



Post Hepatectomy Liver Failure in Nutshell



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Abstract

Hepatic resections are the most complex operative interventions that we do today with a mortality rate as high as 30%. Post-Hepatectomy Liver Failure (PHLF) is a major source of morbidity and mortality after hepatectomies with an incidence of up to 10% of cases. Lower rate of PHLF are reported in East Asian countries (1-2%), but when present, PHLF leads to significant morbidity and mortality.

Keywords: Post hepatectomy liver failure; 50-50 criterion; Hepatic resection

Introduction

Defining what is PHLF and criteria to diagnose it were equally difficult as treating a PHLF. The International Study Group of Liver Surgery: considering the normal postoperative course of serum bilirubin concentration and International Normalized Ratio defined PHLF as the impaired ability of the liver to maintain its synthetic, excretory, and detoxifying functions, which are characterized by an increased INR and concomitant hyperbilirubinemia on or after postoperative day 5 [1].

Criteria to define and diagnose PHLF includes

a) Model for end stage liver disease (MELD) score

MELD is a widely used criteria which incorporates serum creatinine, INR, and bilirubin in a complex mathematical formula computation given by

MELD Score = $10 * ((0.957 * \ln(\text{Creatinine})) + (0.378 * \ln(\text{Bilirubin})) + (1.12 * \ln(\text{INR}))) + 6.43$

b) 50-50 criterion

This does not account for any clinical parameters and relies only on two laboratory values namely Prothrombin Time [PT] and serum bilirubin on post-operative day 5. The association of PT <50% and SB >50 $\mu\text{mL/L}$ on POD 5 was a simple, early, and accurate predictor of more than 50% mortality rate after hepatectomy. These criteria could be identified early enough, before clinical evidence of complications, for specific interventions to be applied in due time [2].

Preoperative risk assessment

CT-based volumetric analysis: A helical CT scan to assess the volume of resection by semi-automated contouring of the liver. Shoup et al observed that the percentage of remaining liver was closely correlated with increasing prothrombin time (>18 seconds) and bilirubin level (>3 mg/dL). PHLF was noted more often in patients undergoing trisegmentectomy especially those with $\leq 25\%$ of liver remaining.

Indocyanine green (ICG) clearance and ICG retention rate (ICG R15): All ICG administered is cleared by normal liver. ICG reflects intra-hepatic blood flow which can be used to assess liver functional reserve in patients with cirrhosis. Application of ICG and ICG R15 to estimating functional hepatic reserve after resection of normal livers in the setting of malignancy is an effective method. ICG elimination is measured by pulse spectrophotometry & indocyanine green plasma disappearance rate (ICG PDR) is determined. The foremost advantage of ICG is that it is a noninvasive tool for prediction of PHLF [3]. When the pre-operative ICG PDR was less than 17.6%/min and the pre-operative serum bilirubin was >17 $\mu\text{mol/L}$, the positive predictive value for post-operative liver dysfunction was 75%, and the negative predictive value was 90%.

Galactosyl human serum albumin (GSA) scintigraphy: $^{99\text{m}}\text{Tc}$ diethylenetriamine-pentaacetic acid-Galactosyl human Serum Albumin (GSA) scintigraphy for the pre-operative evaluation of cirrhotic patients is a valid method for pre-operative

risk assessment. The molecule is taken up by the liver, reflecting the volume of functional liver. Uptake corresponds to bilirubin level, INR, and ICG clearance. GSA is unaffected by hyperbilirubinemia and offers a highly accurate estimation of FLR. In nearly 20% of patients, the severity of liver disease is underestimated by ICG clearance testing, and better represented by GSA scintigraphy.

99mTc-mebrofenin: 99mTc-mebrofenin is excreted into the bile by adenosine triphosphate-dependent export pumps namely the multidrug-resistance-associated proteins 1 and 2, without undergoing biotransformation during transit through the hepatocytes. This preoperative total hepatic uptake rate of 99mTc-mebrofenin correlates well with the indocyanine green

(ICG) clearance rate. In patients with parenchymal disease and hilar cholangiocarcinoma 99mTc-mebrofenin uptake in the future remnant liver on functional hepatobiliary scintigraphy has been proved to be more valuable than measurement of the volume of the future remnant in the assessment of the posthepatectomy risk of liver failure and liver failure-related mortality.

*To avoid irreversible injury to the liver, the Pringle maneuver should be applied in an intermittent manner, and the duration should not exceed a total of 120 minutes. *Pringle maneuver during liver transection is safe and effective and can be employed, in an intermittent manner, during hepatectomy of whatever histology of nontumorous liver [4] (Table 1).

Table 1: Methods and techniques to minimize PHLF

Preoperative
Weight loss in obese patients
Nutritional supplementation
Aggressive management of co-morbid conditions
Portal vein embolization [PVE] to enlarge FLR
Intra Operative
Avoidance of skeletonization of hepatoduodenal ligament unless required for R0 resection
Minimize EBL (resection under low CVP conditions) *
Avoidance of blood transfusions if able
Close attention to hemostasis to avoid post-operative hemorrhage
Postoperative
Early recognition and treatment of post-op hemorrhage
Early recognition and treatment of biliary obstruction or leak
Early recognition and treatment of intra-abdominal infection

Estimation of Remaining Functional Parenchyma

Bismuth et al proposed a formula to estimate amount of functional parenchyma remaining after resection (Mr), Where Me is the quantity of functional liver removed and Mt the total quantity of functional liver. PBC the Paul Brousse Hospital classification.

$$Mr = Me/Mt \times PBC$$

Postoperative mortality or complications are not dependent on the amount of resected parenchyma alone. There was a 5%

mortality even after minimal resection. Postoperative liver failure is precipitated in over 50% of patients by sepsis, hemorrhage or portal thrombosis. Incidence of late liver failure is rare [$< 5\%$] with almost nil mortality when estimated postoperative liver volume $> 35\%$. Normal livers regenerate completely within 3 months, while in cirrhosis or chronic hepatitis it may take up to 9–12 months or even longer to reach preoperative liver volume. The speed of hepatic regeneration appears to be a function of the volume resected.

Treatment of PHLF (Table 2)

Treatment of PHLF remains difficult

Table 2: Consensus definition and severity grading of posthepatectomy liver failure by the ISGLS

Grade A	Abnormal laboratory parameters; requiring no change in the clinical management
Grade B	Deviation from the regular clinical management but manageable without invasive treatment
Grade C	Deviation from the regular clinical management and requiring invasive treatment

- i. Pulmonary, renal and circulatory disturbances should be treated with a goal-directed therapy regime.
- ii. Diuretics and renal replacement therapy have to be used as indicated
- iii. In pulmonary insufficiency, noninvasive or invasive ventilation has to be used.

Specific treatment of hepatic insufficiency

Goal-directed therapy: Human albumin, fresh frozen plasma or AT III to cover the liver function

Liver support systems have been available for some years now: Molecular absorbent recirculating system (MARS), Modified fractionated plasma separation and adsorption (Prometheus) and Bioartificial liver and extracorporeal liver assist device

Liver transplantation: Salvage transplantation as the last resort

Conclusion

PHLF is a severe deadly complication. Mild hepatic insufficiency with a transient hyperbilirubinemia that does not alter the expected post-operative course is quite common. Multi-system failure requiring invasive treatment in ICU and multiple factors increase the risk of mortality. Obesity, diabetes,

neoadjuvant treatment with chemotherapy, underlying cirrhosis, increased age, male gender, need for extended liver resection, and long operation with high intra-operative Estimated Blood Loss. Risk of PHLF can be minimized by accurate preoperative assessment of FLR, induction of hypertrophy of the liver remnant via PVE if the expected FLR is < 20% for a normal liver, < 30% for a steatotic liver and < 40% for a cirrhotic liver. PHLF is rather easy to prevent than to treat [5].

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