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REVIEW

Management of post-hepatectomy complications

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Abstract

Hepatic resection had an impressive growth over time. It has been widely performed for the treatment of various liver diseases, such as malignant tumors, benign tumors, calculi in the intrahepatic ducts, hydatid disease, and abscesses. Management of hepatic resection is challenging. Despite technical advances and high experience of liver resection of specialized centers, it is still burdened by relatively high rates of postoperative morbidity and mortality. Especially, complex resections are being increasingly performed in high risk and older patient population. Operation on the liver is especially challenging because of its unique anatomic architecture and because of its vital functions. Common post-hepatectomy complications include venous catheter-related infection, pleural effusion, incisional infection, pulmonary atelectasis or infection, ascites, subphrenic infection, urinary tract infection, intraperitoneal hemorrhage, gastrointestinal tract bleeding, biliary tract hemorrhage, coagulation disorders, bile leakage, and liver failure. These problems are closely related to surgical manipulations, anesthesia, preoperative evaluation and preparation, and postoperative observation and management. The safety profile of hepatectomy probably can be improved if the surgeons and medical staff involved have comprehensive knowledge of the expected complications and expertise in their management. This review article focuses on the major post-operative issues after hepatic resection and presents the current management.

Key words: Hepatectomy; Postoperative complication; Management

Core tip: Despite technical advances and high experience of liver resection of specialized centers, it is still burdened by relatively high rates of postoperative morbidity and mortality. Common post-hepatectomy complications include fever, hemorrhage, bile leakage, liver failure, pleural effusion, and subphrenic infection. The aim of this study was to summary the causes for post-hepatectomy complications and to discuss the prevention and treatment trick for postoperative complications.

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INTRODUCTION

The era of hepatic surgery began with a left lateral hepatic lobectomy performed successfully by Langenbuch in Germany in 1887. Since then, hepatectomy has been widely performed for the treatment of various liver diseases, such as malignant tumors, benign tumors, calculi in the intrahepatic ducts, hydatid disease, and abscesses.

Operation on the liver is especially challenging because of its unique anatomic architecture and because of its vital functions. Despite technical advances and high experience of liver resection of specialized centers, it is still burdened by relatively high rates of postoperative morbidity (4.09%-47.7%) and mortality (0.24%-9.7%)[1-16] (Table 1). Common post-hepatectomy complications include fever, hemorrhage, bile leakage, liver failure, pleural effusion, and subphrenic infection, which we will discuss.

POSTOPERATIVE FEVER AND INFECTIONS

Venous catheter-related infection

Deep-vein catheterization is routinely performed for hepatic surgery, and venous catheter-related infection is the most common cause of fever after hepatectomy. This source of fever should be considered if the fever cannot be attributed to some other cause. If it cannot, the catheter should be immediately removed and its tip cultured, so that appropriate antibacterial therapy can be instituted promptly[17-21].

Pleural effusion

Reactive pleural effusion may occur after hepatectomy and usually is the result of diaphragmatic injury, obstruction of thoracic venous or lymphatic systems, or surgical manipulation on the hepatic coronary ligament (usually causing a subphrenic fluid collection). The pleural effusion, which most often occurs in the right chest, can cause fever even though it is aseptic. X-ray and ultrasound examinations should be performed promptly in febrile patients in order to determine whether a pleural effusion has developed. If only a small effusion is present it may spontaneously resolve, and if the patient has no significant symptoms or signs, no special treatment will be needed; otherwise, thoracic puncture and drainage of the effusion should be carried out[22-24].

Incisional infection

Incisional infection usually occurs within 1 wk after operation. Swelling and exudation at the incision site, or in the case of severe infection, dehiscence of the wound may be seen. If infection is found, the sutures and necrotic tissue should be removed and adequate drainage established. Antibiotics may be prescribed to help control the infection. If wound dehiscence is present, tension sutures may be placed[25-27]. Albumin may be administered intravenously in order to help relieve intra-abdominal pressure if present[28].

Pulmonary atelectasis or infection

Postoperative atelectasis or pulmonary infection most commonly presents 3-5 d after the operation. Symptoms and signs may include chest tightness, shortness of breath, and cyanosis. Surgical trauma, prolonged bed rest, and limited coughing because of incisional pain are the major factors predisposing to pulmonary atelectasis or infection. The findings of hypoxemia, determined by blood-gas analysis, and abnormalities seen on chest X-ray films, will assist in making the diagnosis. If the pulmonary infection progresses to pneumonia, the patient may have fever, cough, and pulmonary rales; increased bronchovascular shadows and pulmonary consolidation may be seen on chest X-ray films. Analgesic drugs may be given to relieve patient's pain and to facilitate deep breathing; bronchial lavage may be performed for relief of airway obstruction; and antibiotics may be prescribed after sputum culture and testing bacteria for drug sensitivity[28-30].

Ascites

Ascites is common in hepatectomy patients who have associated liver malfunction or cirrhosis. Ascitic fluid may drain from the incision site or the drainage tube[31]. Accumulation of much ascites may result in imbalance of water and electrolytes. Paracentesis for treatment of the ascites usually is not recommended; administration of diuretics and albumin is preferred. However, if the ascites is suspected of being infected and the source of fever, diagnostic paracentesis under ultrasonic guidance should be performed[32-35].

Subphrenic infection

Subphrenic infection is a severe complication of hepatectomy, usually resulting from incomplete or premature removal of a subphrenic fluid collection or a bile leak. Fever, tenderness in the upper abdomen, and abdominal muscle tension are the major manifestations of subphrenic infection. Septicopyemia or septicemia may develop if infection is severe, which may occur with pleural effusion or pulmonary atelectasis[36]. Thorough drainage of the fluid, in addition to anti-inflammatory therapy, is critical in the treatment. Ultrasonic guidance may be useful in the aspiration of subphrenic fluid collections or in the evacuation of abscesses. Open operation may be needed if the infection is severe[37].

Urinary tract infection

Fever, back pain and bladder irritation are the common symptoms of upper urinary tract infection. In contrast, fever is not common in lower urinary tract infection, which is usually manifested by dysuria and urinary frequency and urgency. Treatment of the urinary infection includes anti-inflammatory medications, oral hydration, and medications to relieve cystospasm and symptoms of bladder irritation.

POSTOPERATIVE HEMORRHAGE

Intraperitoneal hemorrhage

The incidence of intraperitoneal hemorrhage ranges from 4.2% to 10%[6,38-41]. Three common reasons for intraperitoneal hemorrhage are: (1) bleeding from the surfaces of the residual liver, which may be a consequence of arterial branch truncation or congestion of the hepatic vein due to stenosis or ligation; (2) incomplete intraoperative hemostasis, which sometimes is due to inappropriate

Table 1 Summary of studies investigating the post-hepatectomy mortality and morbidity

Ref.	Journal	Date of publication	Country of study	NO. of Patients studied	Disease's diagnosis	Mortality and morbidity of hepatectomy
Savage *et al*[1]	*Ann Surg*	December 1991	United States	300	Liver trauma or liver tumors	The operative mortality was 19% (1962-1979) or 9.7% (1980-1988), and the overall complication rate was 12.3%
Wu *et al*[2]	*Zhonghua Waike Zazhi*	May 2002	China	1762	Liver cancer	The total mortality was 0.40%, and the total complication rate was 4.09%
Ishikawa *et al*[3]	*Hepatogastroenterol*	November-December 2002	Japan	139	HCC	The mortality within 30 postoperative days was 2.2%, and complication morbidity was 40.2%
Descottes *et al*[4]	*Surg Endosc*	January 2003	France	87	Benign liver tumors	There was no postoperative mortality, and the postoperative complication rate was 5% (laparoscopic liver resection)
Dimick *et al*[5]	*Arch Surg*	January 2003	United States	569	Malignant or benign liver disease	The overall in-hospital mortality rate was 4.8%
Benzoni *et al*[6]	*Hepatobiliary Pancreat Dis Int*	November 2006	Italy	287	HCC or liver metastasis	In-hospital mortality rate was 4.5%, and the morbidity rate was 47.7%
Benzoni *et al*[7]	*Hepatogastroenterol*	January-February 2007	Italy	134	HCC	In-hospital mortality rate was 7.4%, and the morbidity rate was 47.7%
Mullen *et al*[8]	*J Am Coll Surg*	May 2007	United States	1059	Noncirrhotic patients	The complication rate was 43%, and the 90-d all-cause mortality rate was 4.7% (1.9% patients died of causes unrelated to the liver)
McKay *et al*[9]	*Ann Surg Oncol*	May 2008	Canada	1107	Liver tumor	In-hospital mortality rate was 6.0%, and an overall complication rate was 46%
Feng *et al*[10]	*World J Gastroenterol*	December 2008	China	827	Benign hepatic lesion	In-hospital mortality rate was 0.24%, and the postoperative complication rate was 13.54%
Tomuş *et al*[11]	*Chirurgia (Bucur)*	May-June 2009	Romania	50	Benign hepatic lesion	There was no mortality, and the morbidity rate was 18%
Cescon *et al*[12]	*Ann Surg*	June 2009	Italy	1500	Malignant or benign disease	Overall mortality was 3%, and the morbidity was 22.5%
Huang *et al*[13]	*Chin Med J (Engl)*	October 2009	China	2008	Malignant or benign liver disease	The overall hospital mortality was 0.55%, and the overall postoperative complication rate was 14.44%
Mathur *et al*[14]	*J Gastrointest Surg*	August 2010	United States	3960	Liver tumor	The overall mortality rate was 2.5%, and the overall complication rate was 23.3%
Sato *et al*[15]	*J Gastroenterol*	October 2012	Japan	5270	HCC	In-hospital mortality was 2.6%, and the postoperative complication rate was 14.5%
Dan *et al*[16]	*Chirurgia (Bucur)*	November-December 2012	Romania	133	Benign or malignant tumors	The overall mortality rate was 2.25%

HCC: Hepatocellular carcinoma.

manipulation of the hepatic vein root or trauma to the diaphragm, and increased intrathoracic pressure and vena cava pressure which may lead to bleeding; and (3) vascular sutures loosened or fallen off, an event which usually is ascribed to elevated pressure in the vena cava from patients' body movement, such as turning over or coughing severely. Detachment of the ligature on the short hepatic veins may cause a gap in the vena cava wall. Postoperative intraperitoneal hemorrhage usually occurs within 48 h, and from the residual liver's surface or the diaphragm. Thorough intraoperative hemostasis is critical and must be ascertained before the operation is concluded. When the root of the hepatic vein is manipulated during the operation, hemorrhage from the vein or anterior to the inferior vena cava should be carefully sought by increasing the intrathoracic pressure artificially. Mattress sutures with hepatic needles should be used for the hemostasis, and the traumatized surface can be covered with hemostasis film, gelatin sponge, biological glue, or omentum as means of achieving additional hemostasis[42]. The presence of persistent bloody drainage might indicate that intraperitoneal clots have formed, which may occlude abdominal drains, leading to abdominal distention. Close monitoring of vital signs and transfusion of whole blood, platelets, and plasma are usually recommended as long as the patient's blood pressure and pulse remain stable. Otherwise, secondary open surgery should be considered[43]. We recommend that open surgery to attain hemostasis be performed if blood loss exceeds 1000 mL/h for more than eight hours. In summary, correct timing for operations on infected liver sections, careful manipulation during operation, and thorough hemostasis and drainage are critical for success in attaining hemostasis.

Coagulation disorders

Five common causes of coagulation disorders associated with hepatectomy are: (1) functional failure of the residual liver due to prolonged ischemia, especially in the presence of cirrhosis[44]; (2) massive intraoperative bleeding, or blood transfusion of more than 4000 mL;

(3) consumption of coagulation factors and platelets due to severe infection; (4) overdose of heparin after hepatic artery or portal vein catheterization; and (5) cardiopulmonary bypass or extracorporeal circulation[45,46]. Coagulation time, prothrombin time, platelet count, and fibrinogen level should be tested to aid in making the diagnosis of a postoperative coagulation disorder, and the 3P test may be performed if necessary[47]. Expansion of the circulating blood volume and transfusion of fresh blood should be carried routinely once a coagulation disorder is confirmed, and prompt administration of fibrinogen, prothrombin complex, fresh platelets, and plasma cold precipitates also is important[48-50]. Protamine can be administered to neutralize the heparin if it has been overdosed.

Gastrointestinal tract bleeding

The common causes of gastrointestinal tract bleeding after hepatectomy are: (1) stress ulcer, the most common; (2) portal hypertension due to liver cirrhosis; and (3) congestion of gastrointestinal organs because of secondary portal hypertension due to the limited volume of the residual liver. Gastrointestinal tract bleeding usually occurs within two weeks after operation. It may be manifested by the passage of brown or bloody drainage, hematemesis, melena, deterioration of vital signs, and abdominal pain. If the bleeding is mild, nasogastric suctioning and administration of proton pump inhibitors and hemostatic drugs may be adequate treatment. Somatostatin and ulinastatin may be given if the bleeding is massive. Operation should be considered if the blood pressure and pulse are unstable, or if hemorrhage persists after 48 h of aggressive treatment[51-54].

Biliary tract hemorrhage

Iatrogenic bile duct injury is the most common cause of biliary tract hemorrhage after hepatectomy. Surgical maneuvers, including operating in the hepatic portal region, bile duct exploratory surgery, and placement of T-tubes in the biliary ducts could result in biliary tract hemorrhage. Other common causes are mucosal erosion ulcer and coagulation disorders due to biliary tract infection and inflammation. The major manifestations of biliary tract hemorrhage are right upper quadrant gripping pain, upper gastrointestinal bleeding, and obstructive jaundice. Usually, bleeding of this kind can be treated effectively with appropriate hemostasis, antibiotics, and supportive measures. For patients who have massive biliary tract bleeding or whose bleeding site is unclear (after hepatic artery angiography), explorative operation should be carried out[55-59].

BILE LEAKAGE

The incidence of bile leakage ranges from 4.0% to 17%[60-63]. Common causes of postoperative bile leakage are: (1) truncation of the distal bile duct in the residual liver, the most common cause; (2) leakage at the bile duct-intestinal anastomosis, or incomplete suture around the T-tube; and (3) injury of the bile duct from inappropriate surgical technique. A retrospective analysis by Yoshioka *et al*[64] of 505 hepatectomy cases found that the incidence of bile leakage was 6.7%, with three independent risk factors: (1) multiple hepatectomy ($P = 0.002$, OR = 3.439; 95%CI: 1.552-7.618); (2) traumatized liver surface $\geqslant$ 57.5 cm^2 ($P = 0.004$, OR = 5.296; 95%CI: 1.721-16.302); and (3) intraoperative bleeding $\geqslant$ 775 mL ($P = 0.01$, OR = 2.808; 95%CI: 1.280-6.160)[64]. Another analysis by Sadamori *et al*[65] of 359 hepatectomy cases found that operative time $\geqslant$ 300 min was an independent risk factor for bile leakage after hepatectomy. To help predict if postoperative bile leakage will occur, the residual liver can be covered with wet gauze, which may show the presence of minimal bile seepage. To help avoid postoperative bile leakage, biological glue can be applied to the surface of the residual liver, and a C tube can be placed in the cystic duct for decompression[66,67]. Intraoperatively, bile leakage might be revealed with the use of indocyanine green fluorescein[68-70]. Close postoperative monitoring is mandatory and should include observing for abdominal pain, rebound tenderness, muscle tension, and bile leakage from the drainage tube. Bile leakage also may be evident by the presence of bile in the peritoneal drainage (the concentration of bilirubin in the bile will be higher than in serum). In addition, computed tomography (CT) visualization can be used to determine if the bile duct is occluded and, if so, where the occlusion is located. A drainage tube can remain in the bile duct if there is no sign of peritonitis; the bile leakage may resolve spontaneously within two months. However, if peritonitis develops, open surgery should be performed as soon as possible for thorough cleaning of the abdominal cavity and repair of the damaged common bile duct. Antibiotics may be administered for control of infection, and supportive treatment should be given as usual after a major operation[71,72]. It has been reported that bile leakage occurred in 14 of 96 patients who underwent hepatectomy; nine were treated successfully without operation, but five required a second operation. In general, non-operative treatment was sufficient if the results of ERCP and CT were negative for bile leakage, but operative intervention was needed if conservative therapy failed[73].

LIVER FAILURE

Liver failure is a severe postoperative complication of hepatectomy. It is closely associated with active hepatitis, cirrhosis, limited residual liver tissue, massive intraoperative hemorrhage, the mode and duration of hepatic portal vein occlusion, the kind of anesthesia used, and perioperative medication used. An incidence of liver failure after hepatectomy of about 0.70%-33.83% has been reported[74-77], and the failure was related to inadequate residual liver tissue and functional capacity[78,79]. Comprehensive therapy for liver failure includes postoperative supplementation with albumin, fibrinogen or prothrombin complex; intravenous nutrition; and transfusion of

fresh blood. Prognosis is poor if coagulation disorders develop. Presently, the most effective therapy for liver failure is liver transplantation, but it is associated with a high mortality rate in patients with liver cirrhosis and, therefore, it remains a controversial treatment choice in this circumstance[80-86], Generally, prevention of liver failure is felt to be more important than treatment of it. Some common preventive measures are: careful preoperative assessment of the liver's functional reserve and institution of measures to improve the liver function. Prevention of intraoperative bleeding and the need for blood transfusion also are important in preventing liver failure. In one report, the incidence of postoperative complications increased significantly when the intraoperative blood loss exceeded 1200 mL[11]. Several methods can be used to reduce the chance of intraoperative bleeding: CUSA[87-89], heat solidification technology[90-93], reduction of central venous pressure[94-96], and blocking of hepatic portal blood inflow (with or without control of hepatic blood outflow)[97-101]. For patients with liver cirrhosis, the volume of residual liver and the time of portal occlusion must be strictly assessed. Also, the method used for occluding blood flow to the liver must be appropriately selected. It has been recommended that half hepatic blood flow occlusion should be used for patients with cirrhosis, and hepatic blood inflow occlusion without hemihepatic artery control (hemi-hepatic artery-preserved portal occlusion) used if half occlusion is difficult or inadequate. Hepatic blood inflow occlusion without hemihepatic artery control is simple for operation, with less damage to the liver function; more importantly, the effect of the blood flow blocking is equivalent to the half-hepatic blood flow blocking[102,103]. The procedure for inflow occlusion is the following: the hepatic artery is exposed first, to separate the right and left hepatic arteries from the root of the artery. To restrict blood flow to the right half of the liver, the hepatic portal vein, bile duct, and the right hepatic artery should be tightened together with a catheter; the opposite arrangement is used for restricting blood flow to the left half of the liver, except that the left hepatic artery, instead of the right hepatic artery, is occluded[98]. It is important that the patient receive sufficient oxygen throughout the perioperative period, and that hepatotoxic drugs are avoided.

After hepatectomy, the patient should be closely monitored, with particular attention to abnormalities in levels of consciousness, liver function, the volume and character of drainage fluid, acid-base balance, and serum lactic acid levels. In general, during the first postoperative day, the ideal levels of serum hepatic transaminases, total bilirubin, and prothrombin activity can be expected to remain below 1000 IU/mL, about 2 mg/dL, and about 50%, respectively. Acidosis is very common in liver failure, so the level of serum lactic acid should be carefully monitored. Serum bilirubin level should rapidly decrease; if the level increases abruptly after the second postoperative day the risk of hepatic failure increases. Currently, there is not a unified definition of liver failure after hepatectomy. The international hepatic surgery research team has proposed a definition based on the normal postoperative course of serum bilirubin concentration and international normalized ratio (INR), reflecting the ability of the liver to maintain its synthetic, excretory, and detoxifying functions. Postoperative liver failure is defined as an increased INR and hyperbilirubinemia (according to the normal limits of the local laboratory) on or after postoperative day 5[104]. The severity of post-hepatectomy liver failure is graded based on its effect on clinical management; grade A failure requires no change in the patient' s clinical management; grade B failure requires deviation from the usual management but does not require invasive therapy; grade C requires invasive treatment[104].

CONCLUSION

In conclusion, hepatectomy still has significant associated complications and mortality. These problems are closely related to surgical manipulations, anesthesia, preoperative evaluation and preparation, and postoperative observation and management. The safety profile of hepatectomy probably can be improved if the surgeons and medical staff involved have comprehensive knowledge of the expected complications and expertise in their management.

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