INTRODUCTION

Hepatocellular carcinoma (HCC) is one of the most common causes of cancer related mortality in the world.[1] It is frequently found in patients with chronic liver disease resulting from infection with hepatitis C virus (HCV).[2] In Egypt, between 1993 and 2002, there was an almost twofold increase in HCC amongst chronic liver patients.[3] Cirrhotic patients are frequent candidates for liver related surgery at the Liver institute in Egypt. Liver resection improves overall survival in patients with small, non-invasive and non-metastatic tumors,[3;4] but this surgery may be followed by clinical or subclinical hepatocellular derangements, metabolic abnormalities, haemodynamic changes, coagulation and electrolyte changes due to temporary liver dysfunction frequently encountered in the immediate postoperative period.[5-8] The choice of the anaesthetic technique and management should take this in consideration when planning to minimize perioperative complications of this surgery particularly in cirrhotic patients as any deviation could have a significant impact on recovery, hospital stay and costs. Few studies were designed to address this issue in cirrhotic patients with use of the minimal invasive transoesophageal Doppler to monitor these perioperative haemodynamic changes.[5]

Anatomical and physiological considerations:

1-Anatomical considerations:

The liver is a large abdominal organ in the human body. It accounts for about 2% of the total mass of healthy adults and 5% of neonates. The human liver normally weighs between 1.4–1.6 kg, and is a soft, pinkish-brown organ.[9]

Traditional gross anatomy divided the liver into four lobes based on surface features. The falciform ligament is visible on the front of the liver. This divides the liver into a left and a right anatomical lobe. If the liver is flipped over (the visceral surface), there are two additional lobes between the right and left. These are the caudate lobe and the quadrate lobe. [10]

In contrast, surgical anatomy divides the liver based on the portal venous system. Portal vein distributed within the liver dividing it into eight segments. Each individual segment receives a "portal pedicle" consisting of a portal venous branch, hepatic arterial branch, and a bile duct radicle with segmental drainage through a dedicated hepatic venous branch. The eight functional units embrace the hepatic veins that provide outflow to the inferior vena cava.[11]

2-Physiological considerations:

A- Hepatic blood supply and its regulation:

Approximately 25% of the cardiac output passes through the liver. The blood flow to the liver is derived from two different sources, the hepatic artery and the portal vein. The hepatic artery accounts for only 25-30% of total hepatic blood flow, but it may provide up to 50% of the oxygen supply to the liver. On the other hand, the portal vein supplies up to 75% of total hepatic blood flow. Since the portal vein drains the blood from the stomach, spleen, pancreas, and intestine, it is rich in nutrients but already partially deoxygenated.

Consequently, the portal venous contribution to the hepatic oxygen supply does not usually exceed 50-55%.[10]

Regulation of blood flow through the hepatic artery occurs primarily at the terminal arterioles which are richly supplied with smooth muscle cells.

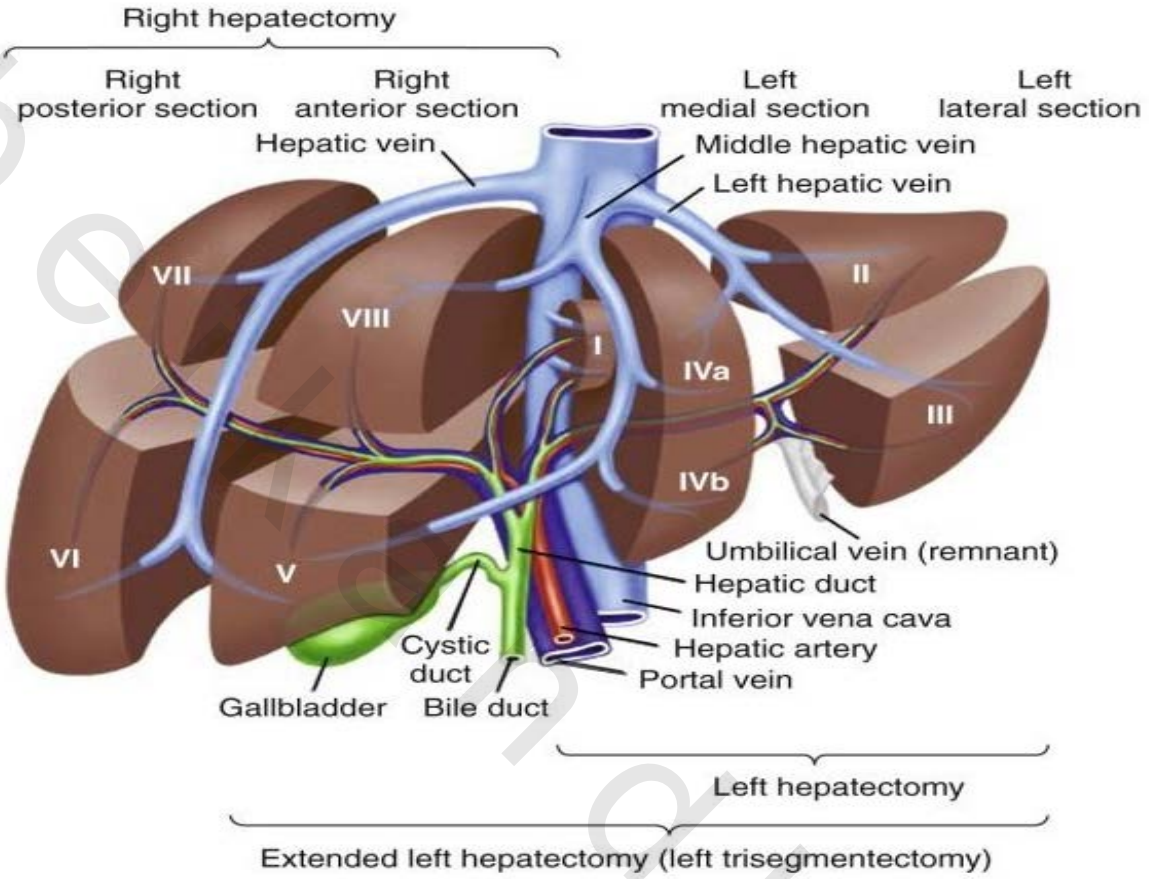

Figure (1) Segmental liver anatomy and the normal portal venous structures. Bracketed text shows hepatic segments resected during partial hepatectomies.[11]

In contrast, portal venous flow is primarily controlled by arterioles in the preportal splanchnic organs. Recent evidence suggests that changes in vascular resistance within this vascular bed may occur not only at the sites of the terminal portal venules but also at the sinusoidal level, which can significantly alter the distribution of flow within the liver. These changes in vascular tone seem to be mediated at least in part by contraction or relaxation of hepatic stellate cells (Ito cells), which are localized within the peri sinusoidal space of Disse.[12]

Factors that may alter hepatic blood flow during anaesthesia and surgery:

1-Effects of volatile anaesthetics:

Volatile anaesthetics can alter hepatic perfusion. However, the relative influence on the two vascular inflows to the liver, and the extent of changes caused, differ between the various agents. Moreover, hepatic arterial flow may simultaneously decrease, in particular in the presence of arterial hypotension. In contrast, total hepatic blood flow is usually well maintained during anaesthesia with isoflurane.[13] There are only a few studies available that analyze the effects of the two newer volatile anaesthetics sevoflurane and desflurane. These studies suggest that both agents may reduce portal venous flow, while blood flow through the hepatic artery seems to remain essentially unchanged. [14]

2-Effects of intravenous agents and muscle relaxants:

Most intravenous anaesthetics and analgesics seem to have no direct effects on the liver circulation. However, reductions in cardiac output or arterial pressure associated with the use of these agents may cause secondary decreases of portal venous and/or hepatic arterial blood flow. Fentanyl does not seem to significantly impair blood flow to the liver, and rocuronium do not impair hepatic perfusion. [15]

3-Effects of ventilation:

Artificial ventilation decrease liver blood flow significantly. This impairment is primarily by reducing cardiac output and simultaneously increasing hepatic outflow resistance, frequently associated with controlled ventilation, particularly when high positive end-expiratory pressures is applied.[16]

4-Effects of surgery:

Surgery causes profound reduction in blood flow through the intestine and the liver. Abdominal surgery, particularly of the upper abdomen, has probably the greatest effect. Haemorrhage produces a greater fall in portal venous than in hepatic arterial blood flow and results in profound impairment of hepatic perfusion both at the level of the macrocirculation[17] and at the microcirculatory level.[18]

5-Other factors :

Diseases of the liver:

Cirrhosis with high intrahepatic resistance often produces dramatic falls in overall hepatic blood flow due to decreased portal venous flow. Hepatic arterial blood, tends not only to remain constant but also may increase. It seems reasonable that all kinds of pathology (diffuse and nodular space occupying) lead to a primary decrease in portal venous flow, and subsequently to an increase in hepatic artery flow. The theoretical explanation of this observation is that all circulatory change can be explained by the adenosine washout theory. [19]

Non anaesthetic drugs:

β-adrenergic blockers (propranolol) has been employed to reduce hepatic (portal) blood flow and used as a therapy for bleeding oesophageal varices. Within 1 hour, 150 mg propranolol reduced cardiac output, portal venous pressure and hepatic blood flow.[20]

Clinical implications of altered hepatic blood flow during anaesthesia and surgery:

Preoperative period.

The major goal in the preoperative period is to identify those patients most susceptible to intraoperative impairment of hepatic perfusion and oxygenation. This group includes all patients with preexisting liver disease. Within this group, mortality can be high from otherwise simple procedures, especially if the liver disease is unrecognized, acute, or has recently worsened. Preoperative evaluation of the patients identified, forms the basis for the optimal timing of surgery. In general, elective operations should be postponed in patients with acute parenchyma liver disease until the hepatic functional reserve has recovered completely. However, if the clinical circumstances do not allow this, then waiting until evidence of acute liver cell necrosis has resolved is recommended in all cases. For patients with chronic liver disease, delay to improve correctable factors may improve the outcome. This preparation of the patient with pre-existing liver disease includes the elimination or reduction of associated risk factors such as ascites, anaemia, coagulation or electrolyte abnormalities, encephalopathy, hyper-bilirubinemia, or nutritional depletion.[21]

Intraoperative period.

The risk of postoperative liver dysfunction is not directly affected by the specific route or brand of anaesthesia selected but rather by the degree of impaired hepatic oxygenation. Therefore, the main aim during the operative period is to keep the hepatic oxygen supply in a normal range. Hepatic oxygen supply depends on oxygen content and the blood flow entering the liver. Consequently, all measures should be taken in order to maintain a normal arterial haemoglobin concentration and Pao_2. The latter should be achieved by careful ventilator adjustment, with the lowest positive end-expiratory pressure possible to avoid any unnecessary increase in intrathoracic pressure. Moreover, the arterial PCO_2 should be kept within normal limits in patients with liver disease to avoid any further disturbance of organ perfusion. The adverse effects of mechanical ventilation on cardiac output should be minimized by appropriate volume replacement therapy and an anaesthetic management that allows for rapid weaning and extubation at the end of the surgical procedure. In addition, the technique chosen should not have major adverse effects on hepatic blood flow. [22]

B-Role of the liver in the haemostatic system.

The liver is the primary site of synthesis of most of the clotting factors and the proteins involved in the fibrinolytic system. These include all the vitamin K-dependent coagulation proteins (factors II, VII, IX, X, protein C, protein S and protein Z), as well as factor V, XIII, fibrinogen, antithrombin, α_2-Antiplasmin and plasminogen.

The notable exceptions are vWF, t-PA, thrombomodulin, TFPI and urokinase plasminogen activator (u-PA). The vWF, t-PA, thrombomodulin and TFPI are synthesized in endothelial cells, while u-PA is expressed by endothelial cells, macrophages, renal epithelial cells and some tumour cells.[23]

Vitamin K, a fat-soluble vitamin, is required to achieve proper levels of procoagulant factors (II, VII, IX and X) and anticoagulant factors (proteins C, S and Z). All the vitamin K-dependent factors have in their amino-terminal several glutamic acid residues that must be converted to gamma-carboxyglutamic acid residues. This process is crucial to allow these proteins to bind calcium ions to form bridges to phospholipid surfaces, which are essential for the formation of activation complexes.

Finally, the liver plays a vital role in the regulation of anticoagulation. Removal of activated clotting and fibrinolytic factors especially tPA, is mediated through the hepatic reticuloendothelial system.[24]

Liver cirrhosis.

In patients with cirrhosis, the Child class and Model for End-Stage Liver Disease (MELD) score have been demonstrated to correlate with preoperative risk.

Cirrhosis causes a hyperdynamic circulation with increased cardiac output and decreased systemic vascular resistance. At baseline, hepatic arterial and venous perfusion of the cirrhotic liver may be decreased: portal blood flow is reduced as a result of portal hypertension, and arterial blood flow can be decreased because of impaired autoregulation.

Moreover, patients with cirrhosis may have alterations in the systemic circulation due to arteriovenous shunting and reduced splanchnic inflow. The decreased hepatic perfusion at baseline makes the cirrhotic liver more susceptible to hypoxemia and hypotension in the operating room.

Anaesthetic agents may reduce hepatic blood flow by 30–50%, and agents such as isoflurane, desflurane, sevoflurane and propofol, which cause less perturbation in hepatic arterial blood flow than other inhaled anaesthetic agents, are preferred for patients with liver disease .[25]

Risk factors for acute intraoperative hypoxemia in patients with cirrhosis include ascites, hepatic hydrothorax, hepatopulmonary syndrome (the triad of liver disease, an increased alveolar-arterial gradient and intrapulmonary shunting), which is found in 5–32% of cirrhotic patients followed at transplant centers, and portopulmonary hypertension, which is found in up to 6% of patients with advanced liver disease and which increases postoperative mortality after noncardiac surgery. [26]

Postoperatively, patients with cirrhosis need to be monitored for the development of signs of hepatic decompensation, including encephalopathy, coagulopathy, ascites, worsening jaundice and renal dysfunction.

When any of these indicators is found, supportive therapy should be initiated immediately. The prothrombin time is the single best indicator of hepatic synthetic function. An elevated serum bilirubin can indicate worsening hepatic function but can be

elevated for other reasons, including blood transfusions, resorption of extravasated blood or infection. Renal function must be monitored closely.

Mortality rates as high as 25% are reported following hepatic resection (i.e., partial resection of the liver) in patients with cirrhosis.[27]

Risk stratification based on the Child class and MELD score have allowed more appropriate selection of patients, thus leading to lower mortality rates. In an analysis of 82 cirrhotic patients who underwent hepatic resection, the perioperative mortality rate was 29% in patients with a MELD score 9 but 0% in those with a MELD score 8. [28]

Another study identified Child class and ASA class, but not MELD score, as significant predictors of outcome following liver resection. In this study, the mean MELD score (6.5) was low, which likely limited the ability of the MELD score to discriminate between risk groups. [29]

In addition to predicting mortality, the MELD score can predict morbidity after liver resection. In one study, the frequency of post-liver resection liver failure was 0%, 3.6%, and 37.5% in patients with MELD scores of less than 9, 9–10, and greater than 10, respectively.[30]

The extent of hepatectomy is also a predictor of mortality, as is a low serum sodium concentration .[31]

Post-resectional liver failure has been defined as a prothrombin-time index of less than 50% (INR _1.7) and serum bilirubin greater than 50_mol/L (2.9 mg/dL), the so-called "50-50" criteria. When these criteria are met, the postoperative mortality rate is 59%, compared with 1.2% in patients not meeting these criteria.[32]

Moemen et al[33] have prospectively introduced a recently modified Child-Pugh scoring system by the addition of four parameters: serum sodium, serum creatinine, white blood corpuscles and arterial /alveolar oxygen tension ratio Pa/AO2. This new scoring proved to be a more accurate predictor of patient outcome.[34]

Haemostasis:

Assessment of the haemostatic process:

A number of laboratory tests are available to measure the functionality of the haemostatic system including tests for platelet function, screening tests for overall coagulation and single factor analyses.[35]

Prothrombin time (PT).

The PT of normal plasma is usually 12–15 secondes but each laboratory must determine its own reference range. It is known that PT varies with commercially available reagents (purified or recombinant tissue factor in a mixture of calcium and phospholipid), resulting in variable sensitivity to changes in the coagulation factors. To standardise the PT results the World Health Organization (WHO) has developed an international reference thromboplastin, and recommends that the PT ratio be expressed as the International Normalized Ratio or INR.[35]

Activated partial thromboplastin time (aPTT).

Mixing assays.

Mixing studies are used to evaluate a prolonged aPTT or, to distinguish between a factor deficiency and an inhibitor

Individual coagulation factor assays.

Specific functional assays have been developed for all the coagulation proteins. Assays of most of the coagulation factors are performed by mixing patients' plasma with plasma that lacks the factor in question, and then an aPTT or PT assay is performed. The formation of clots then depends on the activity of the factor in question from patient's plasma.[21]

Thrombin time.

This assay is normally used to detect defects in fibrin generation. A commercially available reagent containing thrombin is added to citrated plasma. The assay will be sensitive to presence of thrombin inhibitors (heparin), hypofibrinogenaemia or functional defects of fibrinogen.[22]

Activated clotting time.

Activated clotting time (ACT), originally described by Hattersley (1966) is a clotting assay that assesses the initial fibrin clot formation but uses whole blood instead of plasma, which is used in the PT and aPTT.

Platelet function tests

Platelets are activated at the site of injury to form a platelet plug and a procoagulant surface for localising the haemostatic response. Assays are available to measure platelet number, size, and function, including adhesion, aggregation and release. [36]

1. Platelet counts.

2. Bleeding time.

The BT is a measure of the interaction of platelets with the vessel wall and is performed by measuring the BT after a skin incision.

3. Platelet aggregometry.

Platelet aggregation can be measured using platelet-rich plasma (PRP) or whole blood using an aggregometer (modified spectrophotometer), by this technique, the ability of different agonists (e.g. collagen, ADP, epinephrine, ristocetin) to induce platelet aggregation at a range of concentrations is measured as a function of time.[37]

Whole blood assays.

Thrombelastography is a global assay in which the interaction of coagulation factors, platelets, fibrinolytic factors, inhibitors and other factors can be assessed by a viscoelastic

measurement of the fibrin polymerisation. The main uses of the TEG and recently ROTEM have been to monitor blood component therapy during surgery in particular in situations with massive blood loss as hepatic and cardiac surgery or trauma. [38]

Liver Resection in cirrhotic patients.

Indications for partial liver resections:

Liver resection is usually done to remove various types of liver tumors that are located in the resected portion of the liver. Partial liver resections are the treatment of choice for patients with a malignant liver or bile duct tumor. The most frequent colorectal metastasis, hepatocellular carcinoma (HCC) and cholangio-carcinoma.[39]

The body can cope with removal of up to two-thirds of the liver and up to 70%–80% of the normal liver can be resected with functional compensation occurring within weeks of an operation.[39]

The liver has the capacity to grow back within 3 month of the operation, the remainder of the liver will grow in size to near normal. Hepatic resection in non cirrhotic patients is associated with a perioperative mortality rate of 1–2%[40] and the mortality rate in cirrhotic patients is reported to be 8% perioperatively, the incidence of postoperative complications ranges from 20% to 50%.[41]

The guiding principal for hepatectomy in cirrhotic patients is that limited resection should be favored, with as much functional parenchyma spared as possible. In general, even for patients with well compensated Child grade A cirrhosis, resections are tried to be limited to less than two segments of functional liver. Patients with large tumors are more likely to tolerate major resections because little functional parenchyma must be removed along with the tumor. Major hepatic resections involving removal of at least one lobe are now reported to carry an operative mortality of less than 10% in cirrhotic patients.[42]

Estimating the risk of surgery:

The assessment of operative risk and postoperative outcome are markedly influenced by the severity and nature of the underlying liver disease and the type of surgery being considered.[43]

A- Nature of the underlying liver disease.

1-Obstructive jaundice:

The presence of underlying obstructive jaundice markedly increases perioperative mortality, and several studies have reported risk factors for increased mortality in patients with this condition. These risk factors include an initial hematocrit of above 30%, a serum total bilirubin concentration above 11 mg/dl, the presence of malignancy, a serum creatinine concentration higher than 1.4 mg/dl, serum albumin concentration lower than 3.0 g/dl, age older than 65 years, AST above 90 IU/l, and blood urea nitrogen concentration above 19 mg/dl.[44]

2- Acute hepatitis:

Patients with acute hepatitis have increased morbidity and mortality associated with surgery. These increases probably occur as a result of the acute hepatocellular injury and associated hepatic dysfunction. Elective surgery should be postponed until the patient's clinical, biochemical and histological parameters return to baseline. Similarly, overall morbidity and mortality are increased in patients with acute alcoholic hepatitis, and elective surgery is contraindicated in these patients.(39)

3-Chronic hepatitis:

Surgery is considered safe in asymptomatic patients with histological evidence of mildly active hepatitis, whereas symptomatic patients with histological evidence of severely active hepatitis have been shown to be at increased risk from surgery. The presence of underlying hepatic dysfunction increases preoperative risk. In patients with chronic hepatitis caused by either alcoholic or nonalcoholic steatohepatitis.(45)

B- Severity of the underlying liver disease.

The Child-Turcotte-Pugh (CTP) scoring system was the most frequently used tool to predict perioperative risk in cirrhosis patients undergoing abdominal surgery, exclusive of portosystemic shunt procedures. This scoring system assigned points based on levels of serum albumin and bilirubin, the INR, the degree of ascites, and the presence and grade of encephalopathy and stratified risk in order of severity as class A, B, or C. A number of studies have used this system to predict perioperative outcome in cirrhotic patients undergoing a variety of surgeries.(46)

Predicting perioperative risk of cirrhosis and other forms of acute and chronic liver disease further enhanced by the incorporation of the Model for End-stage Liver Disease (MELD) score.(47) The MELD assigns the patient a score of 8–40, which is derived from a complex formula that incorporates three biochemical variables—the serum total bilirubin concentration, serum creatinine concentration, and international normalized ratio. Although the MELD score was introduced as a tool to better prioritize organ allocation for orthotopic liver transplantation retrospective and prospective studies suggest the superiority of MELD to CTP in predicting both intermediate and long-term survival for patients with cirrhosis, acute alcoholic hepatitis and other forms of chronic liver disease.(48)

Possible complications include:

Bleeding During or after the operation which may require blood transfusions or a further operation, blood loss remains one of the main predictors of both perioperative morbidity and mortality after liver resection.(49)

More recent studies with larger numbers of both transfused and non-transfused patients have been able to confirm the detrimental effects of transfusion on the development of postoperative complications and perioperative death after liver resections(50) as several studies have suggested that blood transfusions suppress host immunity via reduction in natural killer cell function, decreased cytotoxic T-cell function, increased numbers of suppressor T cells and decreased function of macrophages and monocytes.(51)

Table 1: **Child Turcotte Pugh Classification. Class A=0 : 1; Class B=2: 4; class C ≥5**[52]

Feature	0	1	2
Albumin	> 3.5 gr/dL (35 g/L)	2.8:3.5 g / dL (28 to 35 g / L)	<2.8 g / dL (28 g / L)
Bilirubin	<2 mg/dL (34 µmol/L)	2 : 3 mg / dL (34 to 51 µmol / L)	>3 mg / dL
Prolongation of prothrombin time	<4 seconds	4 to 6 seconds	>6 seconds
Ascites	None	Controlled	Refractory
Encephalopathy	None	Controlled	Refractory

Evolution of surgical and anaesthetic techniques, better understanding of the segmental liver anatomy, new methods to control haemorrhage, and better patient selection have led to improvement in outcome. Nowadays, liver resections are performed in specialized centers with a perioperative mortality rate of less than 5%; even though the indications for liver resections have been extended, also to high-risk patients.[53]

Bile leak (1 in 10-15 patients) after operation, bile may leak from the cut surface of the liver. The presence of bile and blood in the peritoneal cavity may impair the normal host defense mechanisms and predispose to the development of sepsis, liver failure, and mortality.[54]

Jaundice is due to excess bile that the remaining liver unable to cope with. It is often associated with accumulation of excess fluid in the abdomen and legs. This problem is temporary, until the liver grows and recovers normal function. The risk of developing jaundice depends on the amount of liver that is left behind, and how well it functions.[55]

Chest infection and possibly needing support on a ventilator in the intensive care unit, **wound infection** and **deep venous thrombosis** in the legs.[56]

Anaesthetic considerations:

The preoperative assessment.

Routine preoperative laboratories, which include a complete blood count, serum chemistry, and plasma coagulation studies. The site and volume of planned resection must be carefully assessed in the preoperative period preexisting liver disease warrants careful assessment of coagulation status, pulmonary and renal function, and cardiac status. This may include obtaining a room air arterial blood gas sample and an echocardiogram in addition to the routine preoperative tests. The site and volume of planned resection must be carefully assessed in the preoperative period, this, in addition to the patient's comorbidities.[56]

Patients with significant co-morbidities scheduled for major liver resections need exercise or pharmacologic stress echocardiography for preoperative assessment of the cardiac status. When limitations in cardiac function or reserve are found, adjustments in surgical approach and anaesthetic management can be planned before surgery. Room air-oxygen saturation measured using pulse oximetry may give early indication of impaired pulmonary gas exchange or inadequate ventilatory reserve.(57)

Approximately one third of patients with cirrhosis or non cirrhotic portal hypertension present with varying degrees of hepatopulmonary syndrome. The mild hypoxemia in these patients is due to ventilation/perfusion mismatching, characterized by an increase in pulmonary perfusion secondary to capillary distension, impaired hypoxic pulmonary vasoconstriction, and accelerated transpulmonary blood flow with unchanged alveolar ventilation. Increasing cardiac output with the progression of cirrhosis worsens the diffusion impairment and hypoxia.(58)

Intraoperative management:

Induction and monitoring:

Liver resections are performed under general anaesthesia with endotracheal intubation and controlled ventilation. Isoflurane is the most commonly used agent to maintain anaesthesia. Sevoflurane reduces the increase in postoperative liver enzyme levels, in an air-oxygen mixture, supplemented with an intravenous narcotic. As for neuromuscular blocking agents, the traditional recommendation is to use those that do not depend on hepatic metabolism. Intraoperative monitoring is adapted to the preoperative condition of the patient, the extent of the liver resection, and the anticipated amount of blood loss. For healthy patients with expected blood loss below 1000 ml one can use routine monitoring only: ECG, pulse oximetry, noninvasive blood pressure and capnometry. An arterial catheter is useful in providing beat-to-beat blood pressure monitoring and allows for easy blood sampling and central venous catheter is installed. Pulmonary artery catheterization is reserved for patients with known preoperative left-ventricular dysfunction, anticipated prolonged major vascular exclusion (e.g., vena cava resection and reconstruction), or preoperative sepsis. Point-of-care blood gas, chemistry, and coagulation analysis can be used to detect and correct intraoperative anemia, acid-base, electrolyte, and coagulation disturbances.(58)

Two large caliber venous accesses are preferable because of high and unpredictable blood loss. Prophylactic antibiotic treatment is indicated due to the length of the operation. Forced warm-air devices are applied to the upper and lower parts of the body to maintain euthermia as resections is associated with significant heat losses. Hypothermia inhibits the enzymes of the coagulation cascade and contributes to intraoperative blood loss.(58)

Fluid management:

The use of colloid rather than crystalloid as maintenance fluid reduces extravascular translocation of fluids, which results in less bowel edema, improved mesenteric perfusion, and more rapid restoration of postoperative gut function. Fresh-frozen plasma is used in patients who are coagulopathic and require correction of their coagulopathy.

Keeping the central venous pressure (CVP) low, <5 mmHg, limits the distention of hepatic veins and sinusoids and was shown repeatedly to reduce blood loss during liver surgery.[59] This approach necessitates restricts fluid administration during induction of anaesthesia and hepatic resection to a minimum. Intravenous nitroglycerine is used to reduce the CVP to the target range if fluid restriction alone is ineffective.[60] Once the resection is completed and haemostasis is achieved, euvolemia is restored by fluid expansion, using crystalloid or colloid. The low-CVP approach exposes the patient to the risks of intraoperative hypovolemia, with potentially inadequate organ perfusion, and insufficient volume reserves if a sudden unexpected intraoperative haemorrhage occur. The incidence of perioperative renal failure has not been found to increase significantly when compared with historical controls.[61]

Maintaining haemodynamic stability and adequate urine output (>0.5 mL/kg/hr), augmentation of renal function with an infusion of furosemide, dopamine or mannitol is decided on an individual basis and is not used routinely. The anaesthesiologist should be ready to provide rapid, warm resuscitation. Hypovolemia in the event of an air embolism, can be life threatening. Infusion of fluid should be restricted until after the parenchymal resection.[62]

Blood transfusion and conservation.

Major liver resections may result in significant blood loss, necessitating transfusion of red blood cells in about 25% to 30% of patients[63] For example; healthy donors undergoing right hepatectomies are expected to lose about 600 mL to 900 mL of blood on average.[64]

The presence of a preoperative coagulopathy, malignancy, and the extent of resection were the predictors consistently found to correlate with the need for intraoperative blood transfusion. Transfusion requirements for liver resections are quite unpredictable; however, when blood transfusion is required, the mean volume of packed red blood cells is relatively high.[65]

Strategies to reduce intra-operative bleeding:

- Low CVP.
- Aprotinin.

Significant reductions in blood transfusion requirements have been shown in liver resection using aprotinin. Although serious safety concerns have been raised about the incidence of life threatening allergic reactions, thrombotic potential and renal failure. Lentschener et al[66] cautioned against the routine use of aprotinin in liver transplantation although a recent Cochrane review did not confirm this, the license for aprotonin has effectively been withdrawn because of a 1.5 times increase in mortality compared with tranexamic acid and aminocaproic acid and an inability to identify specific patients who might benefit from the drug .[67]

- Tranexamic acid.

Blood requirements have been shown to be reduced by tranexamic acid in liver transplant and liver resection.[64] Safety concerns have not been proved.[67]

Postoperative care

Most patients can be extubated at the end of surgery and are nursed in a critical care ward. Approximately 20% of otherwise healthy patients may experience postoperative complications after elective liver resections. Although low residual liver volume was found to be associated with postoperative liver failure, the regenerative ability of the liver is remarkable, and the residual healthy liver is expected to double in size within the first week following the resection. A hyperdynamic state with increased cardiac index and augmented splanchnic blood flow persists for at least 3 days postoperatively.[68] This increased blood supply to the residual liver parenchyma ensures rapid growth. Increase in hepatic parenchymal mass does not necessarily result in full restoration of functional ability. Pre-existing cirrhosis or positive virus carrier status limits liver regeneration, and these patients are more susceptible to developing postoperative hepatic failure. The ability of the liver to regenerate is reduced in diabetic patients, who have an increased incidence of postoperative hepatic failure following major resections. [67]

Postoperative pain following liver surgery is significant, and adequate analgesia remains a challenge. Neuraxial anaesthesia has limitations in liver surgery. Many patients presenting for hepatic surgery have a coagulopathy or thrombocytopenia that makes them ineligible for an epidural and the postoperative prolongation in prothrombin time delayed catheter removal in 9% of patients who had three or more segments resected. Opioid i.v. patient-controlled analgesia systems and single-shot neuraxial opioids are alternatives to continuous epidural analgesia.[58]

Glutathione –S- Transferase

Most clinical studies in the field of hepatology, including the monitoring of response in therapeutic trials, employ serum ALT (alanine aminotransferase) as a marker of hepatocellular damage. However, in some infections, such as chronic hepatitis C virus (HCV) infection, serum ALT has been shown not to be a satisfactory marker of histological disease activity.

Recently, GST has been proposed as an alternative marker of hepatocellular damage induced by several drugs.[69]

In general, the size of the serum aminotransferase increase reflects the relative extent of active hepatocellular damage, but not necessarily its aggregate severity.

However, even when combined with markers of hepatic synthetic function, such as serum albumin and prothrombine time, ALT and AST are relatively poor indicators of centrilobular hepatocellular injury because of their uneven distribution.[70]

ALT and AST are distributed mainly within the periportal area and substantial centrilobular necrosis can occur without a concomitant increase in serum aminotransferases.

Limitations for using aminotransferases as markers for hepatocellular injury include their comparatively long plasma half-lives(17 h for AST; 47 h for ALT). Thus, during acute liver damage, abnormalities in serum aminotransferase concentrations often lag behind changes in hepatocellular integrity.[70]

Cytosolic glutathione S-transferases (GSTs) are enzymes that catalyze the nucleophilic addition of glutathione to the electrophilic centers of a wide variety of chemical structures. In addition, GSTs exert part of the glutathione peroxides activity and have an important function in intracellular binding and transport of a wide variety of both endogenous and exogenous compounds.[71;72]

The family of human enzymes is divided into four main classes: a, m, p, and u, each subdivided into one or more isoenzymes.[73]

Glutathione S-transferase a (GST-a) is found at high concentrations in the human liver and is released quickly and in large quantities into the blood stream during hepatocellular damage.[74] Because the half-life of GST-a in plasma is 1 h,[75] its concentration will follow changes in hepatocellular damage more rapidly than aspartate aminotransferase (AST) or alanine aminotransferase (ALT), which have plasma half-lives of; 17 and 47 h, respectively.[74]

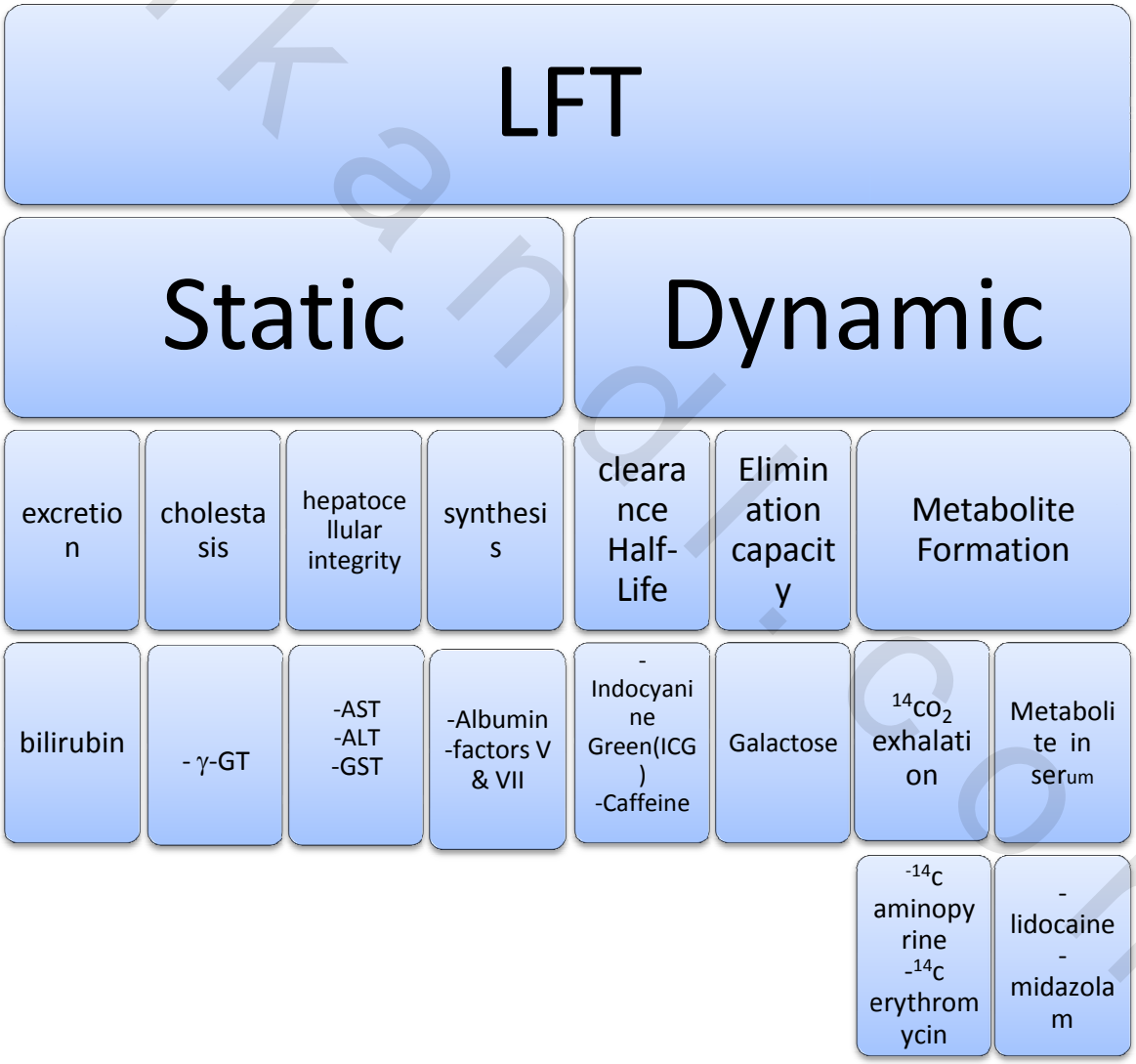

Figure (2): Liver function tests.[69]

The introduction of a commercial ELISA kit [Hepkit; Biotrin International.][76] has facilitated the clinical application of GST-a as a marker for hepatocellular damage. Recent studies demonstrated that the measurement of serum or plasma GST-a may improve the monitoring of hepatocellular integrity in patients with hepatitis C, in anaesthetized patients, in liver transplant recipients, and in women with severe preeclampsia.[77;78]

Glutathione S-transferase is a sensitive and specific biomarker of cell permeability and forms an important high-content parameter in the cluster analysis of toxic responses. Higher GST levels seem to reflect more complex damage.[79]

GST is a potential noninvasive marker of hepatocyte and biliary epithelial cell injury. GST can reveal hepatic effects not detected by alternative testing. The high sensitivity and specificity of GST indicates that unchanging levels almost exclude acute hepatic effects.[80]

GST is one of the key enzymes that keeps the cellular membrane intact. GST which is also known as NonSe-GPx is a part of an antioxidant enzymatic system and plays a role in detoxification of lipid hydroxyl, peroxides.[81] GST is localized in the centrilobular hepatocytes therefore, it is much more specific than both ALT and AST for hepatic damage.[82]

GST is known to be a more important marker for hepatotoxicity associated with volatile anaesthetic agents. In a study of Schmidt et al.[83] an elevation in GST was observed where ALT, AST and GGT levels did not change.

Advantages of using GST in the detection of hepatocellular injury include its low molecular weight (51 kDa), high cytosolic concentration (4%–5% of all hepatocellular protein) and brief half-life in circulation (< 90 min). Since GST is rapidly released into circulation after hepatocellular injury, it can be used as a rapid indicator of changes in hepatocellular integrity.[74] The time course of the changes in GST concentrations implies a minor derangement of hepatocellular integrity that is most likely explained by inadequate hepatocyte oxygenation, rather than an immune response to metabolite-modified hepatic proteins.[74]

Desflurane.

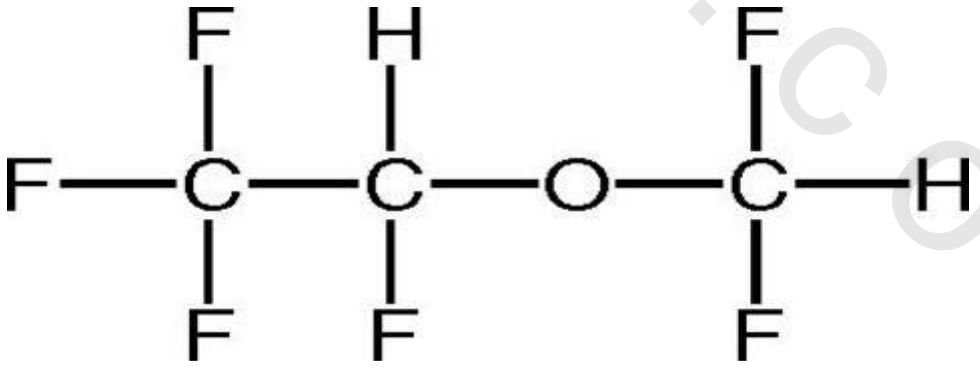

Figure 3: Chemical formula of Desflurane.[87]

In general, volatile anaesthetics have been predominantly used during hepatobiliary surgeries including living donor keratectomy. [84]

Typically, volatile anaesthetics are reported to decrease total hepatic blood supply primarily because of decreased cardiac output and impose various compromising effects on the hepatic oxygen supply.[25]

Volatile agents are frequently used in general anaesthesia practice without complications. However, they continue to have adverse affects on various body systems. Although most of these effects are minimal and reversible, fatal complications such as fulminant hepatitis may occasionally occur most frequently caused by halothane.

Desflurane has been reported to be more innocent than other agents. Nevertheless, there are few reported cases of hepatitis in the literature.[85;86]

The main difference with new inhalational anaesthetics is their resistance against in vivo metabolism.

Volatile agents are known to have an adverse effect on the hepatic antioxidant defense mechanism as well as accelerating peroxidation.[88]

As a result, volatile agents are assumed to cause some structural changes in hepatic tissues.[89]

These changes in hepatic tissues cause the release of many enzymes into circulation. Although it has not been definitively shown to be the case, determination of glutathione S-transferase (GST) levels seems to be a more specific indicator of liver injury.[83]

An increase in GST concentrations may be detected before changes occur in routine liver function tests (aminotransferase activity, bilirubin concentrations).

Subclinical hepatic injury after anaesthesia remains an interesting subject, particularly with the development of new, more sensitive methods of measuring GST levels.

Following hepatic injury, GST quickly enters circulation. Its brief half-life provides early detection of both hepatic injury and recovery.

Minor changes in hepatocellular integrity after halothane, enflurane, sevoflurane and desflurane anaesthesia have been reported by several researchers.[87]

Table 2:physical characteristics of Desflurane.[87]

Some physical constants are:	
Molecular weight	168.04
Specific gravity (at 20°C/4°C)	1.465
Vapor pressure in mm Hg	669 mm Hg @ 20°C
	731 mm Hg @ 22°C
	757 mm Hg @ 22.8°C
	(boiling point; 1atm)
	764 mm Hg @ 23°C
	798 mm Hg @ 24°C
	869 mm Hg @ 26°C
Partition coefficients at 37°C:	
Blood/Gas	0.424
Olive Oil/Gas	18.7
Brain/Gas	0.54
Mean Component/Gas Partition Coefficients:	
Polypropylene (Y piece)	6.7
Polyethylene (circuit tube)	16.2
Latex rubber (bag)	19.3
Latex rubber (bellows)	10.4
Polyvinylchloride (endotracheal tube)	34.7

The administration of desflurane, has been associated with a mild, but statistically significant, increase in GST concentrations.[90]

Hepatic blood flow reduction is thought to be responsible for the increase in GST concentration after anaesthesia.[91]

However, desflurane has been shown to better preserve total hepatic blood flow than halothane or isoflurane in an animal study and appears to have no greater toxicity than currently used inhaled anaesthetics.[92]

In addition, all volatile anaesthetics undergo biotransformation in which their metabolized products are eliminated exclusively by the kidneys.[93]

Desflurane is unique among the class volatile anaesthetics in that it is highly stable and undergoes very little degradation, yielding minimal excretion of organic or inorganic fluoride.[94]

It has been found to be safe in patients with renal failure, and normal renal function is maintained even after prolonged exposure to desflurane.[89]

Furthermore, desflurane has been reported to maintain renal blood flow.[95]

Desflurane is almost neutral to biological degradation with a 0.02% calculated metabolism ratio.[95]

Prolonged administration of volatile anaesthetics may be a risk for hepatic damage, which often remains undetected by standard liver function tests such as aminotransferase activity due to their lack of specificity and sensitivity.[90]

It has been reported that with hepatocellular injury, there is a rapid release of GST, and this could be used as an indicator of changes in hepatocellular integrity.[96]

Compared to other fluorinated agents, desflurane is less soluble in plasma and in tissues. Thus, it has almost absolutely no risk of hepatotoxicity. It may preserve the majority of vital tissues, but human studies are required to identify if it is in any way different from other anaesthetic agents in tissue protection.[97]

Hepatotoxicity with desflurane is theoretically possible because of cross-sensitivity with other inhalation anaesthetics. Nevertheless, since levels of serum trifluoroacetate (TFA), which is a potentially hepatotoxic metabolite, for desflurane is 1,000 times less than those of halothane, this seems a very unlikely possibility.[95]

This feature could be explained by great variability in oxidative biodegradation of these anaesthetics. The level of metabolism is directly related to hepatic injury potential.

Desflurane is resistant to biotransformation. Yet, if a patient is sensitised to trifluoroacetated proteins, minor amounts of conversion to immunogenic metabolites may produce massive hepatotoxicity. The patient may be sensitised to previously used anaesthetics and repeated exposure to desflurane may have produced hepatotoxicity. The basic relationship between exposure and injury is similar to that reported with halothane anaesthesia.[97]

Some degree of disruption in hepatocellular integrity is reported after general anaesthesia with all modern inhalation anaesthetics.[98]

GST levels are used to determine hepatocellular injury, which is more sensitive than the determination of conventional liver enzymes.

The new inhaled anaesthetics, desflurane and sevoflurane, have a lower solubility in blood tissues than all previous volatile anaesthetics.[87]

Impairment of hepatocellular integrity occurs after the administration of general anaesthesia with all modern inhaled anaesthetics .[97]

Several mechanisms have been proposed to account for the hepatotoxic effects of inhaled anaesthetics. One reason seems to be the oxidative biotransformation of inhaled anaesthetics with the formation of toxic metabolites.[99]

Fulminant necrosis and jaundice termed"halothanehepatitis," a very rare but often fatal event, might follow halothane anaesthesia administration.

Highly active oxidative intermediates of halothane metabolism, such as trifluoroacetyl chloride with trifluoroaceticacid(TFA) as an end product, have been identified as promoting this type of liver damage as part of an immune response in susceptible individuals.(99)

The new inhaled anaesthetics differ greatly in their resistance to *in vivo* metabolism. However, small but significant levels of TFA were found after exposure to desflurane.(95)

The metabolism of sevoflurane is approximately 100 times greater (3%–5%), but happens by different mechanisms and will therefore not form TFA.

Hepatotoxicity, ranging from mild, self-limiting disturbances to massive, life-threatening hepatocellular necrosis and jaundice has been associated with the use of inhalational anaesthetics.(98)

The potential of volatile agents to cause hepatic dysfunction is a consequence of their metabolism and even desflurane, with its low solubility in blood and tissues and low hepatic biotransformation, possesses hepatotoxic potential.(87;100) Because of its attractive pharmacokinetic profile, propofol has become a popular drug for induction and maintenance of anaesthesia especially for outpatient surgery. However, propofol still continues to arouse interest as previous studies have yielded conflicting results with respect to its influence on hepatic function and integrity. (100)

Standard enzyme markers, such as alanine and aspartate aminotransferase activity, are limited in their ability to detect minor degrees of anaesthetic-related liver dysfunction.(101;102)

In contrast, plasma alpha glutathione S-transferase (GST) determination is a sensitive and highly specific test for hepatocellular damage and correlates better with drug-induced liver injury.(103)

As it is located predominantly in centrilobular hepatocytes as opposed to the periportal location of the transaminases, GST values allow early detection as well as follow-up of hepatic injury.

Its short plasma half-life allows a quick return to normal when the active phase of hepatic damage is over.(104)

Prolonged administration of volatile anaesthetics may be a risk factor for hepatic damage, which often remains undetected by standard liver function tests such as aminotransferase activity, due to their lack of specificity and sensitivity.(104)

Plasma GST, in contrast, is a highly specific indicator of drug-induced hepatocellular injury that may be particularly relevant since halothane-induced hepatitis is associated with centrilobular necrosis.(104;105)

Reduction of hepatic blood flow with subsequent decreased oxygen availability is believed to be a major cause of the temporary increase in GST concentrations during and after inhalational anaesthesia .[105]

GST is readily and rapidly released from hepatic cytosol into blood in the active phase of anaesthetic-induced liver impairment .[106]

During hypotensive anaesthesia, Piper and colleagues[105] observed a significant increase of GST at the end of surgery, secondary to a direct effect of hypotension and reduced hepatic blood flow, that returned to baseline after 2 h.

Another investigation during spinal anaesthesia showed that the decrease in systemic arterial pressure led to elevated GSTconcentration, whereas the early correction or absence of hypotension preserved hepatic blood flow, and GST values remained unchanged .[91]

According to the data from animals and humans studies, most of the currently available volatile anaesthetics have been shown to preserve hepatic blood flow and function.[8]

Alternatively, total intravenous anaesthesia (TIVA), with the availability of intravenous drugs with more rapid onset and shorter recovery profiles, is now well established in the domain of anaesthesia.

Among these intravenous drugs, propofol is the most commonly used intravenous anaesthetic agent, and it is commonly co administered with an opioid such as fentanyl.[107]

Many known benefits of TIVA include reduced postoperative pain, less postoperative nausea and vomiting, and, most interestingly, less risk of organ toxicity such as hepatic and renal toxicities implicated to arise from volatile agents.[90] However, the impact of TIVA on postoperative liver and renal functions after large liver resections has been less extensively investigated than that of volatile agents.

The liver resection involves the risk of major haemorrhage during the parenchyma resection and the vascular dissection of portal and hepatic veins. These life-threatening intraoperative haemorrhages and subsequent transfusions are often considered major factors of postoperative morbidity and mortality.[108;109]

Therefore, numerous surgical and anaesthetic strategies, such as maintenance of intraoperative low CVP and pharmacological interventions, have been devised to reduce blood loss.[94]

The maintenance of low CVP has been advocated during hepatectomy because elevated CVP is considered one of the major determinants of bleeding from liver parenchyma, and excessive fluid administration can decrease hepatic blood flow and oxygenation and induce graft edema secondary to extravasations of fluid.

The maintenance of low CVP during parenchyma dissection reduces the vena caval distention, aids in mobilization of the liver and dissection of major hepatic vessels, and, most importantly, minimizes hepatic venous bleeding. A number of clinicians have performed restriction of intravenous fluid to maintain low CVP values during extrahepatic

dissection and parenchyma transection and then replacement of the cumulative fluid deficit after the transection for right hepatectomy in living donors.[109]

Target Controlled Infusion

Target controlled infusion (TCI) systems are designed to facilitate the delivery of intravenous anaesthetics. The anaesthetist sets the desired target blood or effect site concentration and the TCI pump adjusts the rate of delivery of the anaesthetic agent according to a pharmacokinetic / pharmacodynamic (PK / PD) model. Different PK / PD models predict different rates of drug transfer and effect site equilibration.

The Diprifusor manufactured by AstraZeneca (Macclesfield, UK) was the first available propofol TCI pump which was based on 'the Marsh PK/PD model'.[110]

More recently, a different PK / PD model, 'The Schnider model', has been introduced into clinical practice.[111]

During induction of anaesthesia, the Schnider model predicts faster propofol effect site equilibration than the Marsh model.

Due to the time period required for the effect site to equilibrate with the central compartment, the effect site concentration correlates better than blood concentration with the clinical effect during induction and recovery.[112;113]

The Diprifusor, the first available propofol TCI pump, uses the Marsh PK/PD model set to the blood target control. The more recently introduced Schnider Model, on the other hand, can be used with either a blood or an effect site target control, although in practice blood control TCI using Schnider has not been documented.

This model is also adjusted for weight, sex, age and lean body mass. Effect site control should deliver faster onset and better titration of anaesthesia, making it a theoretically attractive option for total intravenous anaesthesia (TIVA).

Target-controlled infusion (TCI) devices offer a means for producing relatively stable, controllable plasma concentrations of drugs administered intravenously.[114]

Drug administration by IV boluses produce rapid fluctuations in plasma drug concentrations, whereas a constant rate infusion produces plasma concentrations that slowly rise to reach a stable concentration only after 5−7 drug elimination half-lives (in the usual clinical situation, 3−4 elimination half-lives are the accepted standard).[115]

TCI was introduced for research purposes years ago, with computer- driven infusion pumps using two- or three-compartment pharmacokinetic (pk) models.[116]

A commercial target-controlled infusion system for propofol is now available ('Diprifusor' TCI, Zeneca Pharmaceuticals, Macclesfield, UK) in China .

TCI devices allow the anaesthetist to provide anaesthesia by controlling the theoretical (predicted) concentration of the drug in the central compartment.

Rapid changes in the depth of anaesthesia are therefore possible with similar ease to that achieved with inhalational anaesthesia. But unlike inhalational anaesthesia, where the

end-tidal concentration of vapors can be monitored, on-line blood concentration monitoring is not practical at the present time. The accuracy (predicted vs. measured blood concentration) is not only dependent on the pk parameters, but also on the variability of the pk parameters within the population.

Pharmacokinetic parameters incorporated into 'Diprifusor' TCI systems were proposed by Gepts et al.[116] and may be different from Chinese patients.

By using target-controlled infusion (TCI) techniques, stable effect-site concentrations can be obtained rapidly (depending on the drug onset) and maintained for as long as desired, since these devices deliver IV drugs using a computer-controlled algorithm considering each drug's particular pharmacokinetic and pharmacodynamic properties.[117]

After 15 yr of prototypes and clinical research, the first commercial TCI device (DiprifusorTM) was released in 1996. It has been widely used in the last decade to deliver propofol and markedly improved predictability and titration of propofol during maintenance of anaesthesia while decreasing workload.[118;119]

Recently, a second generation of TCI devices was released, allowing delivery of opioids in TCI mode.[119]

As for propofol, it was expected to improve dose titration, especially when the therapeutic margin is small, like when maintaining spontaneous ventilation during a noxious stimulation.

The Navigator™ Applications Suite software from General electric (GE) enables clinicians to manage anaesthesia in balanced way with pharmacokinetic/ pharmacodynamic modeling and prediction. Hospital specific care protocols, GE's device diagnostics and monitored patient data provide further guidance and assistance to tailor anaesthesia to the patient specific needs.

Navigator Therapy:

- Visualizes pharmacokinetic (PK) and pharmacodynamic (PD) models of select sedation, analgesic and relaxation drugs.
- Displays the modeled synergistic effect of inhaled anaesthetic drugs with four opioids.
- Displays the modeled synergistic effect of propofol with four opioids.
- Projects the future modeled effect site concentrations based on pharmacokinetic models, and the future synergistic effect based on pharmacodynamic models.
- Connects to a range of infusion pumps to minimize manual drug data entry.
- Displays comprehensive trend information on administered drugs.

Navigator Protocol:

- Configurable to give you immediate access to the specific standard operating procedures of your hospital at the point of care.
- Configurable to include emergency treatment protocols, such as resuscitation algorithms, airway management protocols or any other clinically relevant information.

- Index search function to locate the information required.
- Configurable to display measured haemodynamic and ventilation parameters while viewing care protocols navigator device.
- Clear and specific guidance with visual step-by-step instructions on how to resolve a technical alarm with the anaesthesia delivery system.
- Technical instructions quickly available at the point of care.

Propofol.

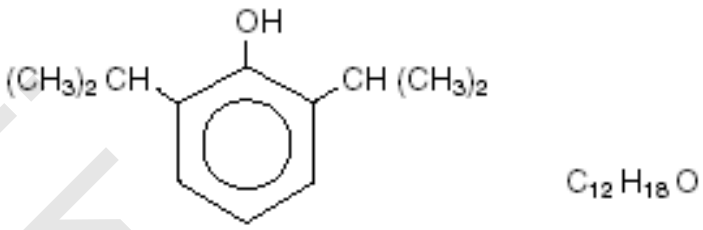

Figure 4: Chemical formula of propofol.

- Diisopropylphenol, a short acting intravenous general anaesthetic that rapidly and smoothly produces sedation and hypnosis within 40 seconds from start of injection.
- Rapidly absorbed and extensively distributed, highly lipophilic,
- Crosses blood brain barrier, highly protein binding 95-99%,
- Conjugated in liver to inactive metabolites and excreted in the kidney as metabolites (50% of the dose).
- Used for induction and maintenance of anaesthesia with a dose of 2-2.5mg/kg and 200mcg/kg/min maintenance.

Fentanyl

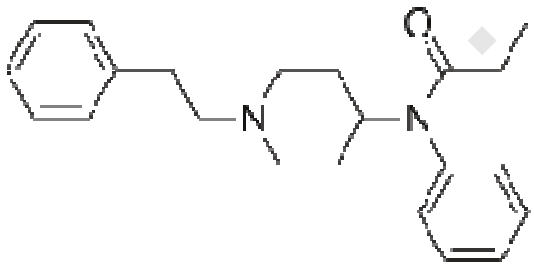

Figure 5: Chemical formula of Fentanyl.

- N phenyl ethyl piperidinyl N phenylpropanamide.
- Also known as Sublimaze , a potent synthetic narcotic analgesic with a rapid onset and short duration of action .
- A strong agonist at the mu –opioid receptors.
- Approximately 100 times more potent than morphine due to its high lipopholicity.

- Mainly used for induction of anaesthesia to produce procedural sedation and as an analgesic.
- Considered the safest opioid medication on the market.
- Dose: 1-4 mcg/kg/dose, infusion 1-5mcg/kg/hr.
- Side effects include respiratory depression, bradycardia, hypotension, urine retention and tolerance.

Haemodynamic monitoring

The most important aspect in monitoring the critically ill patient is the detection of life-threatening derangements of vital functions. Aggressive strategies have been promoted to monitor almost every aspect of the patient's status.(120)

A physical examination remains the cornerstone of assessing patients with haemodynamic compromise, even though signs and symptoms often poorly predict measured haemodynamic variables. Clinical signs and symptoms help to clearly define the clinical problem and its differential diagnosis. As an adjunct, some type of haemodynamic monitoring is often decided upon, depending on the clinical severity of disease and the presentation of the patient, among other factors.(121)

Haemodynamic monitoring can be invasive or non invasive, and continuous or intermittent. Monitoring devices can measure physiologic variables directly, or derived through signal processing.(121)

Techniques of haemodynamic monitoring:

1-Heart rate monitoring:-

The simplest and the least invasive form of cardiac monitoring remains the measurement of heart rate. electronic monitoring devices are used to provide a continuous display of heart rate.(122)

2-Pulse Rate Monitoring

The pulse oximeter plethysmograph trace is the most common source for measurement of the pulse rate. In addition to indicating the pulse rate, this waveform may also provide supplementary diagnostic clues to cardiovascular function.(123)

3-Blood pressure monitoring:-

Mean arterial pressure best approximates the organ perfusion pressure in non cardiac tissues, as long as venous or surrounding pressures are not elevated, can be measured non invasive or invasive.

Because blood pressure is a regulated variable, a normal blood pressure does not necessarily reflect haemodynamic stability.(123)

4-Cardiac Filling Pressure Monitoring:-

Cardiac filling pressures are monitored to estimate cardiac filling volumes, which determine the stroke outputs of the left and right ventricles. According to Frank-Starling principle, the force of cardiac contraction is directly proportional to end-diastolic muscle fiber length at any given level of intrinsic contractility. This muscle fiber length or preload is proportional to end-diastolic chamber volume. Which includes central venous pressure (CVP), pulmonary artery pressure (PAP) and left atrial pressure (LAP) monitoring.(124)

5- The Cardiac Output Monitoring.

There have been several monitors developed that allow the clinician to monitor cardiac output (CO) and the response to fluid therapy. When these monitors are used in conjunction with the administration of fluids and vasopressors to specific therapeutic end points, patient care and outcome may be improved. These interventions termed "goal-directed therapy" have been used widely both in the operating room (OR) and the intensive care unit (ICU). CO methods should be reliable, noninvasive, continuous and compatible in adult and pediatrics.(124)

Transoesophageal Doppler ultrasound

Oesophageal probes were recognized to have two significant advantages over suprasternal probes. The first was that the smooth muscle tone of the oesophagus is a natural means of maintaining the probe in position for repeated measures and the second was that the oesophagus is in close anatomical proximity to the aorta so that signal interference from bone, soft tissue, and lung is minimized.(125)

A modification of the technique (Pulsed Wave Doppler Ultrasound) requires only one crystal emitting pulses of sound that can be gated to blood flow at targeted distances from the probe. The same crystal detects the reflected Doppler frequency shifts. This provides greater spatial resolution but is more cumbersome.(126)

Available models:

There are currently two versions of the TED the CardioQ™ (Deltex Medical, Chichester, UK) and the Hemosonic™ (Arrow International, USA)was developed by Boulnois and tested by Cariou et al).(127) Both have a probe which attaches to a portable monitor, allowing a display of menus, waveforms and derived parameters. Whilst both models have similar monitors, there are differences between the probes. Additionally, there are slightly different names for similar measurements. For example, the CardioQ™ will display the corrected flow time (FTc) whilst the Hemosonic™ equivalent is the LVETc (corrected left ventricular ejection time).(128;129)

The CardioQ™

The disposable CardioQ probe is 6 mm in diameter. Notches on the probe are placed at 35 and 40 cm from the tip to aid the correct insertion depth. The probe has an internal spring coil to provide an optimum balance between the flexibility and rigidity needed to position the probe. At the tip of the probe the Doppler transducer is angled at 45° and provides a continuous ultrasound frequency of 4 MHz there is nomogram to translate

descending thoracic aortic blood flow velocity into an estimate of total left ventricular stroke volume. The nomogram uses the patient's age, height, and weight to generate a calibration factor and does not rely on any other measurement.[130]

Probe placement

Insertion of the oesophageal probe can easily be performed within a few minutes via the oral or nasal route similar to the placement of a gastric tube. Literature suggests that training in not more than 12 patients is needed to achieve adequate probe positioning and reliable CO measurements can be inserted in conscious and anaesthetized patients.[131]

Correct position

With the Deltex CardioQ™ monitor, a green line will outline the velocity-time envelope of the Doppler waveform. White arrows appear at the beginning, peak and end of the envelope to show the points used to measure the time and velocity values. By viewing the waveforms present on the monitor it is possible to see whether the probe is inserted too far (e.g. a trace typical of the celiac artery is seen, or not far enough (e.g. a pulmonary or azygous trace will be seen, even when the probe is inserted to the correct depth, if it is not rotated in the right direction, the signal recorded could be intracardiac.[132]

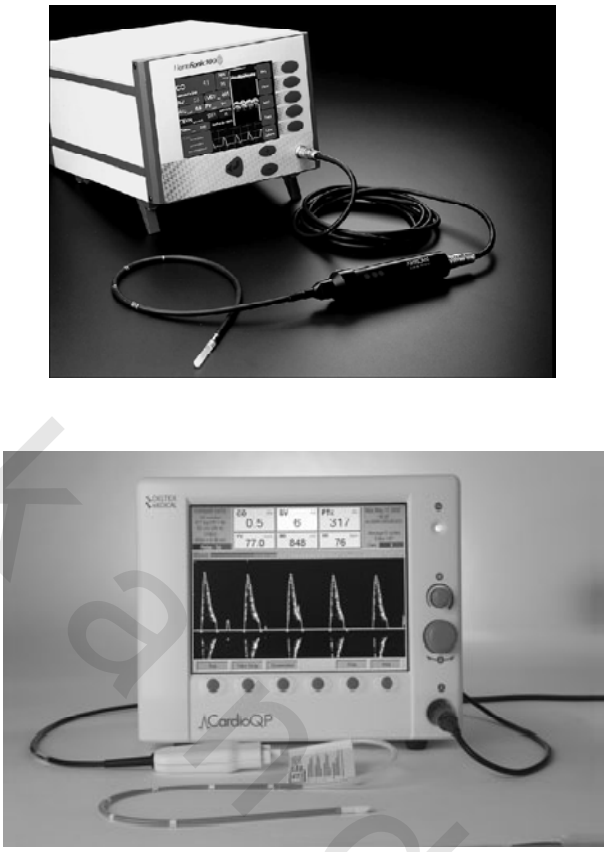

Figure 6: CardioQP monitor with digital values and the Doppler flow velocity curves. The Oesophageal Doppler probe is in front in left side and hemosonic on right side[132]

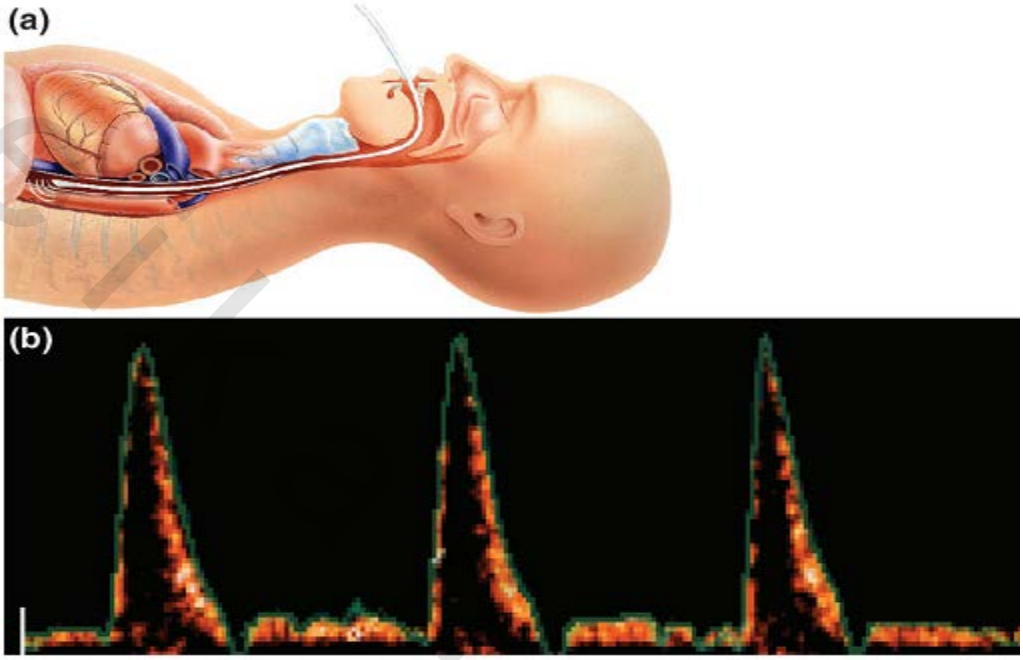

Figure 7: (a) the relation between esophagus and descending thoracic aorta. (b) Characteristic velocity waveform obtained in the descending aorta.[132]