肝內及肝外膽管癌AJCC分期及臨床應用-外科手術治療

中山醫學大學附設醫院 肝膽消化外科

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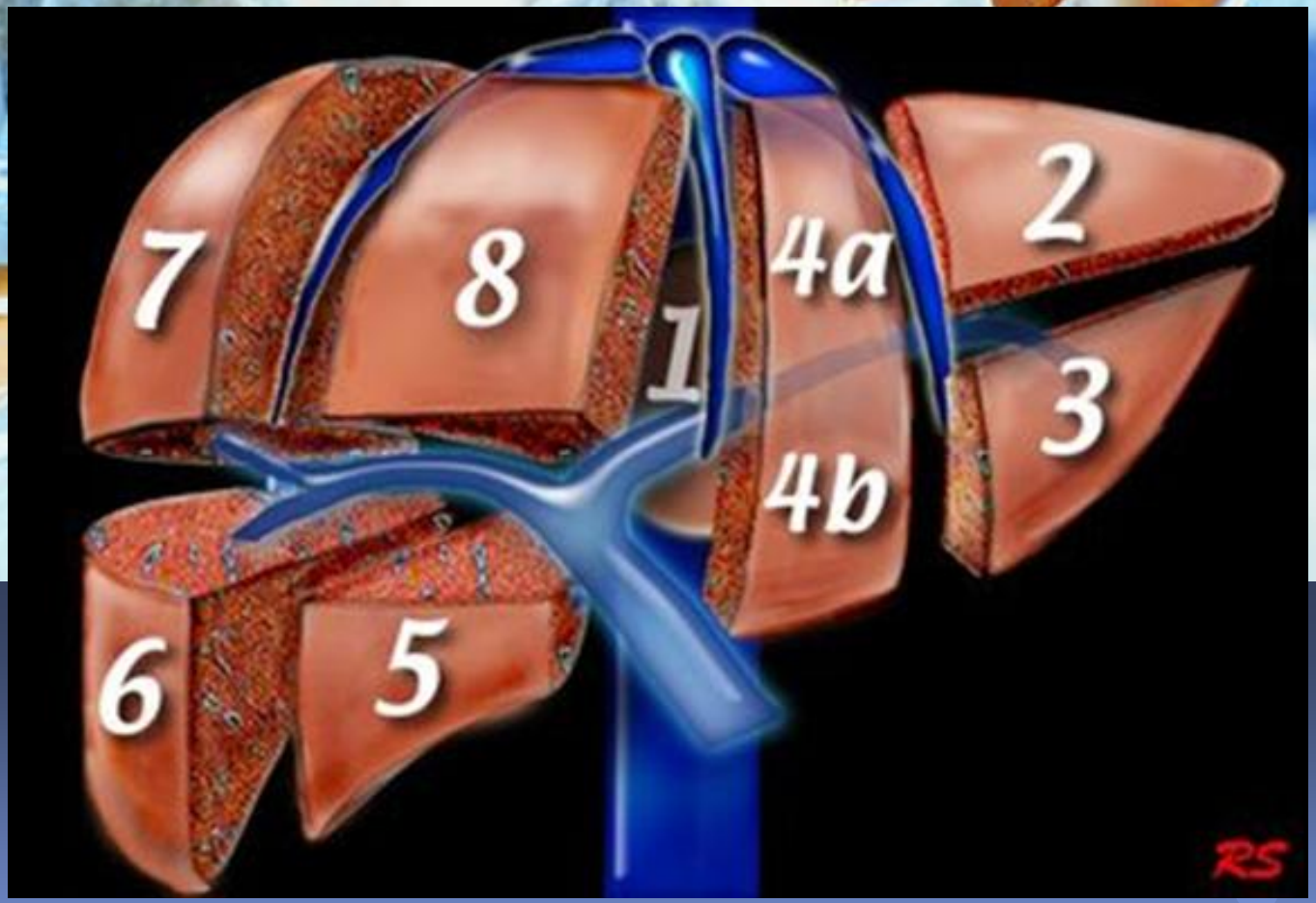
2014-04-12


7
8
1
4a
2
4b
3
6
5
RS

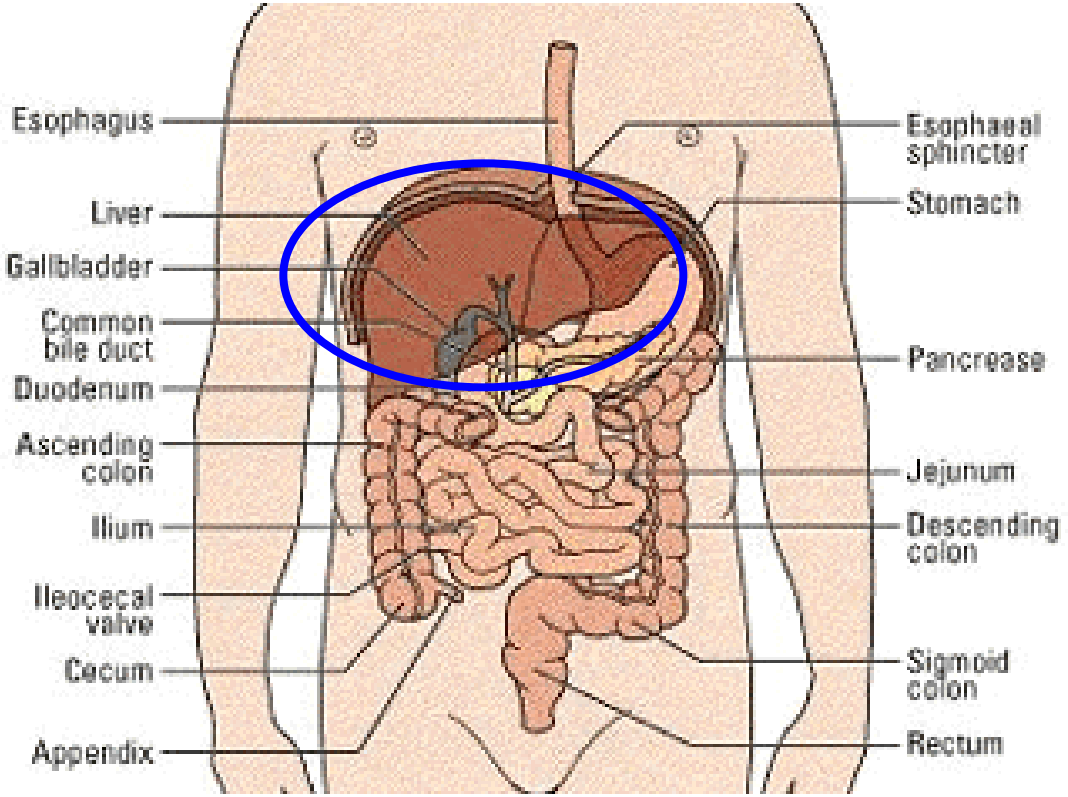
肝臟

人體最大的腺體器官


A

- 新陳代謝中心
  - 佔人體體重的 2.5-3%
  - 約 1500公克
  - 分為左右兩葉
  - 肝小葉是肝臟構造與功能的基本單位

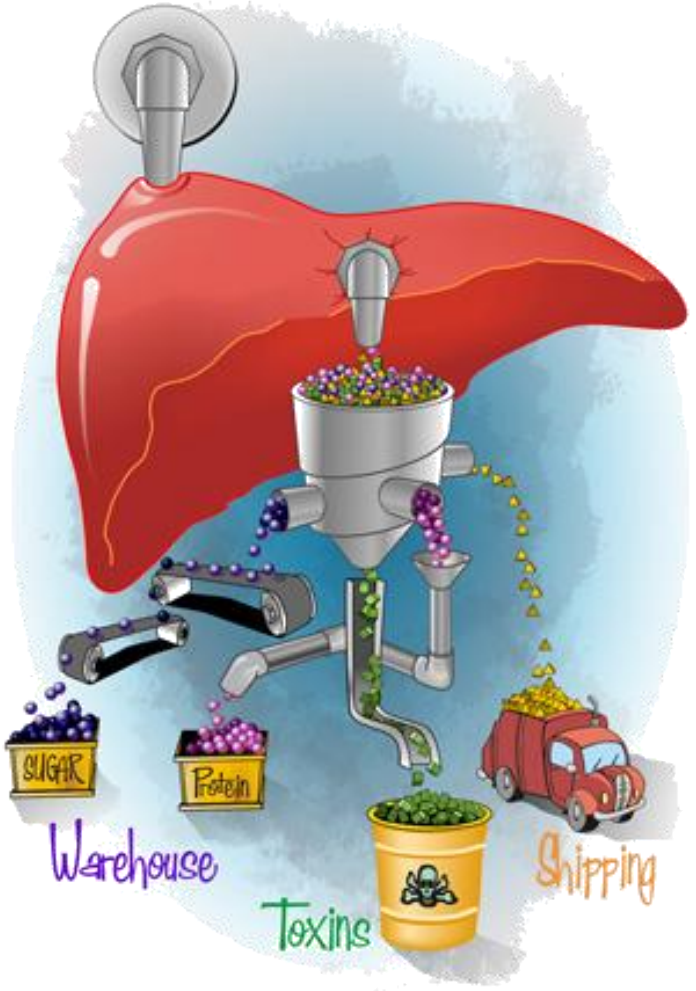
外型位置


Esophagus
Liver
Gallbladder
Common bile duct
Duodenum
Ascending colon
Ilium
Ileocecal valve
Cecum
Appendix
Esophageal sphincter
Stomach
Pancrease
Jejunum
Descending colon
Sigmoid colon
Rectum

生理功能

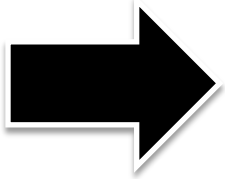
- **重要功能**
  - ✓ 氧化還原功能
  - ✓ 解毒功能
  - ✓ 排泄功能
  - ✓ 儲存功能
  - ✓ 消化功能

- 20%的正常肝細胞即可維持生理功能



肝臟損傷

- **化學性**
  - 藥物
  - 毒素
  - 化學物質
    - 三硝基甲苯、四氯化碳、氯奈、丙烯醛、苯胺、氯仿、砷化氫、二甲基甲酰胺、二硝基酚、乙醛、有機磷、丙烯晴
  - 重金屬
    - 砷、磷、汞、銻、鉛

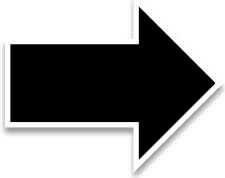


導致結果

- 急性肝中毒
- 腎臟損傷
- 神經系統損傷
- 發炎

肝臟損傷

- **酒精**
  - 過量飲酒
  - 長期酗酒



導致結果

- 影響解毒代謝功能
- 免疫力下降
- 脂肪肝
- 酒精性肝炎
- 慢性酒精中毒
- 肝硬化
- 急性、慢性消化系統傷害
- 心血管疾病

肝臟損傷

病毒感染

- HAV
- **HBV**
- **HCV**
- HDV
- HEV

導致結果

- 肝細胞損傷
- 急性肝炎
- 猛暴性肝炎
- 慢性肝炎
- 肝硬化
- 肝癌

肝臟損傷

(1)肝臟中**三酸甘油酯的合成增加**
三酸甘油酯合成酵素的活性升高、游離脂肪酸的濃度增加。

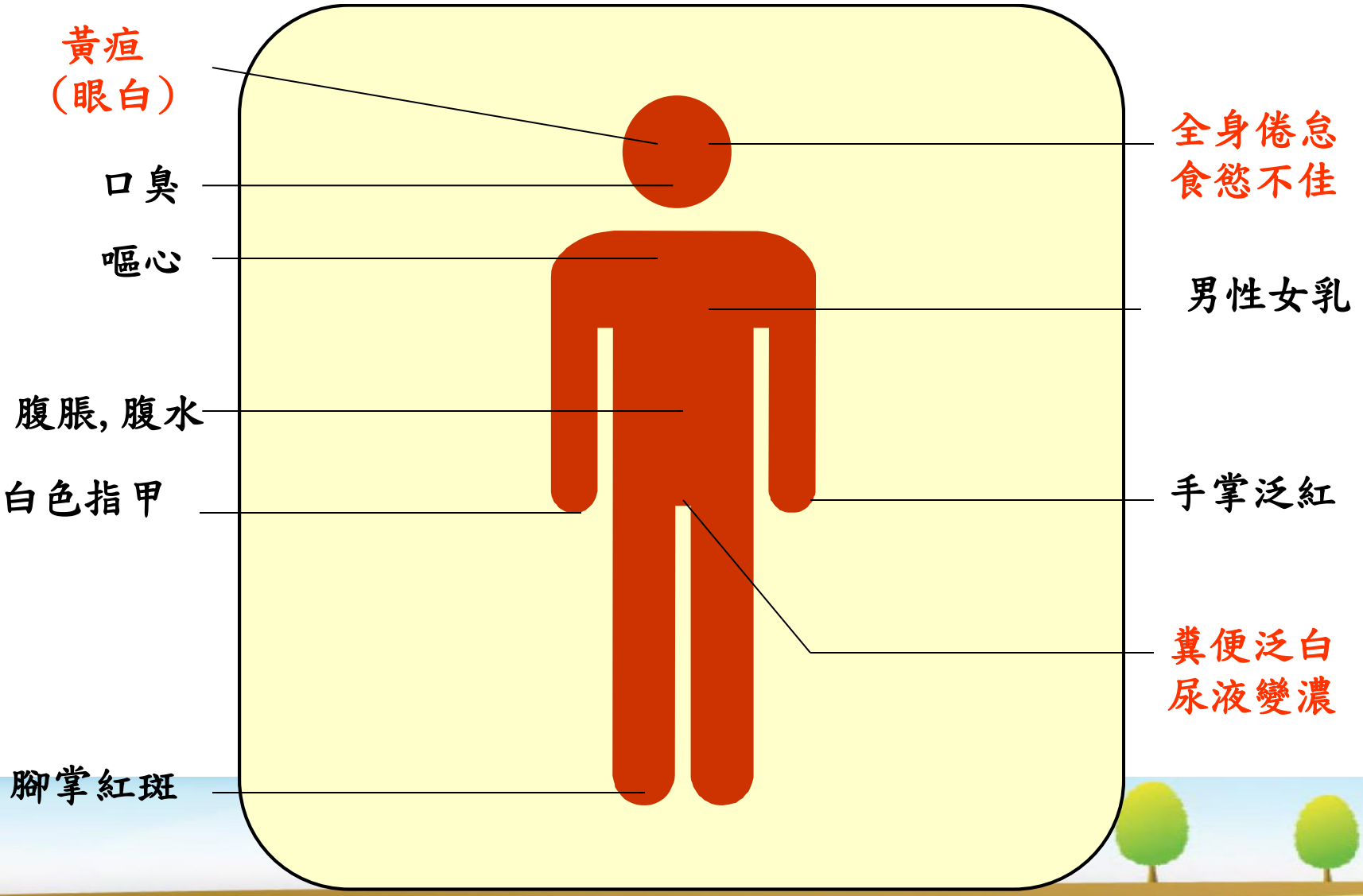
(2)肝臟中**三酸甘油酯的排除降低**
脂肪酸的氧化反應受阻。

(3)肝臟中**脂蛋白的合成與分泌降低**
影響肝臟中脂質的輸出，為造成脂肪肝的主因。

大量的脂質蓄積於肝細胞中所引起的肝臟病變

脂肪肝

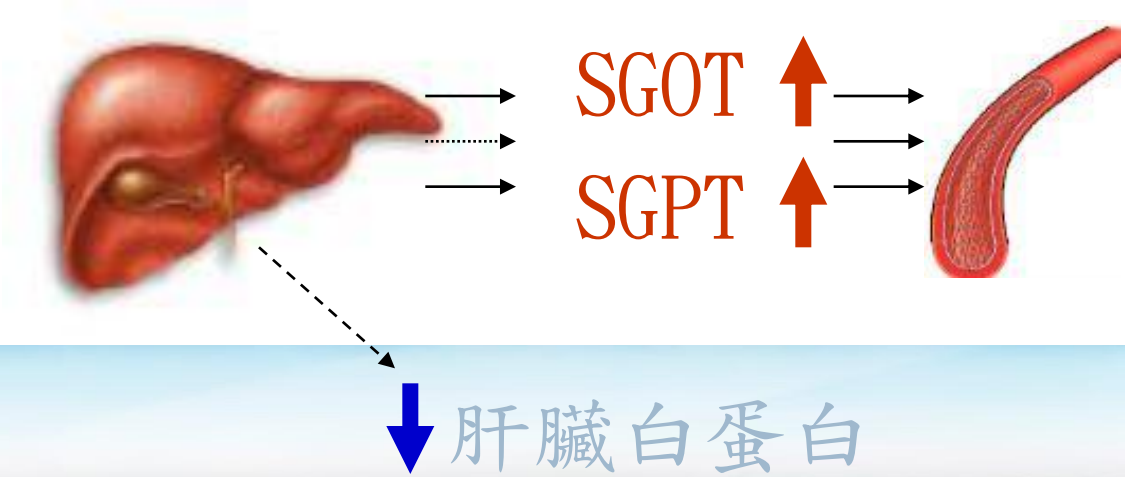
肝臟是沉默的器官



肝功能檢測

- AST（血清麩胺酸基轉氨酶）
- ALT（血清麩胺酸丙酸轉氨酶）
- 腹部超音波
- 病毒抗體抗原
- AFP, CEA, CA19-9

腹部超音波



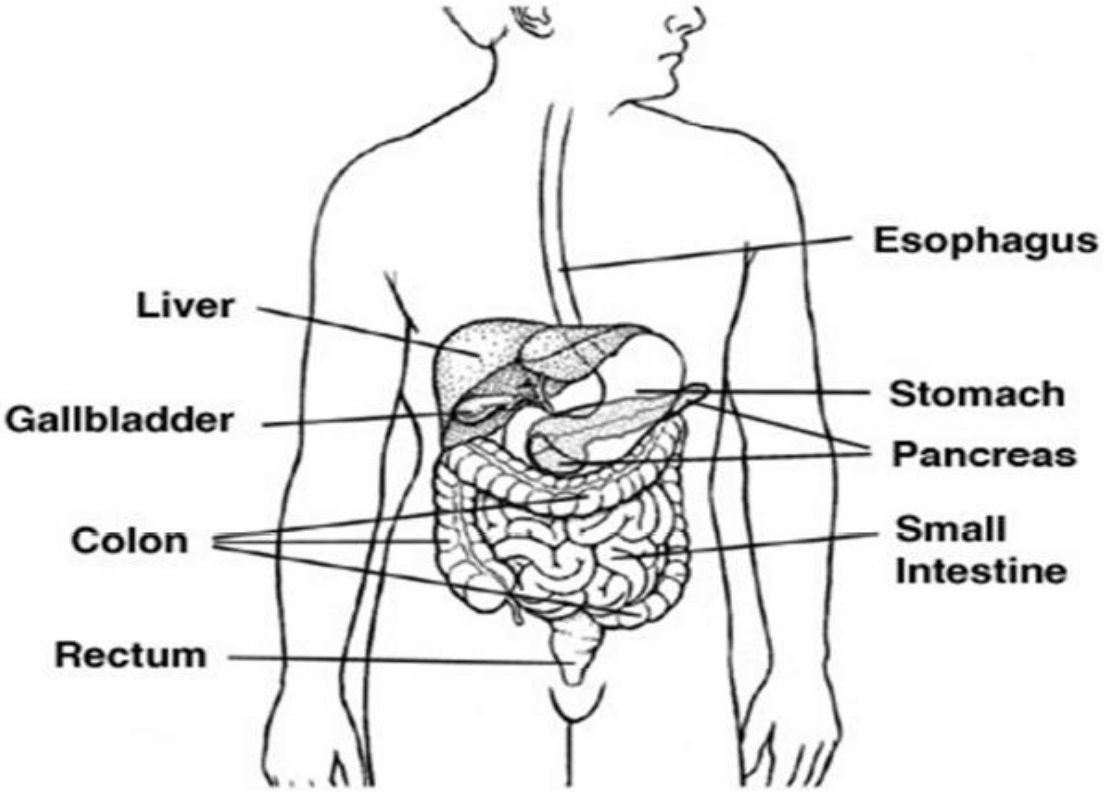
良性肝臟腫瘤

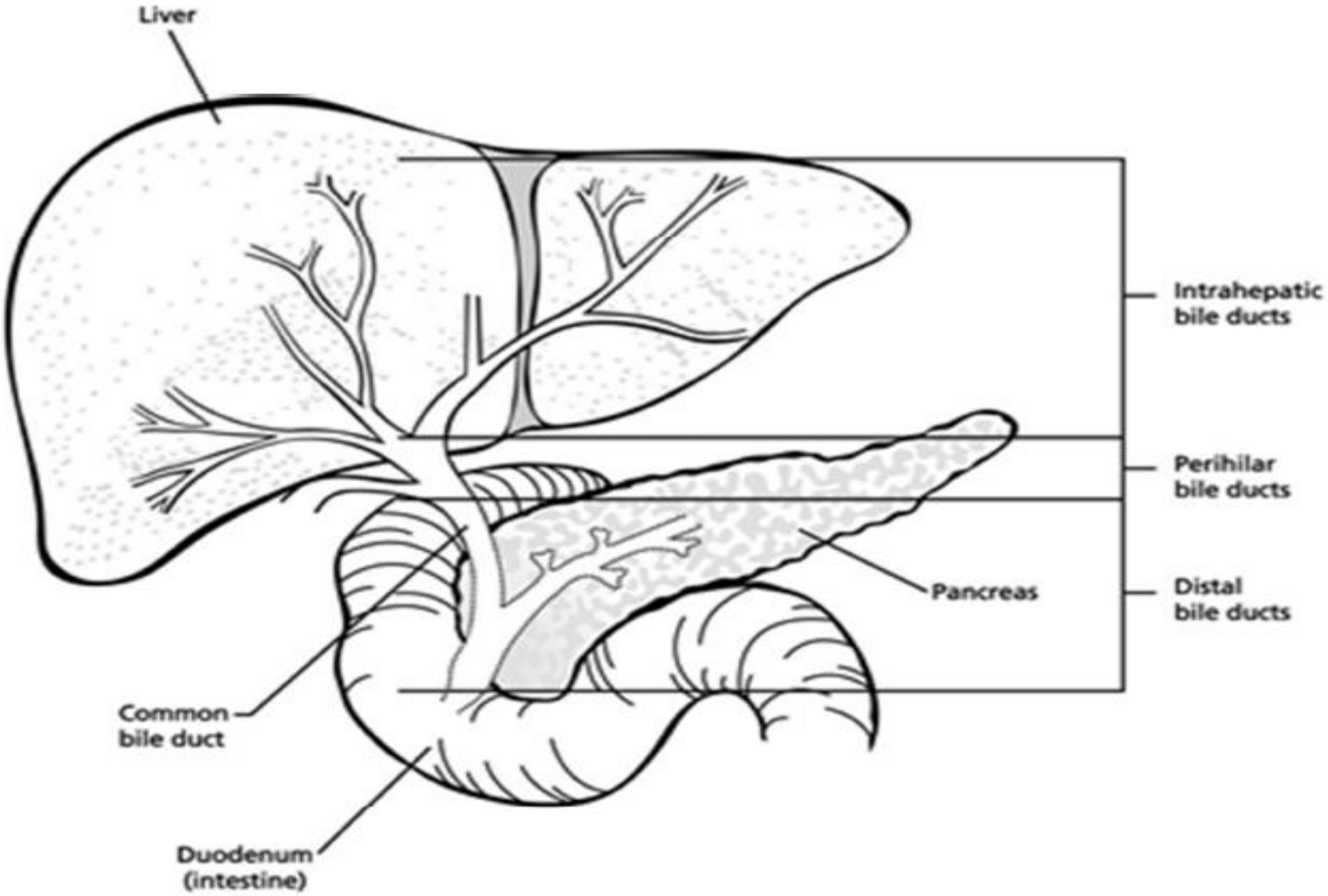
- **血管瘤Hemangiomas** (most common). Symptomatic, Surgical. Rupture rare, most asympt.Women.
- **腺瘤Adenomas** (exclusively in women 30-50, OCP risk factor). 10% malig trans, rupture. Surgical.
- **局部結節增生Focal nodular hyperplasia** (FNH).Women 20-50, stellate scar on CT. Kupffer cells on scan.Non surgical.
- **單純囊腫Simple Cysts**. Surgical if sympt, rupture, infection, bleed, or suspicious. Unroof, oversew.
- **多發性肝囊腫Polycystic liver disease** associated with renal failure. Women 30-80, 50% PC kidneys as well.

惡性肝臟腫瘤

- 肝細胞癌
  - Hepatocellular carcinoma (HCC) most common, men, 40-70. Risks: cirrhosis, Hep B, Hep C, carcinogens, hemachromatosis, tyrosinemia, glycogen storage, Wilson's, adenoma, schistosomiasis, alpha-1 antitrypsin deficiency, blood group B.
- **膽管癌**

What is bile duct cancer ?




Liver
Intrahepatic bile ducts
Perihilar bile ducts
Distal bile ducts
Pancreas
Common bile duct
Duodenum (intestine)

Types of bile duct cancers

- Intrahepatic bile duct cancers : 1/10
- Perihilar (also called hilar) bile duct cancers :
  - 6-7/10
  - The most common, Klatskin tumors
- Distal bile duct cancers : 2-3/10

Histologic types of bile duct cancer

- **Adenocarcinomas** :
  - are cancers of glandular cells that can develop in several organs of the body.

- Bile duct adenocarcinomas develop from the mucous glands that line the inside of the duct. **Cholangiocarcinoma** is another name for a bile duct carcinoma

Epidemiology about bile duct cancer

- **Asia and the Middle East** : much more common
  - because of a common **parasitic infection** of the bile duct.

- The average age
  - Intrahepatic bile ducts : 70 years old
  - Extrahepatic bile ducts : 73 years old .
  - Almost 2 out of 3 people with bile duct cancer : ≥ 65 years old

Risk Factors

- Primary sclerosing cholangitis
- Bile duct stones
- Choledochal cysts
- Liver fluke infections
- Abnormalities where the bile duct and pancreatic duct normally meet
- Cirrhosis
- Polycystic liver disease
- Caroli syndrome

Risk Factors

- Inflammatory bowel disease
- Aging: More than 2 out of 3 patients with bile duct cancer are older than age 65.
- Obesity
- Exposure to Thorotrast
- Family history
- Diabetes
- Viral hepatitis
- Alcohol

Risk Factors

- Smoking
- Pancreatitis (inflammation of the pancreas)
- Infection with HIV
- Exposure to asbestos
- Exposure to radon or other radioactive chemicals
- Exposure to dioxin, nitrosamines, or polychlorinated biphenyls (PCBs)

Gene mutations related to bile duct cancers

- TP53 tumor suppressor gene
- KRAS
- HER2/neu
- c-met

Signs and symptoms of bile duct cancer

- Jaundice
- Itching
- Light colored stools
- Dark urine
- Abdominal pain
- Loss of appetite/weight loss
- Fever
- Nausea and vomiting

Diagnosis

- History and physical exam
- Blood tests
  - Tests of liver and gallbladder function
  - Tumor markers : CEA, CA19-9

Diagnosis

- Imaging tests
  - Ultrasound
  - Computed tomography (CT) scan :biopsy
  - Magnetic resonance imaging (MRI) scan: MRCP
  - Cholangiography: ERCP, MRCP, PTC
  - Positron emission tomography (PET) scan
  - Angiography

American Joint Committee on Cancer (AJCC) TNM system

- Intrahepatic bile duct cancers

- Extrahepatic bile duct cancers:
  - Perihilar tumors
  - Distal tumors.

Staging of intrahepatic bile duct cancer : **T categories**

- **TX**: No description of the tumor's extent is possible because of incomplete information.
- **T0:** There is no evidence of a primary tumor.
- **Tis:** Cancer cells are only growing in the mucosa (the innermost layer of the bile duct) and have not grown into deeper layers of the bile duct. This stage is also known as *intramucosal carcinoma* and was previously called *carcinoma in situ*.
- **T1:** A single tumor that has grown into deeper layers of the bile duct wall, but it is still only in the bile duct. The cancer has not grown into any blood vessels.

Staging of intrahepatic bile duct cancer : **T categories**

- **T2:** Split into 2 groups
- ·**T2a:** A single tumor that has grown through the wall of the bile duct and into a blood vessel.
- ·**T2b**: 2 or more tumors, which may (or may not) have grown into blood vessels

- **T3:** The cancer has grown into nearby structures such as the intestine, stomach, common bile duct, abdominal wall, diaphragm, or lymph nodes around the portal vein.

- **T4:** The cancer is spreading through the liver by growing along the bile ducts.

Staging of intrahepatic bile duct cancer :

N , M categories

- **NX:** Regional (nearby) lymph nodes cannot be assessed.
- **N0:** The cancer has not spread to nearby lymph nodes.
- **N1:** The cancer has spread to nearby lymph nodes.

- **M0:** The cancer has not spread to tissues or organs far away from the bile duct.
- **M1:** The cancer has spread to tissues or organs far away from the bile duct.

Staging of intrahepatic bile duct cancer :

Stage grouping

- **Stage 0 (Tis, N0, M0)**
- **Stage I (T1, N0, M0)**
- **Stage II (T2, N0, M0)**: T2a, T2b, N0, M0
- **Stage III (T3, N0, M0)**:
- **Stage IV:** Split into 2 groups
- ·**Stage IVA (T4, N0, M0) or (Any T, N1, M0)**
- ·**Stage IVB (Any T, any N, M1)**

Staging of perihilar bile duct cancer :

T categories

- **TX**: No description of the tumor's extent is possible because of incomplete information.
- **T0:** There is no evidence of a primary tumor.
- **Tis:** Cancer cells are only growing in the mucosa (the innermost layer of the bile duct) and have not invaded deeper layers of the bile duct. This stage is also known as *intramucosal carcinoma* and was previously called *carcinoma in situ*.
- **T1:** The cancer has grown into deeper layers of the bile duct wall, such as the muscle layer or the fibrous tissue layer.

Staging of perihilar bile duct cancer :

T categories

- **T2:** The tumor has grown through the wall of the bile duct and into nearby tissue.
- ·**T2a**: The tumor has grown through the wall of the bile duct and into surrounding fat.
- ·**T2b**: The tumor has grown through the wall of the bile duct and into nearby liver tissue.

- **T3**: The cancer is growing into branches of the main blood vessels of the liver on one side (the main blood vessels of the liver are the portal vein and the hepatic artery).

- **T4**: The cancer is growing into the main blood vessels of the liver (the portal vein and or the common hepatic artery) or branches of these vessels on 2 sides, OR the cancer is growing directly into other bile ducts while part of the tumor is growing into one of the main blood vessels

Staging of perihilar bile duct cancer :

N, M categories

- **NX:** Regional (nearby) lymph nodes cannot be assessed.
- **N0:** The cancer has not spread to nearby lymph nodes.
- **N1:** The cancer has spread to nearby lymph nodes, such as those along the cystic duct, the common bile duct, the hepatic artery, and the portal vein.
- N2: The cancer has spread to lymph nodes further away from the tumor, such as those around the major blood vessels of the abdomen (such as the aorta, the vena cava, the celiac artery, and the superior mesenteric artery).

- **M0:** The cancer has not spread to tissues or organs far away from the bile duct.
- **M1:** The cancer has spread to tissues or organs far away from the bile duct.

Staging of perihilar bile duct cancer :

Stage grouping

- **Stage 0 (Tis, N0, M0)**
- **Stage I (T1, N0, M0)**
- **Stage II (T2, N0, M0) : T2a,T2b**
- **Stage III:** Has 2 substages:
- ·**Stage IIIA (T3, N0, M0)**:
- ·**Stage IIIB (T1 to T3, N1, M0)**
-
- **Stage IV:** Has 2 substages:
- ·**Stage IVA (T4, N0-1, M0)**
- ·**Stage IVB (any T, N2, M0) or (any T, any N, M1)**

Staging of distal extrahepatic bile duct cancer :

T categories

- **TX**: No description of the tumor's extent is possible because of incomplete information.
- **T0:** There is no evidence of a primary tumor.
- **Tis:** Cancer cells are limited to the mucosa (the innermost layer of the bile duct) and have not invaded deeper layers of the bile duct. This stage is also known as *intramucosal carcinoma* and was previously called *carcinoma in situ*.
- **T1:** The cancer has grown into deeper layers of the bile duct wall, but it is still only in the bile duct.

Staging of distal extrahepatic bile duct cancer :

T categories

- **T2:** The cancer has grown through the bile duct wall but has not started growing into nearby structures.

- **T3:** The cancer has grown into nearby structures such as the liver, gallbladder, pancreas, or duodenum (the first part of the small intestine), but it is not growing into the main blood vessels supplying the stomach and intestines (the celiac artery and the superior mesenteric artery).

- **T4:** The cancer has grown into one or both of the main blood vessels supplying the stomach and intestines (the celiac artery and the superior mesenteric artery).

Staging of distal extrahepatic bile duct cancer :

N, M categories

- **NX:** Regional (nearby) lymph nodes cannot be assessed.
- **N0:** The cancer has not spread to nearby lymph nodes.
- **N1:** The cancer has spread to nearby lymph nodes.

- **M0:** The cancer has not spread to tissues or organs far away from the bile duct.
- **M1:** The cancer has spread to tissues or organs far away from the bile duct.

Staging of distal extrahepatic bile duct cancer

- **Stage 0 (Tis, N0, M0)**

- **Stage IA (T1, N0, M0)**
- **Stage IB (T2, N0, M0)**

- **Stage IIA (T3, N0, M0)**
- **Stage IIB (T1 to T3; N1; M0)**

- **Stage III (T4, any N, M0)**

- **Stage IV (Any T, any N, M1)**

Survival statistics for bile duct cancers

Intrahepatic bile duct cancer

Stage	5-year relative survival
Localized	15%
Regional	6%
Distant	2%

Extrahepatic bile duct cancer

Stage	5-year relative survival
Localized	30%
Regional	24%
Distant	2%

Treatment

- • Surgery
- • Radiation therapy
- • Chemotherapy
- • Palliative therapy

Surgery for bile duct cancer

- *potentially curative surgery* and *palliative surgery*

- **Surgery for resectable cancers**
  - For resectable cancers, the type of operation depends on the location of the cancer

- Surgery for unresectable cancers
  - Liver transplant:
  - Chemotherapy
  - Radiation.

Radiation therapy for bile duct cancer

- **After surgery for resectable cancers:**
  - Adjuvant radiation therapy is helpful, but more research is needed to confirm this.

- **As treatment before surgery for borderline resectable cancers:**
  - *Neoadjuvant therapy*.

- *chemoradiation*. Most often, the chemo drugs used are 5-fluorouracil (5-FU) or capecitabine (Xeloda)

- **External beam radiation therapy (EBRT)**
  - **Three-dimensional conformal radiation therapy (3D-CRT)**
  - **Intensity-modulated radiation therapy (IMRT)**
  - **Stereotactic body radiotherapy (SBRT)**
- **Brachytherapy (internal radiation therapy)**

Chemotherapy for bile duct cancer

- limited.

- **Hepatic artery infusion**

- **Drugs used to treat bile duct cancer**
- ·5-fluorouracil (5-FU)
- ·Gemcitabine (Gemzar®)
- ·Mitomycin C
- ·Doxorubicin (Adriamycin®)
- ·Cisplatin
- ·Capecitabine (Xeloda)
- ·Oxaliplatin

Palliative therapy for bile duct cancer

- **Biliary stent or biliary catheter**
- **Biliary bypass**
- **Palliative radiation therapy**
- **Tumor ablation**

Palliative therapy for bile duct cancer

- **Photodynamic therapy (PDT)**
- **Alcohol injection**
- **Pain medicines**

Treatment of bile duct cancer, by situation

- **Resectable bile duct cancers :** location of the cancer and a person's overall health

- **Unresectable bile duct cancers :** chemo and/or radiation therapy

Targeted therapy

- Nexavar
- Avastin
- Tarceva
- Erbitux
- Vectibix
- Zactima

手術前的檢查及評估:

胸部X光檢查，心電圖，腹部超音波、腹部電腦斷層或肝動脈血管攝影等，磁振照造影檢查則視診斷需要才做。另外，必要時會安排心臟超音波，肺功能測試及骨骼掃描等檢查。

實驗室檢查評估:

血球計數，肝功能生化檢查，凝血功能，及靛氰綠(ICG) 15分鐘滯留率等。

Company Logo

手術切除的技術方法原則

(1) 切除腫瘤必須帶有足夠的外科邊緣（安全邊緣>1公分）

(2) 在安全範圍內儘量採取合乎解剖學的切除

(3) 儘量避免手術期輸血

(4) 為了減少腫瘤手術中因扳動引起的血行散播，扳動肝臟前儘可能結紮預定切除域的門脈分枝

(5) 儘量避免手術中因操作引起腫瘤破裂。

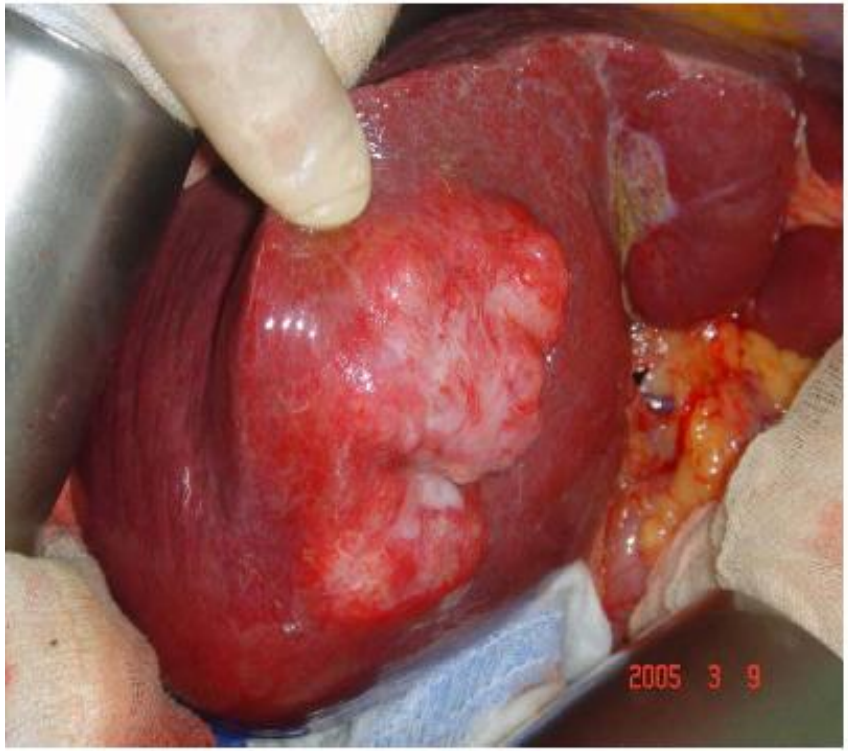
術中儀器的使用有:手術中超音波、超音波碎肝器(CUSA)等

手術期死亡率

手術期死亡率報告介於 1.2 % ~ 5.0 %，

最主要的死亡原因是手術後發生肝功能衰竭。

肝臟手術實例
正常肝 vs. 肝硬化



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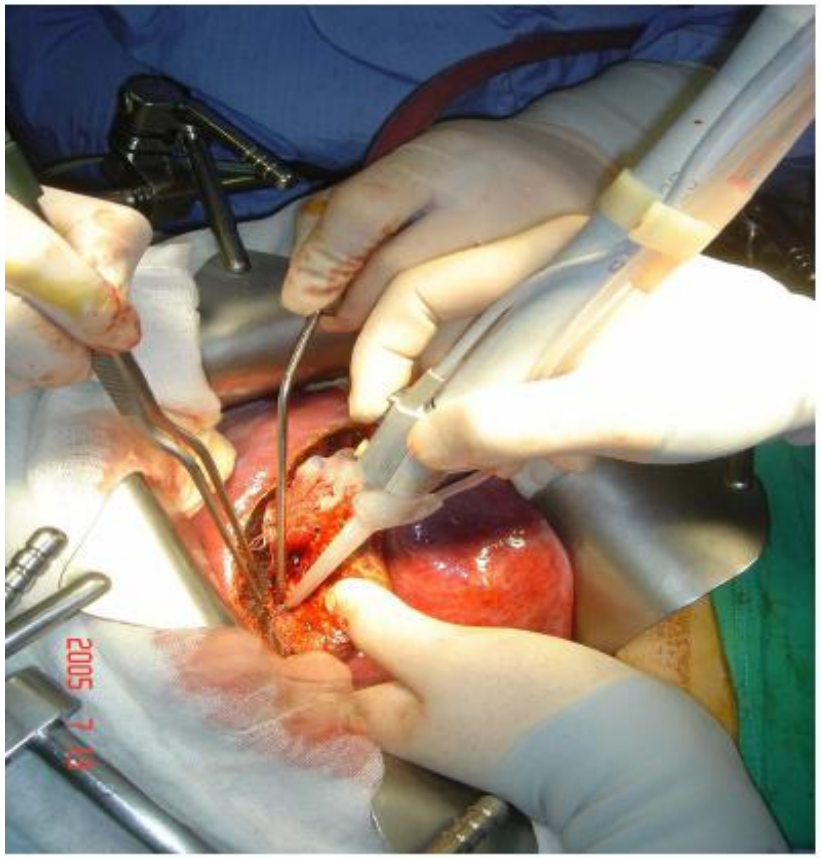
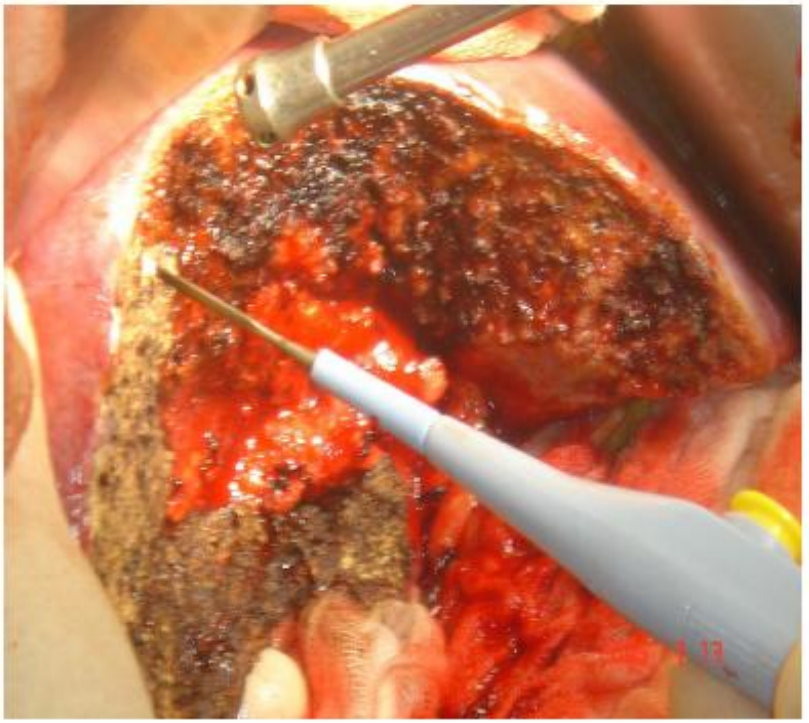
切肝利器
CUSA





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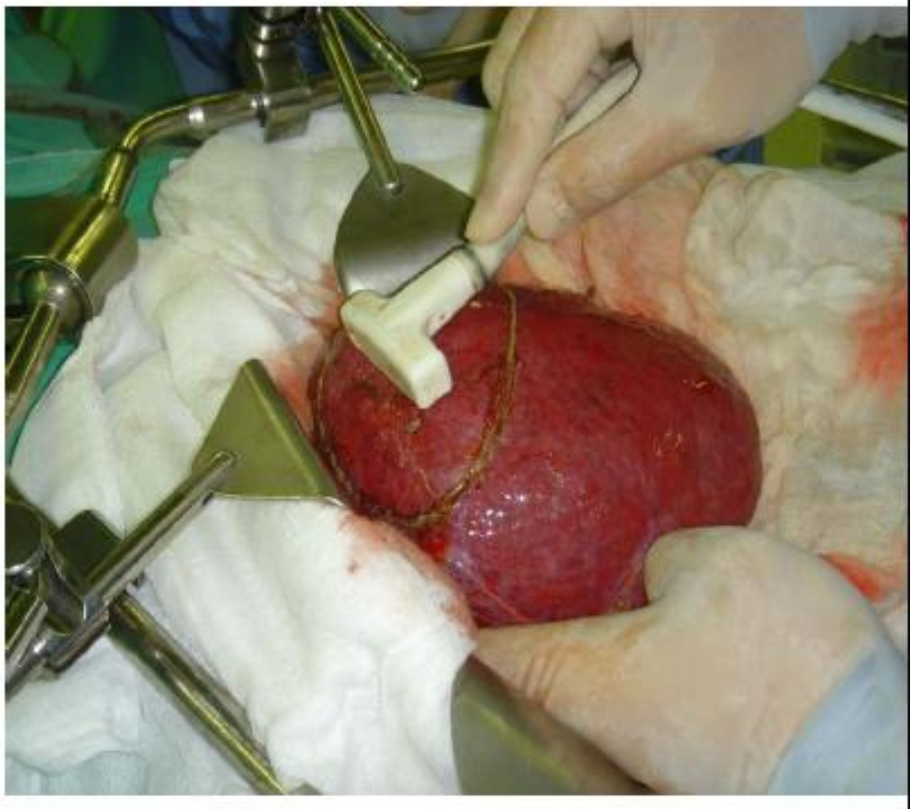
手術中肝臟超音波



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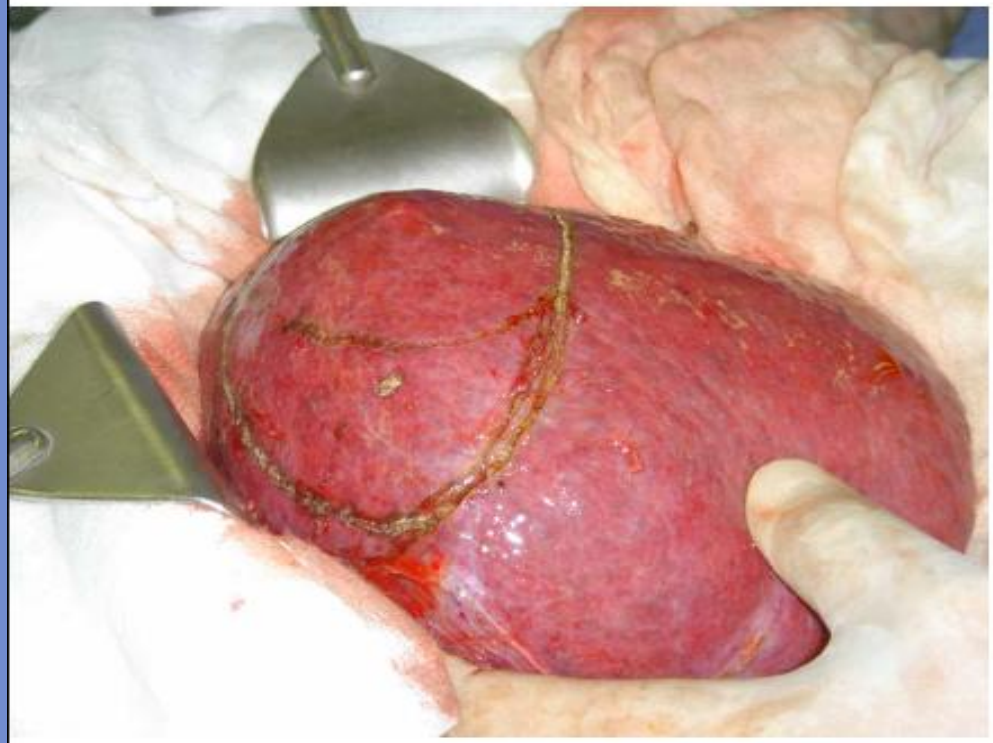
肝臟手術實例
Segmental Hepatectomy



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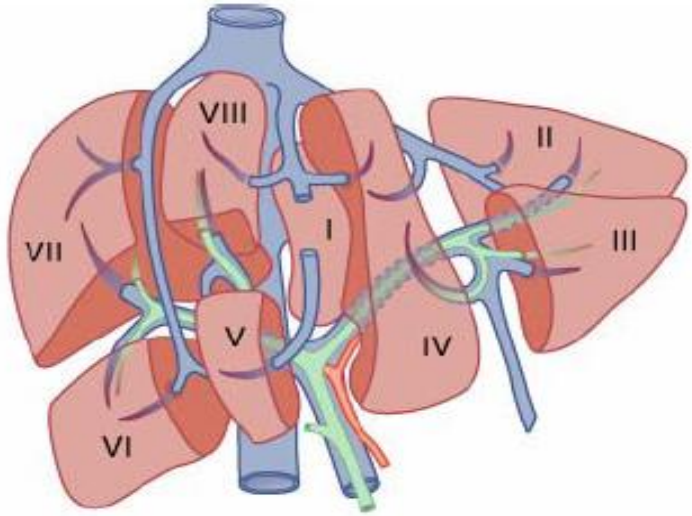
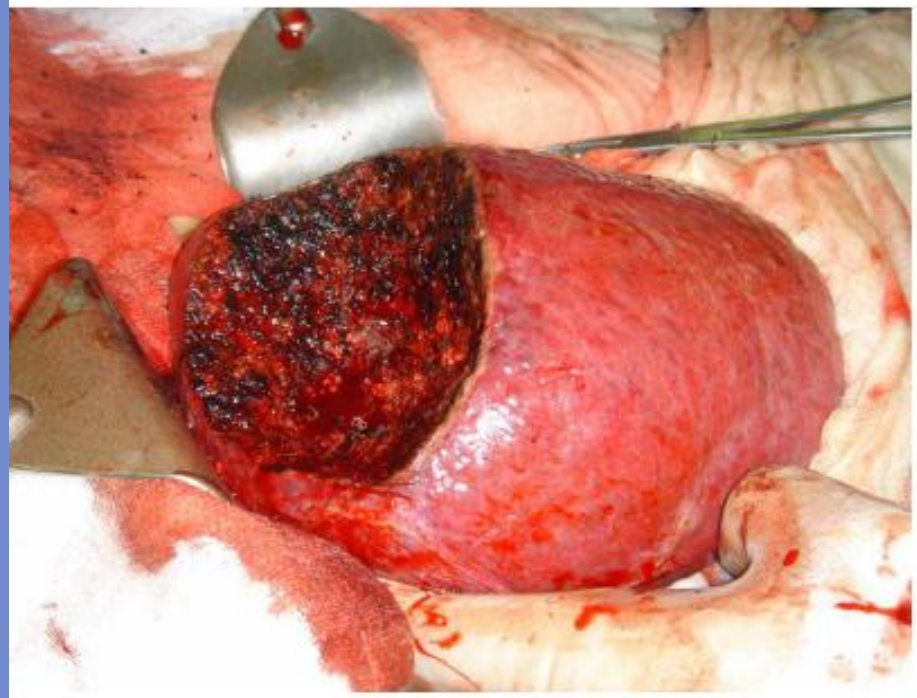
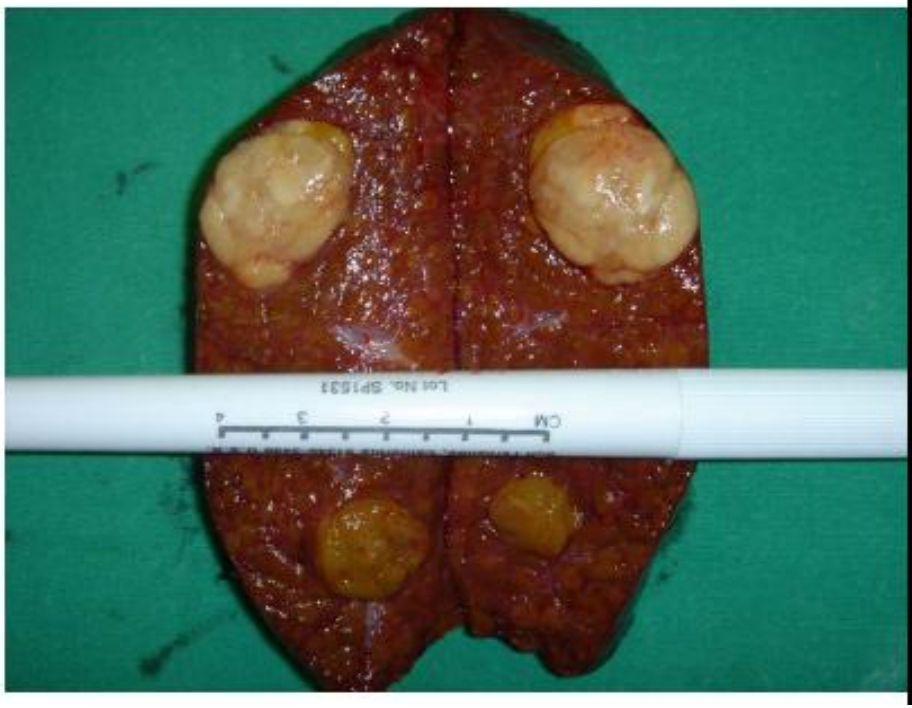


肝臟手術實例
Segmental Hepatectomy





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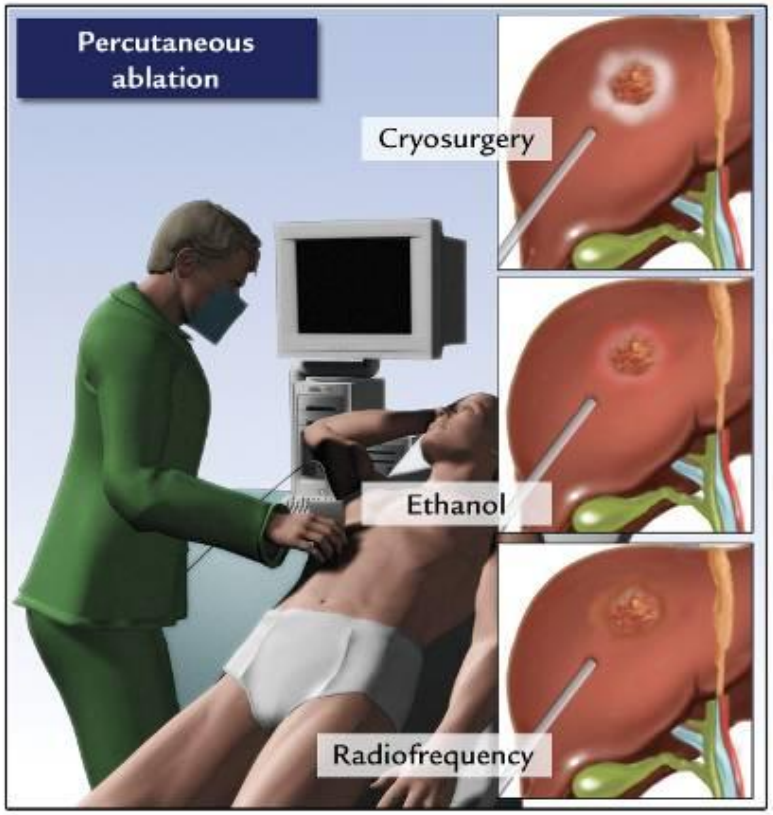
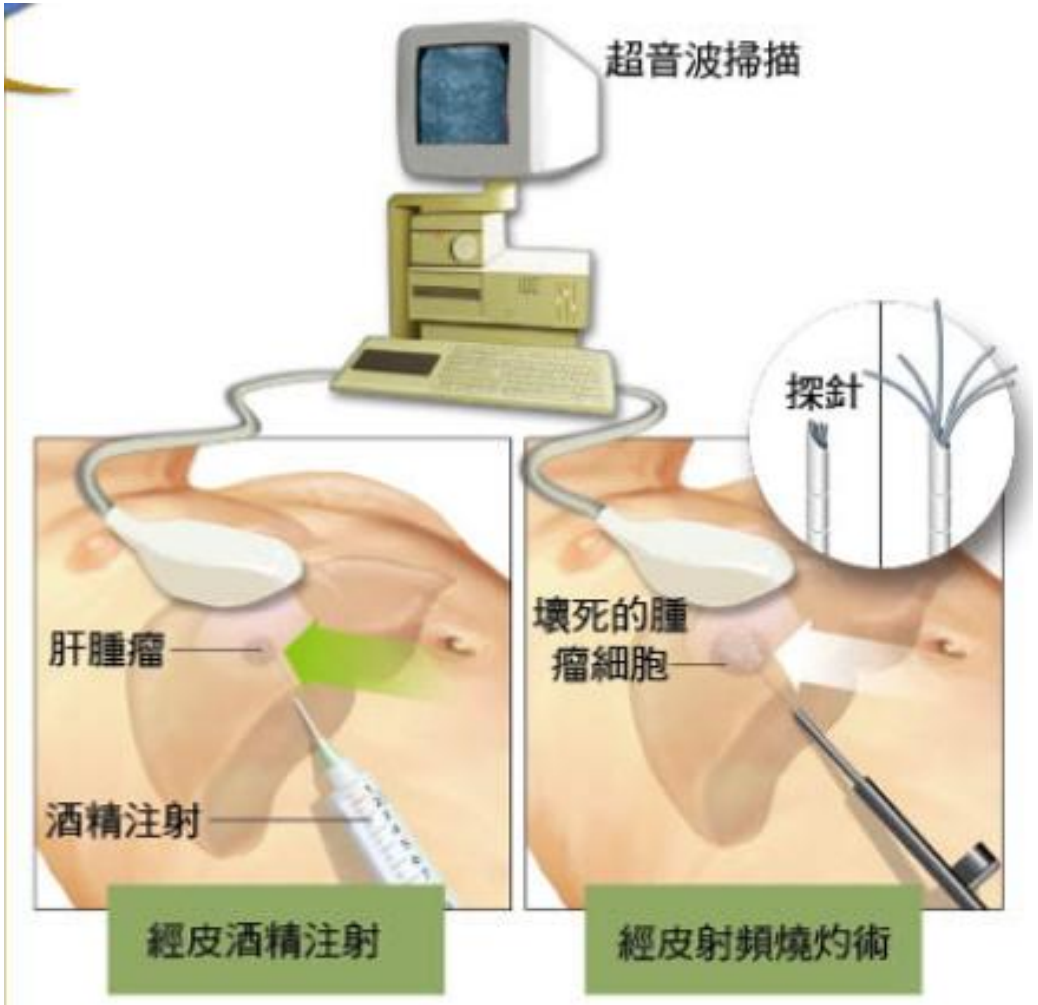
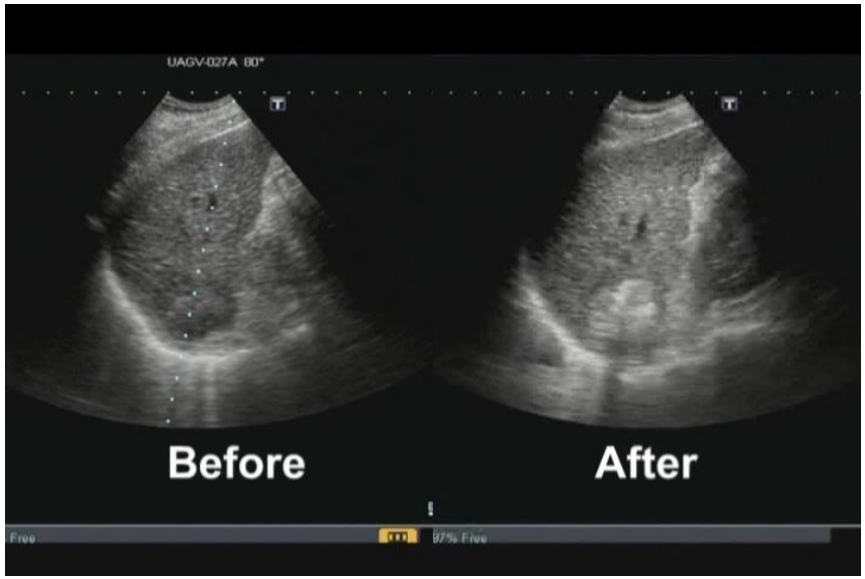
射頻燒灼(RFA)


Percutaneous ablation
Cryosurgery
Ethanol
Radiofrequency


超音波掃描
探針
肝腫瘤
酒精注射
壞死的腫瘤細胞
經皮酒精注射
經皮射頻燒灼術

射頻燒灼(RFA)



結論

外科手術治療(包括肝部份切除及肝移植)可提供部份膽管癌病患治癒的希望。近來由於手術技巧及手術前後對病患照顧方法的進步，手術成績已較以往改善。

為了進一步延長病患術後存活率，術後密切追蹤病患及對復發病患給予適當的治療是必須的。

手術前後輔助性療法(栓塞治療, 電療及化學療法)是否可改善病患的存活率，其方式及效果仍待進一步探討。

戰勝肝癌

- **面對膽管癌，積極樂觀**，目前膽管癌的診斷與治療技術日新月異，治療技術的進步與標靶治療的出現，替膽管癌患者帶來新的曙光與希望。
- 膽管癌治療，最重要的就是與醫師配合、選擇最佳的治療方式，**切勿聽信坊間偏方**，或是擔心害怕而拒絕接受正統治療。
- 只要去做，沒有什麼不可能；成功的唯一秘訣，就是堅持到最後一分鐘。醫師與您一同努力，戰勝肝癌!

努力抗癌

Thanks for Your Listening


Any questions?