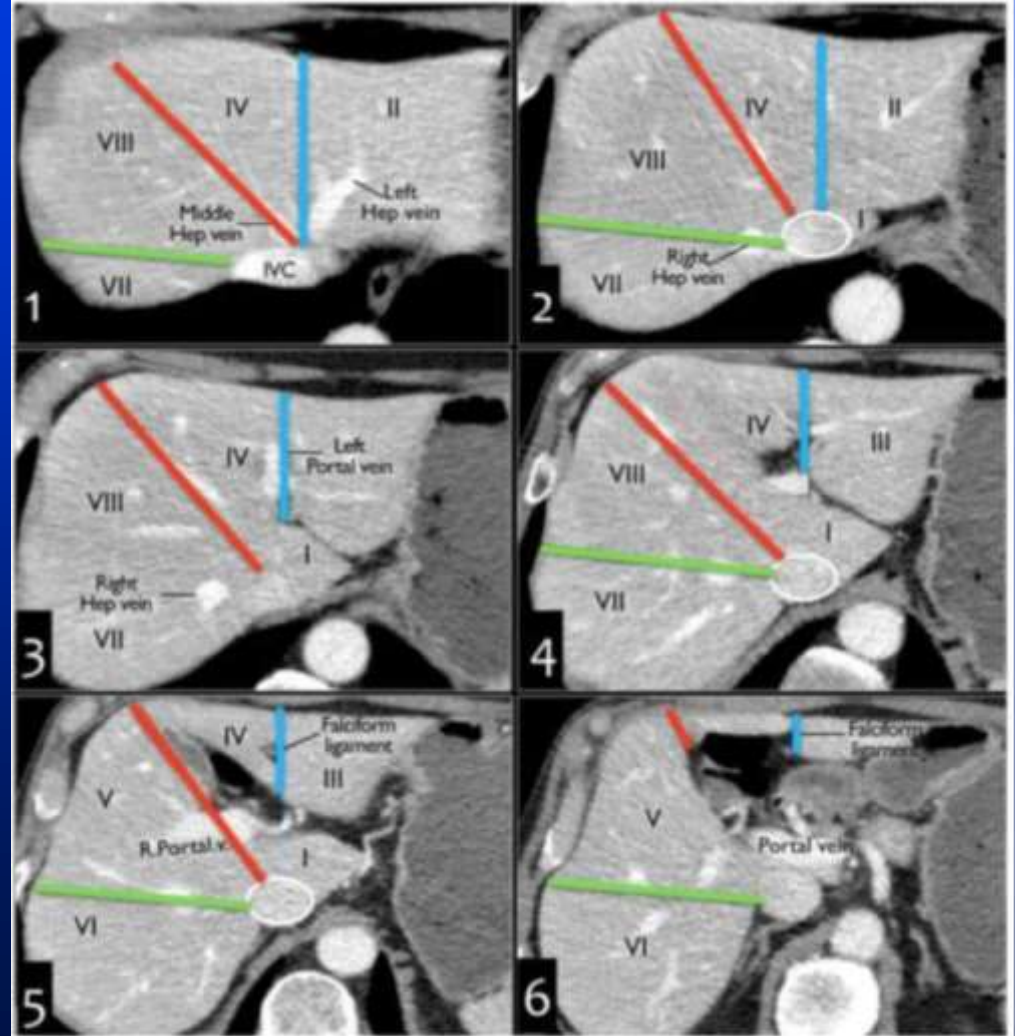
Extended right hepatectomy
Right trisegmentectomy

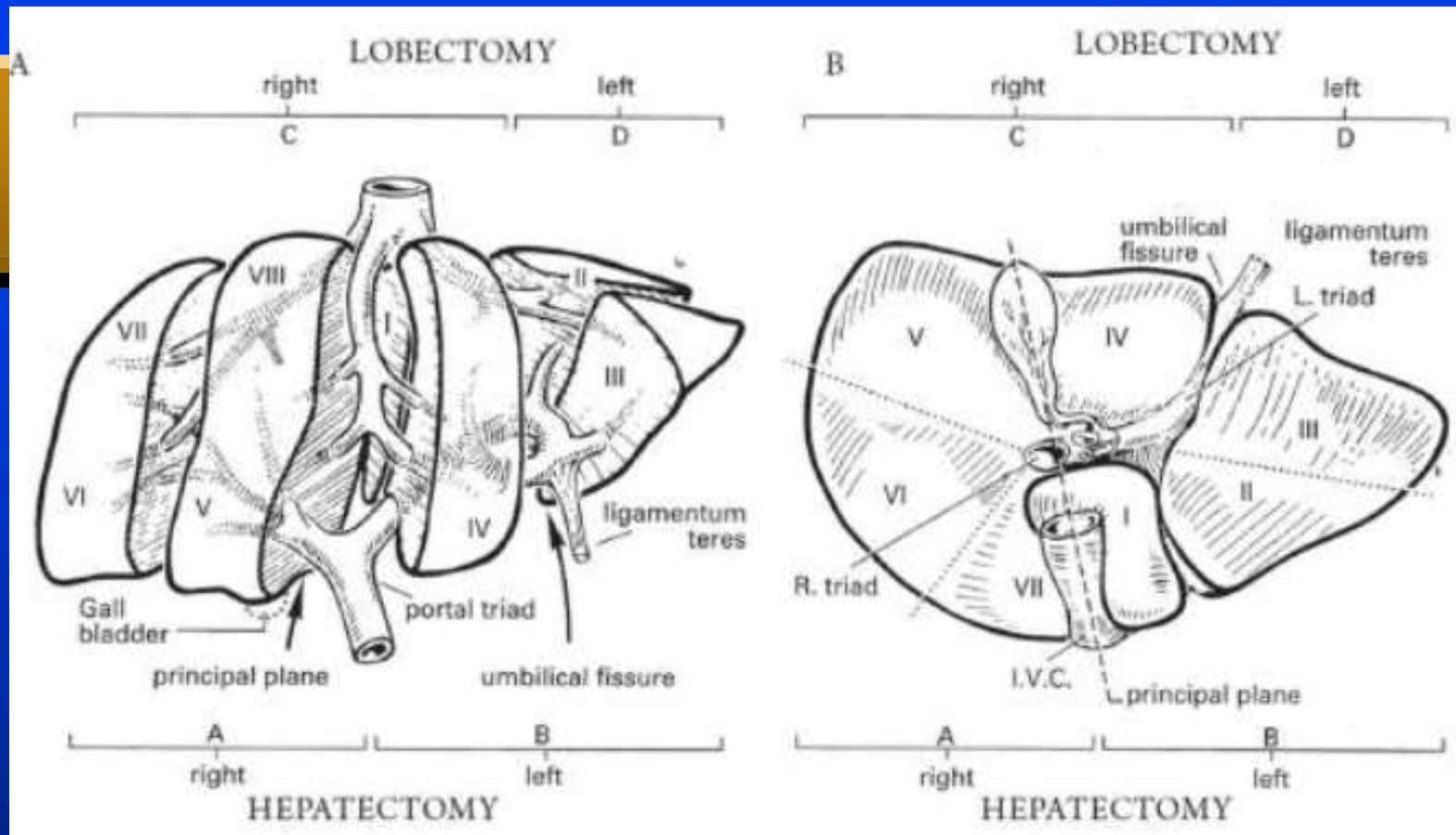
Right hepatectomy



Left hepatectomy

Extended left hepatectomy
Left trisegmentectomy

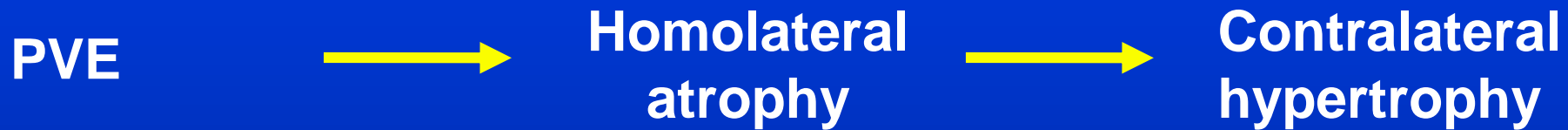




A. Exploded view of the liver demonstrating the distribution of segments separated by the hepatic veins and portal triad structures. The segmental anatomy of the liver forms the foundation for modern hepatic surgery. B. Inferior view of the liver demonstrating the division into the functional right and left hemilivers by the principal plane (Cantlie's line), and into the anatomic right and left lobes by the umbilical fissure. Both views show brackets above and below the figures clarifying the terminology of common liver resections and demonstrating the segments corresponding to each type of resection. (Used with permission from: Blumgart LH, Belghiti J. Surgery of the liver, biliary tract, and pancreas. 4th ed. Philadelphia, PA: Saunders Elsevier, 2007).

The anatomic right and left lobes of the liver are divided by the ligamentum teres and umbilical fissure, where the main vascular and biliary structures to the functional left liver run. However, the true functional division of the right and left liver is divided by the middle hepatic vein. This can be demarcated by a plane extending from the left side of the gallbladder fossa anteriorly, to the left side of the inferior vena cava posteriorly (known as Cantlie's line). The right and left liver are further subdivided into segments which follow the distribution of the portal triad structures. The right, middle, and left hepatic veins drain into the vena cava and run within the corresponding scissurae.

PVE (Portal vein embolization)- RATIONALE



“... to initiate compensatory hypertrophy of the future remnant liver, thus preventing postoperative liver failure.”

Makuuchi et al. Surgery 1990; 107: 521-7

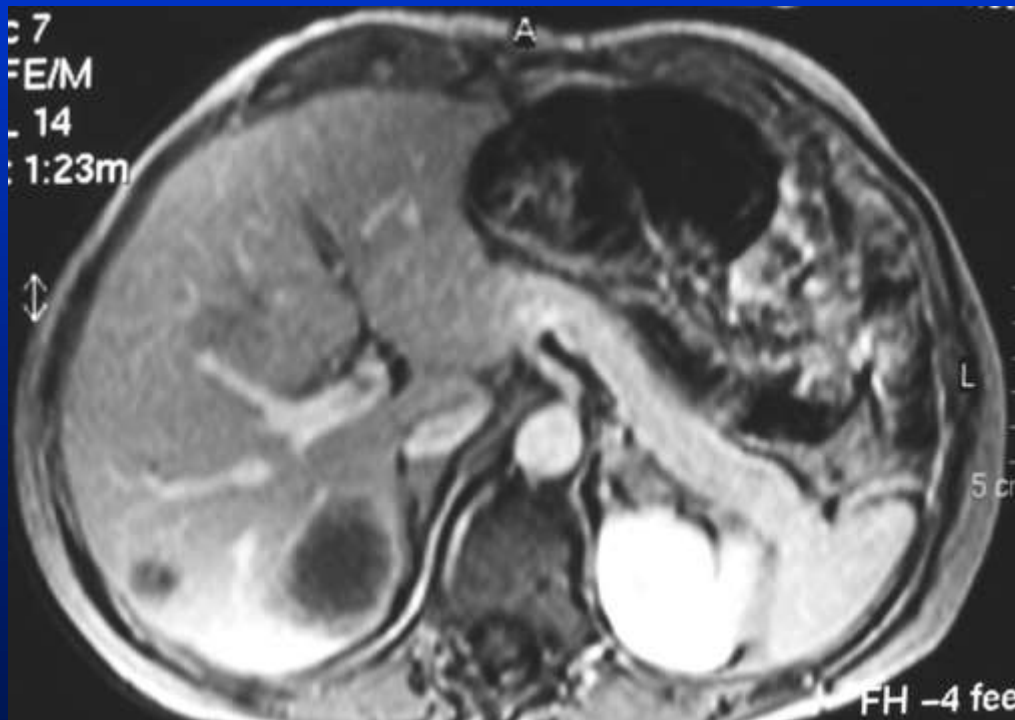
PVE - TECHNIQUE

- Under local anaesthetic
- Under US guidance
- Percutaneous transhepatic puncture of LPV
- Portal Angiogram
- PVE
- Check Portal Angiogram



PVE – VOLUMETRIC STUDY

Pre-PVE



Post-PVE



PVE – BUT?...

- During liver regeneration following portal embolisation the growth rate of liver metastases is more rapid than that of liver parenchyma.

Elias et al. Br J Surg 1999; 86: 784-88

- Proliferative activity of intrahepatic colorectal metastases after preoperative hemihepatic portal vein embolisation.

Kokudo et al. Hepatology 2001; 34: 267-72

ABLATION TECHNIQUES

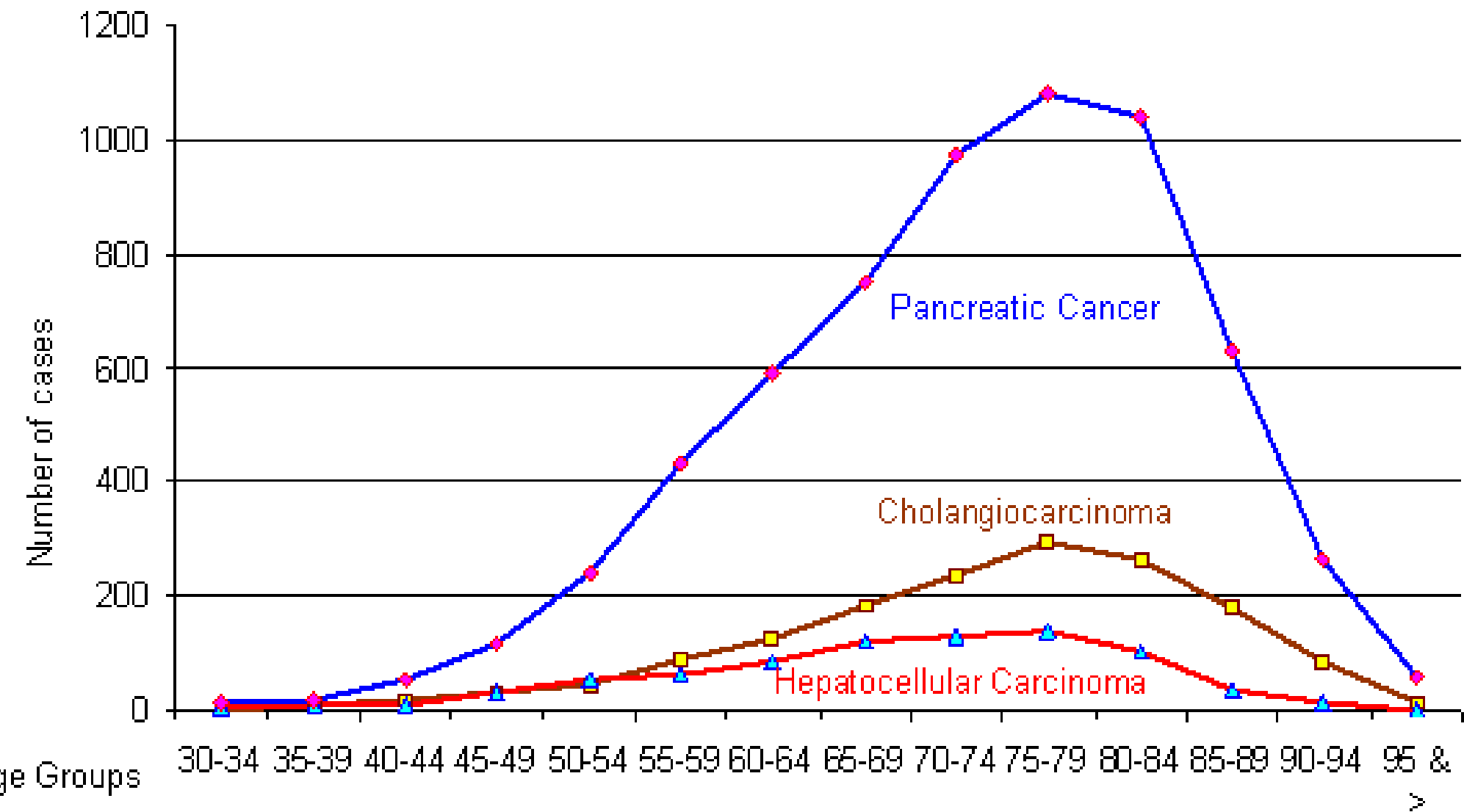
- **Cryotherapy**
- **Thermal ablation**
 - Radiofrequency ablation (RFA)
 - Interstitial laser photocoagulation (ILP)
- **Microwave coagulation**
- **Electrolysis**

No randomized trial ever performed

DISCUSSION

- **Concurrent vs staged resection**
- **Extrahepatic disease**
 - Lymph node involvement
- **Type of liver resection**
- **Use of adjuvant chemotherapy**

Age-specific mortality from HPB Cancer in England and Wales in 2003



HEPATOCELLULAR CARCINOMA

- **Incidence**
 - World-wide 250 000 - 1 000 000 per annum
 - Europe 30 000 / year
- **Male:female ratio 4-5:1**
- **Africa and Asia, earlier age at presentation**
- **Associated with cirrhosis ~80% cases**
- **Overall European survival:**

| | 1 year (%) | 5 year (%) |
|----------------------|------------|------------|
| Primary liver cancer | 16 | 5 |
| Biliary tract cancer | 26 | 12 |
| Pancreatic cancer | 15 | 4 |

HEPATOCELLULAR CARCINOMA

- **Hepatitis B and C**
- **Alcohol**
- **Any cirrhosis (including biliary atresia)**
- **Haemochromatosis**
- **Non-cirrhotic**
 - » Older population
 - » Fibrolamellar HCC

HEPATOCELLULAR CARCINOMA: CLINICAL PRESENTATION

- **Silent**
- **Anorexia and malaise**
- **Distension**
- **Pain**
- **Weight loss (preterminal)**
- **Spontaneous rupture**
- **Jaundice**
- **Paraneoplastic (hypoglycaemia)**

HEPATOCELLULAR CARCINOMA: PATHOLOGY

- **Massive (younger / non cirrhotic)**
- **Nodular (cirrhosis) - most common**
- **Diffuse - may mimic appearance of cirrhosis -
poor outlook**
- **Portal vein invasion - intrahepatic spread**
- **Hepatic vein invasion - systemic spread**
- **Lymph node metastases in 30%**



STAGING / IMAGING OF HEPATOCELLULAR CARCINOMA

- **AFP**
- **Ultrasound**
- **Chest and abdominal CT**
- **MR with higher tesla**
- **Angiography**

HEPATOCELLULAR CARCINOMA: PATHOLOGY

- **Favourable prognosis**

- **Macroscopic** - single, small tumour, capsule, no vascular invasion

- **Microscopic**

- **No micro-satellites**

- No capsular invasion**

- No vascular invasion**

- Well differentiated**

- Clear resection margin**

- Fibrolamellar tumours**

HEPATOCELLULAR CARCINOMA: NATURAL HISTORY

Survival in relation to size tumour (Untreated)

| STUDY | SIZE | No. | 1-YEAR | 2-YEAR | 3-YEAR |
|----------------------|--------|-----|--------|--------|--------|
| Ebara <i>et al</i> | <3 cm | 22 | 91% | 56% | 13% |
| Barbara <i>et al</i> | <5 cm | 39 | 81% | 56% | 21% |
| Okazaki <i>et al</i> | < 5 cm | 6 | 100% | 67% | 17% |

TREATMENT OF ADVANCED HEPATOCELLULAR CARCINOMA

- **Best option: Surgery**
 - Majority of patients not suitable
 - » Extent of tumour
 - » Poor liver function
 - Field change / recurrence
 - Resection vs Transplantation

SURGICAL RESECTION OF HEPATOCELLULAR CARCINOMA

- **5 year survival ranging from 40-50%**
- **Operative mortality 5-20%**
- **Recurrence rate > 50%**
- **Specialised surgery**
- **Use of embolisation**



NON-SURGICAL TREATMENTS OF HEPATOCELLULAR CARCINOMA

- Arterial chemo - / embolisation
- Percutaneous ablation - RFA / alcohol
- Chemotherapy
- Internal radiation therapy
- Hormonal therapy
- Interferon
- Immunotherapy
- Gene therapy

STRATEGIES TO INCREASE RESECTABILITY

- **Neo-adjuvant chemotherapy**
- **Portal vein embolisation**
- **Two stage hepatectomy**
- **Ablation techniques**

CHOLANGIOCARCINOMA

- **15-20% of liver primaries**
- **Incidence 0.01-0.46%**
- **Risk factors**
 - Biliary stasis
 - Stones
 - Infection
 - Primary sclerosing cholangitis
 - Choledochal cyst
- **Carcinogens**
 - Asbestos
 - Dioxin
 - Nitrosamines
 - Thorotrast

CHOLANGIOCARCINOMA

- **Change in practice**
 - Increasing incidence and referral
 - Younger patients
 - Importance of liver resection
 - Development of adjuvant therapies

CHOLANGIOCARCINOMA

- **Classification of perihilar disease - Bismuth**

TYPE

- I** below confluence of RHD and LHD
- II** reaching confluence, but not involving RHD and LHD
- III** occlude CHD and either RHD (IIIa) or LHD (IIIb)
- IV** multicentric or involve both RHD and LHD

CHOLANGIOCARCINOMA

- **Assessment of resectability**
 - Tumour markers
 - Liver function tests
 - Ultrasound
 - Chest and abdominal CT scan
 - MR cholangiography
 - MRA and V
 - ERCP and endoscopic ultrasound and biopsy
 - Laparoscopy

CHOLANGIOCARCINOMA

- **Clinical assessment**
 - Overall condition
 - Age ?
 - Relief of biliary obstruction
 - Cardio-respiratory status
 - Renal function

CHOLANGIOCARCINOMA

- **Hilar cholangiocarcinoma**
 - Extends horizontally along bile ducts
 - Spreads via lymphatics and nerves
 - Boundary between diseased and healthy tissue unclear

CHOLANGIOCARCINOMA

- **Surgical options**
 - Local resection
 - Combined bile duct and liver resection
 - » Right better than left
 - » PV reconstruction
 - » Caudate resection
 - ± pancreatico-duodenectomy
 - Ex-vivo resection and reimplantation
 - Liver transplantation
 - » ± pancreatico - duodenectomy

CHOLANGIOCARCINOMA

- **Conclusions**

- Improved staging
- Radical resections – clear margin
- Sufficient residual functioning liver
 - » Stenting – selective or general
 - » Portal vein / hepatic artery embolisation
- Development of adjuvant therapies
 - » Chemotherapy
 - » Radiotherapy / brachytherapy