Preservation of liver function during hepatic resection

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Keywords: liver function, hepatic resection, liver resections

S Afr J Anaesth Analg 2011;17(2):202-204

Most liver resections will be performed to remove malignant tumours with curative intent. In general, benign liver lesions will seldom require surgery. Apart from some symptomatic neuroendocrine tumours, partial resection or "debulking" is rarely used.

In the setting of malignant liver tumours, the basic requirements are:

- The indication for surgery is reasonable.
- The surgeon and the institution are adequately trained in liver surgery, with all required resources being available.
- The lesion/s can be fully resected with a margin of one centimetre, ideally.
- Sufficient liver remains to sustain the patient until regeneration occurs.
- The remnant liver has adequate inflow and outflow.

In addressing the concept of preservation of liver function in hepatic resections, all the above factors are relevant. The indication for resection should be appropriate, and the procedure should be correctly performed, and the patient managed in the postoperative phase by a multidisciplinary team experienced in dealing with liver disease.

Types of liver tumours

Liver tumours can be broadly classified as being either benign or malignant. Malignant tumours are then subdivided into primary and secondary malignancies.

Benign tumours

- Haemangioma;
- Focal nodular hyperplasia;
- Adenoma;
- Cystic lesions.

Malignant tumours

- Primary: hepatocellular carcinoma;
- Cholangiocarcinoma;
- Secondary (metastatic).

Indication for surgery

The most common benign tumours are haemangiomas and focal nodular hyperplasia, and seldom require surgical intervention, intractable pain being the rare exception. Adenomas in males and those that are larger than two centimetres in females, or with complications, should be resected.

Primary liver cancers are suitable for resection depending on the size, position and number and state of the underlying liver.

Secondary or metastatic cancers may be considered for resection in certain circumstances. The original cancer and its biological behaviour is probably one of the most important determinants of the indication for resection. Certain primary tumours, such as colorectal cancer, have been found to respond favourably to resection of liver metastases with a five-year survival of 25-60% of all cases being reported. Other primary cancers that may be considered for resection of liver metastases include renal, adrenal, breast, melanoma and neuroendocrine malignancies.

Extent of resection

Patients with normal liver parenchyma should be able to tolerate resections of up to 75% of total liver volume, provided that the remnant liver retains an adequate arterial and portal venous inflow, and that hepatic venous outflow is preserved. Also, the remnant liver should not be compromised during and after surgery by factors such as hypoxia, hypotension, drug toxicity and sepsis.

The liver is able to regenerate following resection. This should take place within the first two to three weeks

following surgery. However, until regeneration occurs, sufficient hepatic reserve is required to sustain the patient in the early postoperative phase.

Patients with cirrhosis have a significantly reduced tolerance to resection. The Childs status is used as a guide to determine the extent of possible resection. Childs A patients can usually tolerate resections of 40-50%, and Childs B, up to 25%. Childs C patients should not be subjected to hepatic resection as the risk of postoperative liver failure is high.

Better understanding of the segmental liver anatomy has improved the ability to resect what is required, while avoiding unnecessary loss of normal liver parenchyma. Segmental, sectoral and multi-segment resections are increasingly used to attain oncological objectives, while preserving maximal liver function. Non-anatomical resections of small peripheral lesions may also be performed in conjunction with larger resections to preserve liver parenchyma. Combined resection and radio-frequency or microwave ablation may also be used to maximise the remnant liver.

State of the liver

Established cirrhosis is usually apparent with blood and radiological investigations. However, subtle liver dysfunction may be difficult to determine in the preoperative setting. The obesity epidemic has been associated with a significant increase in the incidence of non-alcoholic fatty liver disease and steatohepatitis. Chemotherapeutic agents such as oxaliplatin and irinotecan, commonly used in the adjuvant, neoadjuvant and palliative treatment of colorectal cancer, can also lead to liver injury, and are associated with steatohepatitis and blue liver syndrome respectively. This has led to a new entity now referred to as chemotherapy-associated steatohepatitis.

The impaired liver has a reduced capacity to cope with surgical resection and is also less able to regenerate fully following major resection. Therefore, the state of the underlying liver must be carefully assessed prior to any planned resection. Some data has emerged that preoperative administration of omega-3 fatty acids and low-fat diets may result in a significant improvement in the fatty liver.

Intraoperative strategies to maintain liver function

During surgery, it is necessary to maintain adequate hepatic perfusion pressure gradients and oxygenation throughout, in order to limit liver injury. At times during the operation, it is necessary to occlude inflow to the liver using a Pringle manoeuvre to limit bleeding from the resection margin. This results in total hepatic ischaemia, which is usually well tolerated for a period of time. The normal liver may tolerate total inflow occlusion for up to one hour, particularly if this occurs at intervals with periods of reperfusion in between.

Ideally, ischaemia of the remnant liver should be limited as much as possible. The extent of ischaemic injury may be reduced by ischaemic preconditioning of the liver, where total inflow is occluded for 10 minutes, followed by a period of reperfusion of 20 minutes prior to further inflow occlusion. Thereafter, the liver is better able to tolerate ischaemic insult.

However, the abnormal liver is much less tolerant of ischaemic injury and inflow occlusion should be limited. Ischaemic preconditioning has also been shown to be of benefit in cirrhotic and steatotic livers. The use of selective inflow occlusion avoids any ischaemic injury to the remnant liver, as only the inflow to the lobe or segment to be resected is occluded. This technique requires experience and knowledge of the segmental liver anatomy. It is a valuable technique to use to avoid unnecessary ischaemia of the remnant liver.

One of the major potential risks to the patient during liver resection is excessive bleeding. This can lead to significant arterial hypotension with resultant hepatic hypoperfusion. Bleeding from hepatic arteries and portal veins can be controlled by inflow occlusion at the hepatic hilum, but bleeding from divided hepatic veins is much more difficult to control. The major contributor to hepatic venous bleeding is central venous pressure, and is it necessary to keep this low throughout the procedure, with 3-5 cmH_2O being recommended. The anaesthesiologist has a vital role to play in reducing intraoperative bleeding by maintaining low venous pressures, while still ensuring adequate inflow and hepatic perfusion pressures.

Intraoperative ultrasound is routinely used during liver resection, not only to detect tumours not seen on preoperative imaging, but also to visualise portal and venous anatomy. This tool helps to guide resection so that the remnant liver has adequate inflow and outflow. The judicious use of blood components and cell-saved blood may be required to maintain systemic and hepatic perfusion pressures, thereby indirectly preserving liver function.

Postoperative care after liver resection

Efforts to maintain liver function do not cease at the end of the surgical procedure and the anaesthetic. The post-hepatectomy patient remains in danger of complications which could place the remnant liver at

risk of further injury: the second hit phenomenon. This is particularly true where a major or extended resection has occurred, and the remaining liver parenchyma is barely sufficient to sustain adequate hepatic function until regeneration begins to occur. Care must be taken to avoid hypotension, hypoxia and sepsis, all of which could place the remnant liver at risk of further injury. Early recognition and management of bleeding is essential to prevent shock, and limit the need for blood products which may have further injurious effects. Care must also be taken with the use of potentially hepatotoxic drugs.

Other complications which may jeopardise the remnant liver include portal vein and arterial thrombosis. These can be readily diagnosed by duplex ultrasound. Regular monitoring of hepatic synthetic and conjugating function is required to identify impending liver failure.

Conclusion

Liver resection can almost always be performed safely with low mortality, limited morbidity and maintenance of liver function. However, this achievement requires correct indications for surgery, appreciation of the state and anatomy of the liver, intraoperative techniques to maintain liver perfusion and limit injury, and careful monitoring in the postoperative phase to prevent further injury to the remaining liver. This surgery should be performed by experienced practitioners in a multidisciplinary setting in a centre of excellence.