



Preoperative assessment of liver function and perioperative management of posthepatectomy liver failure

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The current state of hepatectomy and posthepatectomy liver failure (PHLF)

PHLF is the status of disfunction in synthesis, excretion and detoxication. According to International Study Group of Liver Surgery (ISGLS), PHLF is defined by an increased bilirubin level and international normalized ratio (INR) on or after postoperative 5 days, and is graded by clinical severity from grades A to C (1,2). Grade A is the condition without any treatment. Grade B deviates from normal postoperative management and requires blood products, diuretics, oxygen administration, and so on. Grade C is the status with multiple organ failure which requires intensive management including respirator, dialysis, and liver transplantation, etc. Perioperative mortality rates in A, B and C were estimated 0%, 12%, and 54%, respectively (1). Although PHLF has decreased due to extensive studies of risk factors for PHLF and improvements in surgical techniques, it remains high for several types of procedures. According to a nationwide survey of board-certified training institutions by the Japanese Society of Hepato-Biliary-Pancreatic Surgery, 90-day mortality rates is 10.3% and 6.7% after left trisectionectomy and hepatopancreatectomy, respectively (3). Further, the mortality rates after associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) was reported over 5% (4).

In order to prevent PHLF, Scientific and Research Committee of the European-African Hepato-Pancreato-

Biliary Association (E-AHPBA), the Board of Directors of the European Society of Surgical Oncology (ESSO), and the Secretary General of the European Society for Surgical Research (ESSR) concisely summarized the necessary preoperative examinations and assessments, treatment policies including a strategic map as a consensus guideline (5).

Risk factors of PHLF and preoperative assessment of liver function

Preoperative risk factors for PHLF includes cirrhosis, residual liver function, cholangitis, jaundice, biliary drainage, performance status malnutrition and sarcopenia etc. Operative time, blood loss, portal vein reconstruction, and combined with pancreaticoduodenectomy were reported as intraoperative factor. Further, postoperative risk factors include infectious complications or postoperative bleeding. These risk factors differ depending on diseases. When we assess the preoperative liver function and extract risk factors for PHLF, it is first necessary to classify the type of diseases; hepatocellular carcinoma (HCC), bile duct cancer (BDC) and metastases of other diseases (especially colorectal cancer). Preoperative liver functional assessments are listed in *Table 1*, which is also recommended in the guideline (5). First, the patient's general condition is evaluated by the life intensity and performance status. Further, the assessment of nutritional status, sarcopenia, obesity, and frailty are needed. Liver function is evaluated with clinical scoring [Child-Pugh

Table 1 Measures of preoperative liver function

Assessment modality	Details
General status of patients	Nutritional status, sarcopenia, frailty, obesity, etc.
Classification of diseases	HCC/BDC/metastases of other cancer
Comorbidity	Diabetes, hepatitis, cancer, steroids, etc.
Laboratory examination	AST, ALT, bilirubin, albumin, CHE, Plt, PT/INR, hepatitis, etc.
Clinical scoring	Child-Pugh classification, liver damage, MELD score, etc.
Image examination	Cirrhosis, varices, splenomegaly, ascites
Liver function	ICG, 99mTc-GSA liver scintigraphy
Others	Volumetry, liver stiffness measurement, hepatic biopsy

HCC, hepatocellular carcinoma; BDC, bile duct cancer; AST, aspartate aminotransferase; ALT, alanine aminotransferase; CHE, cholinesterase; Plt, platelet; PT/INR, prothrombin time/international normalized ratio; MELD, model for end-stage liver disease; ICG, indocyanine green.

Table 2 Preventive measures for PHLF

Timing	Measures
Preoperative	Volumetry, three-dimensional simulation, PVE Development of nutritional status, sarcopenia strength training Biliary drainage, control of cholangitis, bile returning
Intraoperative	Reduce bleeding, transfusion
Postoperative	Early resumption of diet, prevent infectious complication

PHLF, posthepatectomy liver failure; PVE, portal vein embolization.

scoring, liver damage, model for end-stage liver disease (MELD) score, etc.], imaging tests (cirrhosis, ascites, varices, dilatation of bile duct, etc.), indocyanine green (ICG) and 99mTc-GSA liver scintigraphy. If hepatectomy is planned, volumetry is needed. Liver stiffness measurement (LSM) or hepatic biopsy are done when necessary.

Preventive measures are listed in *Table 2*. The assessment of future liver remnant (FLR) is estimated volumetry, ICG and ^{99m}Tc-GSA liver scintigraphy. ICGK <0.05 is often used as a cut-off value to predict PHLF and in-hospital death (6). Preoperative portal vein embolization (PVE) is suggested for hepatectomy in which resection rate is 50–60%. Further, in recent years, advances in three-dimensional (3D) simulation have made it possible to perform hepatectomy that closely approximate the preoperative plan. 3D simulation enables surgeons to identify accurately which vessels to preserve or remove, that prevent extended hepatectomy or congested liver, and contributes reducing PHLF (7,8).

Several studies reported that patients with sarcopenia had longer postoperative hospital stay and are more PHLF. Preoperative strength training and improvement of nutritional status are suggested to prevent PHLF. For patients with BDC with develop obstructive jaundice, the usefulness of preoperative biliary drainage, control of cholangitis, and bile returning has been reported (9,10). Because postoperative infectious complications aggravate PHLF, early detection and drainage of intrabdominal abscesses, use of appropriate antibiotics, early postoperative resumption of diet to prevent bacterial translocation are needed. Some studies reported the effectiveness of preoperative bile juice culture (10).

Future challenges

There are still some future research questions that need to be assessed. One of the major challenges is hepatectomy in conjunction with systemic therapy, including molecular

target drug and immune checkpoint inhibitors (ICI). In recent years, the development of ICI has been remarkable. There are still few research reports regarding the timing of hepatectomy during systemic therapy and the drug holiday period. Further, development of malnutrition and sarcopenia associated with systemic therapy should also be considered. Further investigation and large-scale clinical trials are required.

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