Hepatic resection: An insight

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ABSTRACT

Over a long period of years, surgery of the liver was associated with a high complication rate, and therefore was the domain of a small number of specialists. Thanks to our better understanding of the biological, anatomical, technical and pathological aspects of hepatic resection, most complications can now be avoided. The main thrust of this article is to make valuable information available for younger colleagues, with emphasis on providing a differentiated synopsis of the problems of this formidable surgery with particular reference to practical situations.

Key Words: Hepatic resection, liver neoplasms, hydatid cyst, liver trauma

INTRODUCTION

Surgical removal of portions of the human liver was recorded in the 18th and 19th centuries and Langenbuch[1] is credited with the first successful elective hepatic resection. Subsequently many pioneers of modern hepatic resection were largely responsible for the evolution of classical hepatic resection techniques. However it was Couinaud[2] who provided the precise anatomical terminology on which modern hepatic resectional surgery is based.

Hepatic resection for removal of lesions of the liver maybe necessary for a wide variety of conditions. It is the accepted mode of therapy for many primary and metastatic tumours of the liver but rare for benign lesions. The philosophy of hepatic resection is based on biological, anatomical, pathological and technical considerations.

BIOLOGICAL CONSIDERATIONS

Liver is the only solid organ with the capacity to regenerate and resection is therefore possible. Resection is rare for benign lesions, but is the only chance for cure in malignant lesions. In fact resection is often the best palliation in malignancy.

The functional reserve of the liver determines the success of hepatic resection on the other hand the large functional reserve delays the clinical presentation with hepatic dysfunction. Hence hepatocellular carcinoma presents at a very late stage in its natural history because of the lack of symptoms in the early stage. A non cirrhotic liver may tolerate resection up to 80% of its volume.[3] The enormous regenerative capacity enables functional compensation within a few weeks. There is experimental evidence of 50% parenchymal regeneration in 6 months and complete liver volume restoration after one year. A favourable outcome cannot be taken for granted in hepatic resection. Only if reduction of the functional liver parenchyma is less than 50%, can the risk of clinically significant liver insufficiency be virtually disregarded. There is virtually no risk if most of the specimen volume has been replaced by an extensive tumour. In such patients compensatory hypertrophy of the unaffected residual liver has already occurred and the loss of functional parenchyma is limited. A comparable resection performed for multiple or unfavourably located small lesions, however carries a much greater risk of postoperative liver failure. The amount of liver that can be resected safely depends on the degree of cirrhosis,
the functional liver reserve and the regenerative response to the surgical insult.\cite{4,5} In the cirrhotic liver there is much less effective liver regeneration and impairment of liver function is greater, may last longer and result in terminal liver failure. Postoperative liver failure and postoperative mortality is related to the degree of pre-operative liver decompensation and to the extent of non-tumorous liver parenchyma removed.

ANATOMICAL CONSIDERATIONS

Hepatic resection should always be segment based. Non-anatomical resections of the liver are not favoured as cutting across liver segments inevitably jeopardizes the blood supply as also the venous drainage. Segmental liver resection could be resection of a single segment or a combination of segments. All segments can be resected individually without compromising the remaining liver. This anatomical approach allows segments containing tumour to be removed while preserving liver substance, important in patients with primary liver disease. Segment based liver resection is mandatory to ensure adequate clearance and less bleeding.

Non-anatomical liver resection has limited indications like when the lesion is located at the edge of the liver or when it is located in between or at two or more intersegmental planes. A non-anatomical resection should be a ‘box’ resection and not a wedge to avoid inadequate clearance in the depth of the wedge. These resections are however associated with an unacceptable recurrence rate.

The nomenclature for the extent of hepatic resection is based on The Brisbane 2000 Terminology of Liver Anatomy and Resections.\cite{6}

Looking at the spectrum of hepatic resections and the anatomical degree of difficulty for each, easiest is Left lateral sectionectomy (segment 2,3) followed by Right hemihepatectomy (segment 5,6,7,8). Left hemihepatectomy (segment 2,3,4) then Extended hepatectomy (segment 4 to 8 in right and segment 2 to 5 and 8 in left) and lastly Right anterior sectionectomy (segment 5, 8) which is the most demanding. Right hemihepatectomy is easier than left since the line of resection is straight unlike in a left hemihepatectomy where it is oblique so as to preserve the caudate lobe (segment 1).

TECHNICAL CONSIDERATIONS

Hepatic resection should be done only in centers trained to do so. A good preoperative workup, special technical expertise and excellent postoperative care are extremely essential. Hepatic resection for malignant tumors of the liver must be guided by the principle of complete tumour removal with at least a 1 cm margin of parenchymal transection clear of the tumor. Patients with metastatic neuro-endocrine tumors undergoing palliative resections often have tumors which are amenable to enucleation as are benign lesions like hepatocellular adenomas. Only in debatable cases is a formal hepatic resection necessary.

WHAT MAKES HEPATIC RESECTION SAFE?

1. Improved understanding of the biological, anatomical, pathological and technical aspects.
2. Good pre operative workup, special technical expertise and excellent postoperative care.
3. Adequate exposure and good retraction.
4. Complete mobilization of the liver.
5. Minimal blood loss (MBL) programme strategies: Relatively high intraoperative blood loss historically has been a common complication of hepatic resection, frequently resulting in the need for transfusion of blood. Strategies in the minimal blood loss (MBL) programme for liver resections implemented in 1991,\cite{7} include preoperative autologous blood donation and serial intraoperative manoeuvres, including the administration of aprotinin (serine protease inhibitor which minimizes hepatocellular injury and reduces blood loss), low CVP anaesthesia (less than 6mmHg) temporary hepatic vascular inflow occlusion (Pringle manoeuvre), ultrasonic dissection (CUSA) and the use of cell saver to cycle autologous blood intra operatively.
6. Inflow occlusion\cite{8} or Total vascular exclusion.\cite{9}
7. Use of laparoscopic or operative ultrasound for intra operative mapping of segments.
8. Parenchymal transection along anatomical planes using CUSA or Water jet.
9. Use of Staplers to divide vascular pedicles.
10. Use of Tissue glue, Argon plasma coagulation for haemostasis on the raw surface.

Approach to segmental resection
a. Using intra operative ultrasound (IOUSG): mapping out the segments after marking the portal vein branches and hepatic veins. Especially helpful in cirrhotic liver since anatomy is altered.
b. Glissonian approach: lowering the hilar plate and identifying the pedicles, ligating them and then resecting the devascularised segment. Useful in
Complications of hepatic resection
Principal hazards of hepatic resection include biliary leakage as well as bleeding from hepatic veins or inferior vena cava (IVC) during parenchymal transection. This is especially likely to occur during major resection for high posteriorly placed tumours where there is little clearance between tumour margin and the passage of the hepatic veins into the IVC or when tumours are closely adherent or adjacent to the IVC. Infection is a threat after liver resection in patients with biliary obstruction, especially in the presence of previous intervention (PTC or ERCP) and in the cirrhotic patients. Ascites and pleural effusion also occur. The perioperative mortality in patients without primary liver disease is about 2% and the morbidity about 20%. Mortality and morbidity rates are much higher in patients with primary liver disease and when central resections with bile duct reconstruction are carried out.

HEPATIC RESECTION IN CIRRHOTIC LIVER: SPECIAL CONSIDERATIONS

Hepatic resection in cirrhotic liver is difficult but not impossible. In the cirrhotic liver because of the compromised liver function, the functional reserve is less, thus indicating a higher chance of developing post resectional liver failure. The more cirrhotic the liver, the worse is the liver function before operation and the less is the functional reserve. Additionally, it is more challenging because of the intra operative difficulties in mobilising the liver and transecting the liver parenchyma. There may be increased blood loss associated with portal hypertension. Postoperative hepatic failure with increased susceptibility to infection are major concerns. There is a significant relation between intra operative blood loss, postoperative rise in serum bilirubin and postoperative mortality. Abdominal infection may trigger postoperative liver failure. Cirrhosis also predisposes to multi organ failure following hepatectomy. In cirrhotic patients liver function is the main prognostic factor, serum bilirubin the single most important prognostic factor and liver resection should not be carried out in patients with serum bilirubin more than 2 mg%. In the cirrhotic liver therefore, resection should be restricted to patients with good performance status (KPS score>70) and in patients with good liver function (serum bilirubin < 3 mg%, minimal ascites, platelet > 50,000, serum albumin > 3 gm% and INR <1.3).

The intra operative mobilization should be limited and removal of the liver tissue should allow tumour clearance but preserve maximal residual volume. An intraoperative USG helps identify small tumours which may not be visible or palpable in a cirrhotic liver on gross examination and helps to identify lesions which are not demonstrated pre operatively. Intra operative USG has been shown to alter the surgical management plan in 18% of cirrhotic patients. Intra operative USG also helps define optimal resection margins.

In cirrhotics always maintain a good outflow channel by preserving hepatic veins carefully, the pre existing portal hypertension causes liver congestion, and damage to the hepatic veins will cause more bleeding from the raw surface of the divided liver. If the outflow is getting jeopardized limit the resection. Intra operatively shorter duration of inflow occlusion (Pringle’s manouvre <20 minutes) and minimal blood loss (<500 cc) along with experienced surgeon are associated with good outcome. Hepatic resection leads only to a small increase in portal pressure in the normal liver. However in the cirrhotic liver there is further aggravation of portal hypertension related to the amount of parenchyma removed and to an incapacity of the remaining liver to drain the splanchnic bed. The increase in portal pressure may also be related to the increased risk of variceal hemorrhage after liver resection in patients with cirrhosis. Ascites is a frequent complication following liver resection in the cirrhotic patient and occurs in 80% of cases. This is favoured by an increase in the portal pressure and severance of lymph vessels in the hepatic pedicle and liver ligaments. The gross abdominal distension post operatively interferes with ventilatory function and can cause burst abdomen. Leakage of ascites leads to major protein and fluid electrolyte loss. In addition ascites may be infected and this may prove irreversible.

PATHOLOGICAL CONSIDERATIONS

Hepatic resection is the treatment of choice for malignant tumours and is rarely indicated for benign lesions. A rational approach for the diagnosis and management of these lesions is as shown in the algorithms given. (Figure 1, 2, 3)
HEPATIC RESECTION FOR MALIGNANT LESIONS

Hepatocellular Carcinoma (HCC)
Surgical resection is the standard effective treatment. Partial hepatectomy or total hepatectomy with liver transplantation are the only treatment options which have the potential to cure. Partial hepatectomy entails an anatomical resection according to that described by Couinaud’s segments. It has a postoperative mortality rate of 0.5% to 21.5% depending on the percentage of patients of cirrhosis and age more than 70 years. Total hepatectomy with liver transplantation is followed in patients with end stage cirrhosis and single tumour less than 5 cms. in size or not more than 3 tumour nodules with a collective size of less than 9 cms.\(^{[12]}\) Best results are seen in fibrolamellar HCC and small incidentalomas found unexpectedly within the explanted liver. Hepatitis B is now no longer considered to be a contraindication to liver transplantation because of the advent of anti viral drugs like Lamivudine and recently Adefovir dipivoxil.

There are two approaches which can be adopted to improve on the results of partial hepatectomy viz. use of adjuvant therapy and extending the limits of liver resection.

1. Adjuvant therapy: 50 mci of transarterial lipiodol iodine-131 within six weeks of liver resection for HCC has been shown to be of definite benefit.\(^{[13]}\)
2. Extending the limits of liver resection.
   a. En bloc resection of adjacent organs involved by the tumour.
   b. Shrinkage of large tumours:
      Systemic chemotherapy with Cisplatin, 5-FU, Adriamycin and Interferon or Transarterial chemoembolisation (TACE): Contraindicated in portal vein thrombosis.
      Hepatic arterial infusion of chemotherapeutic agents.
      Transarterial Yttrium 90 microspheres
   c. Compensatory hypertrophy of the non involved liver:
      Embolising the portal vein supplying the part of the liver containing the tumour.

Palliative cytoreductive surgery for good risk surgical patient is beneficial. The safer option is always selected and can be a combination of non-anatomical box resection for some lesion in combination with...
microwave coagulation and enucleation of the tumour. Other options include percutaneous microwave coagulation or percutaneous ethanol injection.

Hepatic resections for liver metastasis
The role of hepatic resection in the treatment of colorectal metastasis is now well established based on prospective data on resected patients compared with unresected patients with a similar stage of the disease. Other than metastasis from colorectal and neuroendocrine tumours, the role of hepatic resection has not been defined for metastasis from other primary sites.

Hepatic resections for Carcinoma of the gall bladder
For Nevin’s stage II/III resection of hepatic segments 4b and 5 is advocated while for stage IV more radical resection in the form of a right hemi-hepatectomy is performed.

Hepatic resection for hilar cholangiocarcinoma
Surgical treatment of hilar cholangiocarcinoma includes removal of the affected hepatic duct and different types of liver resection according to the extension of the tumour together with the caudate lobe, and the dissection of the lymphatics and perineural tissue around the hepatoduodenal ligament, coeliac trunk and pancreatic head.

Hepatic resection for benign lesions
Benign liver neoplasms are being increasingly diagnosed nowadays since imaging techniques and laboratory tests are employed very extensively to investigate obscure visceral symptoms. During these investigations it can happen that a liver lesion is diagnosed. This lesion, cystic or solid when discovered in the liver of a healthy person is called a hepatic ‘incidentaloma.’ The natural history and clinical behaviour of benign hepatic tumors during long term follow up may not justify primary surgical treatment in most cases but in symptomatic patients, in cases of diagnostic doubts or for tumors with a known malignant potential resection is indicated.

Benign liver conditions constitute a substantial component of liver pathologies and represent a management challenge. These include:
1. Benign Liver Neoplasms: (a) Adenomas, (b) FNH, (c) Haemangiomas (d) Biliary cystadenomas and (e) Liver cysts-Simple hepatic cysts, Polycystic liver disease and Parasitic cysts.

Indications for the operative treatment of benign tumors are influenced by the level of diagnostic accuracy and some general factors. Most solid benign liver masses can be managed conservatively with observation provided the diagnosis has been reasonably established by imaging techniques. A focal liver lesion with an equivocal diagnosis on preoperative imaging should be removed. In benign liver neoplasms the trend towards resection is increasingly justified because precise preoperative diagnosis of benign liver tumors remains difficult despite sophisticated imaging modalities, so much so that malignant tumors can go unrecognized. Moreover hepatic resection can be carried out safely these days. On the other hand however a temptation to resect benign lesions must be resisted unless there is a clear indication.

In benign liver conditions liver resection maybe necessary in the management of some complex benign biliary strictures especially when associated with unilateral liver atrophy and in cases of hepaticolithiasis in association with Recurrent pyogenic cholangitis and in Caroli’s disease.

Hepatic adenoma (HA)
Giant HA, surface HA are associated with a particularly high incidence of rupture with intraperitoneal haemorrhage (30%). Also possibility of malignant transformation into HCC exists (10%). HA with a diameter > 5 cm. need to be resected since lesion size may be an important indicator of malignancy and potential for rupture. In multiple liver adenomata resection of the largest adenomata is recommended, including repeated resection in the same patient.[14-16] Surgical treatment options are either enucleation or formal segmental hepatic resection which could be even laparoscopic.[17]

Focal nodular hyperplasia (FNH)
Majority are asymptomatic or incidental findings at laparotomy but can be symptomatic in 10% of patients and complications include intraperitoneal hemorrhage, due to spontaneous rupture, or intralesional infarction. Rarely, progressive FNH may lead to hepatic failure and liver transplantation may be of value. Resection is rarely indicated, if lesion is anatomically friendly in patients with unremitting symptoms. Hepatic artery embolisation may produce relief in symptomatic patients unfit for surgery.

Although the clinical and biochemical characteristics
of fibrolamellar carcinoma are non specific, the radiological appearances of tumour on imaging can mimic FNH.\[18\] Thus all patients with undetermined presumed benign liver lesions should be operated on and are best treated by surgical excision.

Haemangiomas

The unknown natural history and risk of complication of large haemangiomas may pose therapeutic dilemmas. Most haemangiomas less than 5 cm in diameter should be regularly observed if the diagnosis is secure. Those more than 5 cm in diameter can be conservatively managed unless they are symptomatic or exhibit rapid growth or have a potential for exposure to trauma. The treatment of giant symptomatic haemangiomas is still largely controversial. Resection is indicated only in patients with severe symptoms like persistent pain of progressively growing tumor or complications of the haemangioma like rupture, Kasabach-Meritt syndrome or CCF. Spontaneous rupture is truly exceptional and is reported in less than 1% of large haemangiomas.

Biliary cystadenoma

Biliary cystadenomas represent a rare benign cystic hepatic neoplasm with premalignant potential. The malignant counterpart is biliary cystadenocarcinoma which is believed to arise from the premalignant form. Major indications for surgery are pain, rupture, hemorrhage, infection, and strong suspicion of malignancy. Differentiating cystadenoma from cystadenocarcinoma by imaging criteria may not be possible in many patients. This concern is considered of less therapeutic than academic importance since treatment is similar in both the tumors because of the premalignant nature of biliary cystadenomas. However cystadenomas and cystadenocarcinomas have to be differentiated from other cystic liver lesions which too may be difficult because of significant overlap in clinical presentation and radiological appearances. Metastatic tumors that undergo cystic degeneration can mimic biliary cystadenomas and cystadenocarcinomas. Both biliary cystadenoma and its malignant counterpart cystadenocarcinoma are slow growing and appear as unilocular or multilocular cystic intrahepatic masses making distinction difficult from simple hepatic cysts especially in the unilocular form thus high index of clinical suspicion and surgical resection for equivocal lesions is advisable.

Hepaticolithiasis

Hepaticolithiasis occurs predominantly in the left lobe and definitive treatment entails removal of stones and treating associated bile duct strictures. Hepatic resection is curative when stones are in the left lobe of liver. The extent of resection is limited in biliary cirrhosis or when stones are present in both lobes. Recurrence is common, there is also 5% risk of development of cholangiocarcinoma and the possibility of secondary biliary cirrhosis. Intrahepatic stones are often associated with Caroli’s disease. Stones in this setting may co-exist with cholangiocarcinoma.\[19-21\]

Liver abscess

Image guided aspiration and catheter drainage with antibiotics are unlikely to be curative in two exceptional situations: secondary infection of a hepatic malignancy and hepatic abscess associated with chronic granulomatous disease of childhood or Caroli’s disease. Hepatic resection is advisable in these situations.

Intrahepatic biliary strictures

Segmental hepatic resection may serve an important role in carefully selected patients with high intrahepatic ductal injuries associated with vascular injury leading to a atrophy-hypertrophy complex causing episodic cholangitis and abscess.

Polycystic liver disease

Combination of surgical resection and fenestration has been the treatment of choice for symptomatic polycystic liver disease. Patients in whom there is no parenchymal sparing or those with failed fenestration maybe offered liver transplantation.\[22\]

Hydatid cyst

While no treatment is required for dead calcified cysts and modalities like the PAIR technique i.e. Puncture under sonographic guidance, aspiration of hydatid fluid, Instillation of protoscolicidal agent, Re-aspiration without drainage and Albendazole, can be successfully employed in uncomplicated unilocular cysts,\[23\] surgery remains the treatment of choice in most cases.

Surgery has the potential to remove the cysts completely and lead to complete cure. It could be ‘radical’ surgery like total cystopericystectomy or conservative surgery like subtotal pericystectomy and partial cystectomy with omentoplasty. Liver hydatidosis cannot properly be considered a “benign disease” as it is progressive, often recurrent (10% to 20%), may cause life-threatening complications, and carries a mortality rate that reaches 10% in recurrences.\[24,25\] To alleviate these concerns hepatic resection may exceptionally be required in particular situations like multiple cysts of a hemiliver or cyst...
occupying an entire peripheral segment. In these cases resection should be performed with the aim of compensating a pericystectomy which would leave a deep residual cavity or portions of suspended or ischaemic liver.\[24\] (Figure 4)

*E.multilocularis* infection causes alveolar hydatid disease which behaves like a tumour and rapidly progresses with metastases to other organs.\[25\] Partial hepatectomy has to be done because of the infiltrative nature of the disease. Occasionally univesicular cysts without daughter cysts are difficult to differentiate radiologically from simple cysts, on the other hand cystic form of embryonal sarcoma can mimic hydatid disease adding to the diagnostic dilemma.\[26\]

**Hepatic Resection for Liver Trauma**

In contrast to former beliefs it is the minority of patients who require surgical intervention for their liver injury. As the proportion of patients undergoing successful conservative management increases, the indications for operation are those patients who remain unstable despite resuscitation attempts and are therefore likely to have a high grade hepatic injury,\[27\] and those who require operative intervention for concomitant injuries and may have any grade of hepatic injury.

Historically a wide variety of operations and techniques have been described and utilized in the management of liver injuries- selective hepatic artery ligation, atrio-caval shunting, total vascular exclusion, veno-venous bypass, omental packing, gauze packing, mesh wrapping, hepatorrhaphy, hepatotomy and direct suturing and anatomical and non-anatomical resection, but with varying degrees of success.

Non-anatomical resections, hepatotomy and direct suture ligation and anatomical resections are selectively utilized and should be performed by experienced surgeons who are familiar with liver anatomy and surgical techniques. Anatomical resections are currently performed in 2-4% of patients with liver trauma with a reported mortality rate approaching 50% and are generally performed when haemostasis has not been achieved by any other means.\[28\]

**HEPATIC RESECTION IN CHILDREN**

Primary liver tumours account for approximately 15% of abdominal tumours in childhood and maybe either epithelial or mesenchymal in origin and are benign or malignant. Secondary hepatic tumours such as neuroblastomas may also affect this age group. Hepatoblastoma is the most common malignant hepatic tumour representing 0.8% to 1% of all childhood tumours.\[29\] Preoperative chemotherapy is effective in reducing the size by 35-95% and this is followed by hepatic resection. Liver transplantation is an alternative and survival after transplant for extensive malignant lesion is greater than 50%.\[30\] Hepatic haemangiomas account for 10% of liver masses in children. In some cases arterio-venous communications result in CCF, which if untreated, may lead to early death within the first few weeks of life in over 75% of cases.

**WHERE ARE WE TODAY?**

The field of liver resection and liver transplantation have acted complementary to each other and it is now commonplace to have combined hepatobiliary and liver transplantation surgical units. On the one hand, ideas regarding organ preservation during ischaemic period have been borrowed from the transplant field to perform extended resections under prolonged ischaemia,\[31\] while on the other hand surgeons have used the experience gained in liver resections to split livers for use in paediatrics or multiple recipients as well as to perform live related liver transplantation. Also, the revolution is laparoscopic surgery has not left liver surgery alone. Besides the use of laparoscopic USG to stage liver tumours, laparoscopic hepatic resection is now being increasingly described for both, benign and malignant lesions.

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