REVIEW

Acute renal injury after partial hepatectomy

Luis Alberto Batista Peres, Luis Cesar Bredt, Raphael Flavio Fachini Cipriani

Luis Alberto Batista Peres, Department of Nephrology, University Hospital of Western Paraná, State University of Western Paraná, Cascavel, Paraná 85819-110, Brazil

Luis Cesar Bredt, Department of Surgical Oncology and Hepatobiliary Surgery, University Hospital of Western Paraná, State University of Western Paraná, Cascavel, Paraná 85819-110, Brazil

Raphael Flavio Fachini Cipriani, Department of General Surgery, University Hospital of Western Paraná, State University of Western Paraná, Cascavel, Paraná 85819-110, Brazil

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Abstract

Currently, partial hepatectomy is the treatment of choice for a wide variety of liver and biliary conditions. Among the possible complications of partial hepatectomy, acute kidney injury (AKI) should be considered as an important cause of increased morbidity and postoperative mortality. Difficulties in the data analysis related to postoperative AKI after liver resections are mainly due to the multiplicity of factors to be considered in the surgical patients, moreover, there is no consensus of the exact definition of AKI after liver resection in the literature, which hampers comparison and analysis of the scarce data published on the subject. Despite this multiplicity of risk factors for postoperative AKI after partial hepatectomy, there are main factors that clearly contribute to its occurrence. First factor relates to large blood losses with renal hypoperfusion during the operation, second factor relates to the occurrence of post-hepatectomy liver failure with consequent distributive circulatory changes and hepatorenal syndrome. Eventually, patients can have more than one factor contributing to post-operative AKI, and frequently these combinations of acute insults can be aggravated by sepsis or exposure to nephrotoxic drugs.

Key words: Hepatectomy; Liver resection; Acute renal injury; Hepatorenal syndrome; Kidney

Core tip: In the specific scenario of liver resections, there are limited and heterogeneous data regarding the occurrence of acute kidney injury (AKI) in the post-operative period, and its clinical relevance (mortality, morbidity and hospital stay) were not conclusively explored and clarified. Difficulties in the data analysis related to postoperative AKI after liver resections are mainly due the scarce data published on the subject.

INTRODUCTION

Currently, partial hepatectomy is the treatment of choice for a wide variety of primary liver tumors (benign or malignant), tumors of the bile ducts and secondary malignant liver tumors. The partial liver resections may also be necessary in the management of complex cystic liver diseases, benign biliary structures, some cases of hepatic trauma and more recently with living donor liver transplantation[1]. With the refinement of surgical techniques, improved selection of patients to procedure, advances in anesthetic support and perioperative care, this traditionally complex and feared operation has become a routine procedure in the past 20 years, with acceptable mortality rates ranging from 3.1% to 4.5%[2-4].

Among the possible complications of major surgical procedures, including the partial hepatectomy, acute kidney injury (AKI) should be considered as an important cause of increased morbidity and postoperative mortality[5,6], with an incidence ranging from 10% to 30% after major operations[7,8]. Literature data report an incidence of 1% of AKI in the postoperative major non-cardiac surgery without liver resection[6] about 20% after cardiac surgery[9-11] and 50% after liver transplantation[12-18].

In the specific scenario of liver resections, there are limited and heterogeneous data regarding the occurrence of AKI in the postoperative period, with an incidence ranging from 0.9% to 15.1% of the patients[19-23], and its clinical relevance (mortality, morbidity and hospital stay) were not conclusively explored and clarified.

Difficulties in the data analysis related to postoperative AKI after liver resections are mainly due to the multiplicity of factors to be considered in this surgical patients, such as general medical conditions and comorbidities, nutritional disorders, metastatic malignancy with low physiological reserve systems, immunological disorders, chemotherapy treatment, functional capacity and volume of liver parenchyma to be preserved, and the perioperative hemodynamic effects of the different modalities of partial hepatectomy. Moreover, there is no consensus of the exact definition of AKI after liver resection in the literature, which hampers comparison and analysis of the scarce data published on the subject[22].

Despite this multiplicity of risk factors for postoperative AKI after partial hepatectomy, there are main factors that clearly contribute to its occurrence. First factor relates to large blood losses with renal hypoperfusion during the operation[20], that very often can be associated by the deleterious renal effects of red blood cell transfusion[23], and in some occasions this renal hypoperfusion occurs in patients with increased renal susceptibility to ischemia, usually elderly patients with underlying cardiovascular or renal disorders, or eventually it may be drug-induced[21-24]. Second factor relates to the occurrence of post-hepatectomy liver failure (PLF) with consequent distributive circulatory changes and hepatorenal syndrome (HRS)[20]. Eventually, patients can have more than one factor contributing to post-operative AKI, and frequently these combinations of acute insults can be aggravated by sepsis[20-24] or exposure to nephrotoxic drugs, such as aminoglycosides[25].

The aim of this review is to present the definition of postoperative AKI after partial hepatectomy, the different pathophysiological mechanisms for its occurrence and methods for preventing these events.

DEFINITION OF POSTOPERATIVE AKI AFTER PARTIAL HEPATECTOMY

AKI is characterized by the deterioration of kidney function over a period of hours to days, resulting in the failure of the kidney to excrete nitrogenous waste products and to maintain fluid and electrolyte homeostasis[26]. In recent years, several criteria have been proposed for the diagnosis of AKI in general population, particularly the "Risk, Injury, Failure, Loss of Renal Function and End-Stage Renal Disease" (RIFLE) criteria[27], the "Acute Kidney Injury Network" (AKIN) criteria[28] and more recently, the criteria suggested by a panel of experts, which combine the AKIN and the RIFLE criteria, thus proposing a new classification: The "Kidney Disease Improving Global Outcomes" criteria[29] (Table 1).

The first question regarding the definition of postoperative AKI after partial hepatectomy, would be determining which of these proposed AKI criteria is most appropriate for these patients undergoing liver resection. Whereas acute tubular necrosis (ATN), resulting from hypoxic damage to the renal medulla, is considered as a major cause of postoperative AKI[30], different from general population, liver resections are often performed in the presence of functional deficit of the hepatic parenchyma, as in fibrosis, steatosis, cirrhosis, chemotherapy-induced injury and also in biliary obstruction[2]. Moreover, the recent technical improvements in liver surgery have resulted in an expansion and more liberal indications for major hepatectomies in patients with these underlying liver conditions[2,3,31-34], however, the risk of postoperative complications, such as AKI, have remained important concerns[3,31,35].

In the specific case of hepatocellular carcinoma, the tumor generally appears in a cirrhotic liver, which is a contributor to unfavorable postoperative results in large procedures[36], regarding renal dysfunction, AKI is a common and potentially fatal event in patients with cirrhosis[37-39], with a reported prevalence of 14%-50% in patients with cirrhosis[40-45], this wide range in prevalence is likely due to different study populations and varying definitions of renal dysfunction. Studies evaluating survival predictors in cirrhosis, renal dysfunction was a

Table 1 Current diagnostic criteria for acute kidney injury in general population

	RIFLE criteria[27]	AKIN criteria[28]	KDIGO criteria[29]
Diagnostic criteria	Increase in SCr to ≥ 1.5 times baseline, within 7 d; or GFR decrease > 25%; or urine volume < 0.5 mL/kg per hour for 6 h	Increase in sCr by ≥ 0.3 mg/dL (26.5 mmol/L) within 48 h; or increase in sCr ≥ 1.5 times baseline within 48 h; or urine volume < 0.5 mL/kg per hour for 6 h	Increase in sCr by ≥ 0.3 mg/dL (26.5 mmol/L) within 48 h; or increase in SCr to ≥ 1.5 times baseline, which is known or presumed to have occurred within the prior 7 d; or urine volume < 0.5 mL/kg per hour for 6 h
Staging	Risk: sCr increase 1.5-1.9 times baseline; or GFR decrease 25%-50%; or urine output < 0.5 mL/kg per hour for 6 h	Stage 1: sCr increase 1.5-1.9 times baseline; or sCr increase ≥ 0.3 mg/dL (26.5 mmol/L); or urine output < 0.5 mL/kg per hour for 6 h	Stage 1: sCr increase 1.5-1.9 times baseline; or sCr increase ≥ 0.3 mg/dL (26.5 mmol/L); or urine output < 0.5 mL/kg per hour for 6-12 h
	Injury: sCr increase 2.0-2.9 times baseline; or GFR decrease 50%-75%; or urine output < 0.5 mL/kg per hour for 12 h	Stage 2: sCr increase 2.0-2.9 times baseline; or urine output < 0.5 mL/kg per hour for 12 h	Stage 2: sCr increase 2.0-2.9 times baseline; or urine output < 0.5 mL/kg per hour for ≥ 12 h
	Failure: sCr increase ≥ 3.0 times baseline: or GFR decrease 50%-75%; or sCr increase ≥ 4.0 mg/dL (353.6 mmol/L) with an acute increase of at least 0.5 mg/dL (44 mmol/L); or urine output < 0.3 mL/kg per hour for ≥ 24 h; or anuria for ≥ 12 h	Stage 3: sCr increase 3.0 times baseline; or sCr increase ≥ 4.0 mg/dL (353.6 mmol/L) with an acute increase of at least 0.5 mg/dL (44 mmol/L); or urine output < 0.3 mL/kg per hour for ≥ 24 h; or anuria for ≥ 12 h	Stage 3: sCr increase 3.0 times baseline; or sCr increase to ≥ 4.0 mg/dL (353.6 mmol/L); or initiation of renal replacement therapy; or urine output < 0.3 mL/kg per hour for ≥ 24 h; or Anuria for ≥ 12 h

AKIN: Acute Kidney Injury Network; GFR: Glomerular filtration rate; KDIGO: Kidney Disease Improving Global Outcome; RIFLE: Risk, Injury, Failure, Loss, End stage renal disease; sCr: Serum creatinine.

powerful predictor of death, as Child-Pugh score[46-48].

Along with parenchymal dysfunction, the portal hypertension levels and its hemodynamic consequences are directly related to the degree of underlying liver injury[49-51], as it is observed in cirrhosis and others conditions, such as severe steatosis and chemotherapy-induced injury[52]. The types of chemotherapy-induced liver toxicity include steatosis[53], sinusoidal changes[54], steatohepatitis[55], and hemorrhagic central lobular necrosis[52]. Steatosis represents fatty changes in the liver, with the presence of fat droplets within the hepatocytes[56], and it has been shown that steatosis may interfere with circulation through sinusoids and impair regeneration, and in addition the liver's protective mechanism against oxidative stress appear to be impaired[57,58]. The morbidity following liver resection associated with steatosis has been reported by Belghiti *et al*[2], in this study with 747 patients, the mortality rate was higher in patients having steatosis than in those with no steatosis, 22% *vs* 8%, respectively (*P* = 0.003). Likewise, according to Behrns *et al*[32] in 135 liver resections, morbidity was seen in 29% and 10% of the patients with steatosis and without steatosis, respectively.

Besides the fact that a significant portion of patients eligible for partial hepatectomy have underlying chronic liver disease or were exposed to systemic therapies with liver toxicity, the hemodynamic changes in patients after major liver resections may have similarities with those of patients with cirrhosis or acute liver failure, and depending on the remnant liver volume and functional quality of parenchyma (steatosis/cirrhosis) the clinical effects may be more evident[59].

In 1953, Kowalski and Abelmann[60] reported the results of a study which have demonstrated that cardiac output in cirrhotic patients was significantly higher compared with healthy volunteers. The reason for this so-called hyperdynamic state is that patients with cirrhosis develop portal hypertension with resultant splanchnic vasodilation and pooling of blood secondary to increased resistance to portal flow. This is due to (1) vasodilators such as nitric oxide, carbon monoxide, and endogenous cannabinoids[61,62]; and (2) vasodilation from inflammatory cytokines such as tumor necrosis factor-alpha and interleukin-6 induced by bacterial translocation from the gut[63]. As a result, the concentration of cyclic guanosine monophosphate cyclic is increased, resulting in splanchnic vasodilation, decrease in central and arterial blood volume, low capillary pressure, low central venous pressure (LCVP), low systemic vascular resistance, and reduction of mean arterial pressure[64]. This compensatory increase in cardiac output *via* activation of the sympathetic nervous system by carotid baroreceptors maintains sufficient renal perfusion, however, with decompensation of cirrhosis and increasing severity of portal hypertension, the compensatory increase in cardiac output is inadequate to maintain circulatory blood volume and adequate renal perfusion[65]. Therefore, it would be reasonable that diagnostic and staging AKI criteria that consider this circulatory impairment could be better applied in patients undergoing liver resections, particularly large resections and those with chronic liver disease.

It is extremely important to point out that in the case of patients with chronic liver disease, isolated dosages of serum creatinine (sCr) levels can not reveal the actual renal function of the patient, because: (1) there is decreased creatine formation in the secondary muscles loss of muscle mass[66]; (2) is increased renal tubular secretion of creatinine (Cr)[67]; (3) increasing the circulating volume of distribution in cirrhosis can dilute the sCr[68]; and (4) interference in the measurement of Cr due to elevated bilirubin[69]. As a result, the serum levels of Cr in patients

with cirrhosis overestimate glomerular filtration rate (GFR). Therefore, a dynamic definition referring to the elevation of serum Cr of $\geq$ 50% of preoperative levels to a final value $\geq$ 1.5 mg/dL (133 mol/L) could be more suitable for these patients, and clinical studies have shown that AKI according to these criteria was a strong predictor of hospital mortality in patients with liver disease[70-72].

Another situation relates to the measurement of urine output of patients with chronic liver disease and ascites, since these patients can often present oliguria with high sodium retention, but they can still maintain a relatively normal GFR[73]. On the other hand, these patients can also have an increased diuresis because of diuretics therapy.

Thus, the current criteria suggested by the "International Ascites Club" for definition of AKI in cirrhotic patients do not include unreal measurements for these patients[68] (Table 2), and apparently would be the most appropriate criteria for the diagnosis and management of AKI after partial hepatectomy, especially in cases of large resections and underlying chronic liver disease.

HEMODYNAMIC INSTABILITY AND RENAL HYPOPERFUSION

Although the extent of liver resection correlates with the magnitude of the procedure, and patients undergoing resection of more than three segments or an additional extrahepatic procedure have an increased risk of complications[74-76], this is not a rigid rule. For example, an isolated resection of segment Ⅰ is technically more demanding than a right hepatectomy, similarly, resection of segments Ⅳ, Ⅴ, Ⅷ or posterior right segments (segments Ⅵ, Ⅶ) may be technically more difficult than the left or right hepatectomy, although the transection area is larger. Therefore, a minor hepatectomy should not be considered as an operation of less magnitude, and most important, the prevention of intraoperative hemorrhage should not be neglected. If excessive blood loss persists and a reduction in oxygen delivery is not corrected, the renal medulla may be susceptible to ischemic ATN[77], and as a result, patients may suffer from AKI. The results of two large studies[3,31] suggest that a blood loss of 1250 mL is the cutoff value for major complications after liver resections, such as AKI. Furthermore, red blood cell transfusion, that can be necessary in the case of haemorrhage, can be an additional risk factor for postoperative AKI[78].

Increased susceptibility to renal hypoperfusion
The kidneys are most vulnerable to moderate hypoperfusion when autoregulation is impaired. Factors increasing susceptibility to renal hypoperfusion may be seen in elderly patients or in patients with atherosclerosis, hypertension, or chronic renal failure, in whom hyalinosis and myointimal hyperplasia cause structural narrowing of the arterioles[79-81]. Increased susceptibility to renal

ischemia may also occur in malignant hypertension because of intimal thickening and fibrinoid necrosis of the small arteries and arterioles[82]. In addition, in chronic kidney disease, afferent arterioles in the functioning glomeruli become dilated with impairment of the kidney's ability to autoregulate the glomerular filtration rate in low-perfusion states[83].

Impaired decreasing of afferent arteriolar resistance can occur when a patient is receiving nonsteroidal anti-inflammatory drugs or cyclooxygenase-2 inhibitors, which reduce the synthesis of prostaglandins in the kidneys, as consequence a decreasing in glomerular capillary pressure occurs in occasions of low-perfusion states[82,84-86]. In other situations, calcineurin inhibitors[87], and radiocontrast agents[88] can act through various vasoconstrictor mediators to increase afferent arteriolar resistance, the later may have direct toxic effects on the tubules as well[81,82,88-92]. Decreased renal perfusion may also may have an exaggerated drop in the GFR in low-perfusion states as a consequence of not raising efferent arteriolar resistance by angiotensin Ⅱ in patients who are receiving angiotensin-receptor blockers or angiotensin-converting-enzyme inhibitors.

Red blood cell transfusion and postoperative AKI
Despite the deleterious effect of hemodynamic instability in renal perfusion, red blood cell transfusion, that can be necessary in the case of haemorrhage, can be an additional risk factor for postoperative AKI[78]. Although the exact causal link between red blood cell transfusion and postoperative AKI is not fully elucidated, there are several mechanisms that may be implicated: Deficiency in 2,3-diphosphoglycerate with impaired oxygen unloading from hemoglobin, less deformability of stored red blood cells with obstruction of smaller capillaries[93] stored red blood cells hemolysis with an increase in circulating free iron[94]. Other mechanisms might include loss of the ability to generate nitric oxide, release of procoagulant phospholipids, increased adhesiveness to vascular endothelium, and accumulation of proinflammatory phospholipids[93,95-98].

POSTHEPATECTOMY LIVER FAILURE AND HEPATORENAL SYNDROME

Apart from blood loss, that can leads to ATN because of severe hemodynamic instability, others risk factors for postoperative AKI after partial hepatectomy would be those that favor PLF, characterized by jaundice, coagulopathy, encephalopathy, ascites, and renal and pulmonary failure, all of which may become apparent only 3 to 5 d after surgery[1]. These risk factors for PLF are well described, such as a small volume of remaining liver with marked volume reduction of organ parenchyma[35,99,100] associated to parenchymal cell injury due portal hyperperfusion[59,101], liver cirrhosis or steatosis[102,103], and liver toxicity induced by chemotherapy[104]. In patients with liver cirrhosis, the postoperative liver failure may occur

Table 2	International Club of Ascites new definitions for the diagnosis and management of acute kidney injury in patients with cirrhosis[68]
Baseline sCr	A value of sCr obtained in the previous 3 mo, when available, can be used as baseline sCr. In patients with more than one value within the previous 3 mo, the value closest to the admission time to the hospital should be used. In patients without a previous sCr value, the sCr on admission should be used as baseline
Definition of AKI	Increase in sCr ≥ 0.3 mg/dL (≥ 26.5 mmol/L) within 48 h; or a percentage increase sCr ≥ 50% from baseline which is known, or presumed, to have occurred within the prior 7 d
Staging of AKI	Stage 1: Increase in sCr ≥ 0.3 mg/dL (26.5 mmol/L) or an increase in sCr ≥ 1.5-fold to twofold from baseline
	Stage 2: Increase in sCr > two to threefold from baseline
	Stage 3: Increase of sCr > threefold from baseline or sCr ≥ 4.0 mg/dL (353.6 mmol/L) with an acute increase ≥ 0.3 mg/dL (26.5 mmol/L) or initiation of renal replacement therapy
Progression of AKI	Progression: Progression of AKI to a higher stage and/or need for RRT
	Regression: Regression of AKI to a lower stage
Response to treatment	No response: No regression of AKI
	Partial response: Regression of AKI stage with a reduction of sCr to ≥ 0.3 mg/dL (26.5 mmol/L) above the baseline value
	Full response: Return of sCr to a value within 0.3 mg/dL (26.5 mmol/L) of the baseline value

AKI: Acute kidney injury; RRT: Renal replacement therapy; sCr: Serum creatinine.

due the compromised liver microcirculation, with less resistance to ischemia-reperfusion injury[105] and impaired regeneration[106], in addition, portal hypertension, if present, is associated with a poor outcome because of compromised portal flow and the risk of postoperative upper gastrointestinal bleeding[107].

Liver steatosis is usually related to obesity, the presence of metabolic disorders, or the intake of alcohol or drugs, and this liver disorder increases the operative risk of partial hepatectomy[2,53,108]. The extent of liver resection in these patients with steatosis in order to avoid PLF is unclear, but the severity of fatty infiltration must be considered: Mild steatosis (up to 30% of hepatocytes containing fat) represents a minimal additional risk, in moderate steatosis (30% to 60% containing fat) caution is necessary, thus, a conservative resection should be favored, and patients with severe steatosis (more than 60% of hepatocytes containing fat) should undergo only limited resection[108].

Regarding the chemotherapy-induced liver aggression, the rates of complications and death after major liver resection are likely to be increased[55,109]. Oxaliplatin can induce a veno-occlusive syndrome, occasionally associated with nodular regenerative hyperplasia, these vascular obstructions result in a bluish appearance of the liver (blue liver syndrome)[54,110,111], and irinotecan can cause chemotherapy associated steatohepatitis[112], and liver impairment can be amplified after partial hepatectomy in both situations, triggering PLF[113].

A major concern regarding PLF is the onset of HRS. HRS is a reversible functional renal impairment that occurs in patients with advanced liver cirrhosis or hepatic failure. It is characterized by marked decrease in GFR and renal plasma flow in the absence of other cause of renal failure[114] (Table 3). The pathophysiological alterations of SHR consist of intravascular hypovolemia with activation of the renin-angiotensin-aldosterone system and vasoconstrictive sympathetic nervous system, leading to renal vasoconstriction of the afferent vessels and subsequent decrease in GFR[20]. Two subtypes of HRS have been identified: SHR type 1 is characterized by a rapidly progressive renal insufficiency defined as a doubling of the initial serum creatinine to a level greater than 2.5 mg/dL or 220 μmol/L in less than 2 wk, it is associated with very poor prognosis, and SHR Type 2 is characterized by a moderate renal insufficiency (Cr greater than 1.5 mg/dL or 133 μmol/L), follows a steady course or slowly progressive, often associated with refractory ascites[114].

KEYPOINTS FOR PREVENTION OF AKI AFTER PARTIAL HEPATECTOMY

Despite the fact that patients can have more than one factor contributing to post-operative AKI after partial hepatectomy, eventually aggravated by sepsis[20,21-24] or exposure to nephrotoxic drugs[25], there are particular risk factors that must be controlled and specific operative and non-operative procedures that must be undertaken for prevention of post-operative renal injury in these patients (Figure 1).

Vascular control of the liver
For prevention of intraoperative blood loss with consequent hemodynamic instability during the partial hepatectomy, there are intraoperative maneuvers that may be crucial in the moment of parenchymal transaction, such as vascular control of the liver[21].

The vascular control of the liver is an effective method to reduce bleeding during the hepatectomy. While various techniques have been proposed, the two most widely used methods are the vascular inflow occlusion and complete vascular exclusion[115,116]. Occlusion of the hepatic vascular inflow[117] by the application of tourniquet in hepatoduodenal ligament[118] is the oldest and simplest way to reduce blood loss during hepatectomy. The "Pringle maneuver" can be used continuously to normal livers under normothermic conditions for a maximum of 60 min, and for 30 min in cirrhotic or steatotic livers, although longer periods have already been described[119-122].
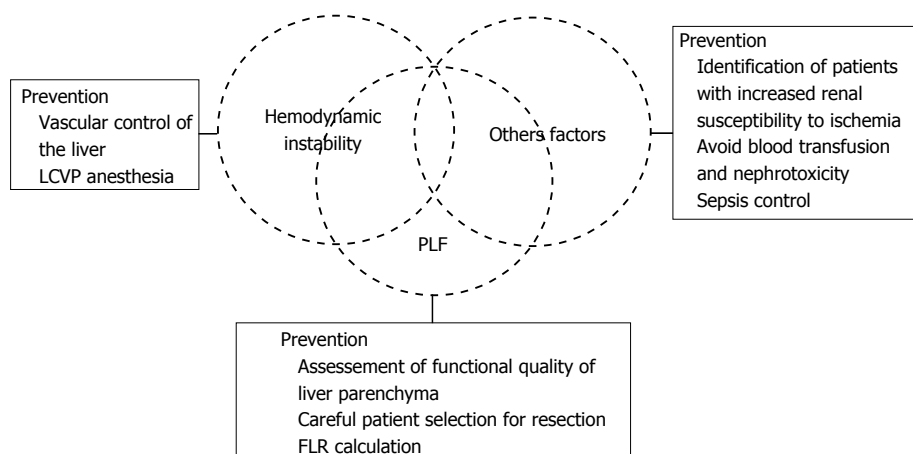
Figure 1 Main risk factors and prevention of acute kidney injury after partial hepatectomy. LCVP: Low central venous pressure; PLF: Posthepatectomy liver failure; FLR: Future liver remnant.

Table 3 Diagnostic criteria of hepatorenal syndrome type of acute kidney injury in patients with cirrhosis[68]
HRS-AKI
Diagnosis of cirrhosis and ascites
Diagnosis of AKI according to ICA-AKI criteria (Table 2)
No response after 2 consecutive days of diuretic withdrawal and plasma volume expansion with albumin 1 g/kg bodyweight
Absence of shock
No current or recent use of nephrotoxic drugs (NSAIDs, aminoglycosides, iodinated contrast media, *etc.*)
No macroscopic signs of structural kidney injury, defined as
Absence of proteinuria (> 500 mg/d)
Absence of microhaematuria (> 50 RBCs per high power field)
Normal findings on renal ultrasonography
Patients who fulfil these criteria may still have structural damage such as tubular damage. Urine biomarkers will become an important element in making a more accurate differential diagnosis between HRS and acute tubular necrosis

HRS: Hepatorenal syndrome; AKI: Acute kidney injury; ICA: International club of ascites; NSAIDs: Non-steroidal anti-inflammatory drugs; RBCs: Red blood cells.

According Belghiti *et al*[123] there is no significant difference in blood loss during surgery using the Pringle maneuver continuously or intermittently (15 min of ischemia for 5 min reperfusion). These concerns about longer periods of hepatic vascular inflow is mainly because that obstruction of the portal blood flow causes venous congestion of the bowel, and in combination with warm ischemic liver injury it results in a flush of anaerobic metabolites and cytokines back into the circulation on the clamp release[124]. In the total vascular exclusion[125], the occlusion of the hepatic vascular inflow is combined to hepatic venous exclusion. The complete hepatic ischemia can be associated to hypothermic perfusion with cooled preservation solution[126] and extracorporeal venovenous bypass, with "*ex situ*" liver resection[127] or "*in situ*" liver resection[128].

LCVP anesthesia

During the parenchymal transaction, a LCVP prevents the back bleeding from hepaticveins[19,129,130], and along with vascular control of the liver, these techniques test the patients cardiovascular reserve[21]. LCVP anesthesia is based on patients being maintained in hypovolaemic state until liver resection has been completed[19,129], this is in contrast to most other major surgical procedures, where patients receive large volumes of crystalloid and colloid during the peri-operative period[21]. Moreover, vasodilators are often used to further reduce central venous pressure (CVP), leading to distributive changes in blood flow[129], and whereas these techniques are applied for haemorrhage control and consequently promoting AKI prevention, a potential consequence of such circulatory changes is ATN, with subsequent renal impairment or failure[20]. The kidneys are at greater risk with abrupt fall in blood pressure, if the mean arterial pressure reaches values below 80 mmHg, there is a significant decrease in GFR[24].

In the study of Wang *et al*[131], the maintenance of CVP $\leq$ 4 mmHg has reduced blood loss during partial hepatectomy, and has shortened the length of hospital stay, with no detrimental effects on hepatic or renal function. According to Melendez *et al*[19], in 496 liver resections with an anesthetic protocol of fluid restriction, with the use of nitroglycerin, furosemide, and with the maintenance of a systolic blood pressure of 90 mmHg, the median volume blood loss was 645 mL and the incidence of AKI was 3.1%. A study with 2116 LCVP-assisted hepatectomies reported an estimated mean blood loss of 300 mL (IQR: 200-600 mL), 90-d mortality of 2%, and postoperative AKI of 16% in the whole cohort (13% at risk, 2% at injury and 1% experienced failure)[132]. A study reported a low incidence of AKI requiring renal replacement therapy after liver resection (< 1%), confirming that the routine use of LCVP anaesthesia in combination with intermittent inflow occlusion is safe[21].

Although there are strong evidences that LCVP during partial hepatectomy can minimize blood loss and mortality[19], it is not clear whether it would play a role

in AKI prevention, as renal perfusion pressure can be decreased during relative hypovolemia, thus, further studies are required to prove this hypothesis.

Prevention of post-hepatectomy liver failure

In order to reduce the incidence of PLF, a careful pre-operative planning and patient selection is mandatory. In the case of underlying cirrhosis, the best candidates for surgical resection are the exclusive Child-Pugh A patients with normal bilirubin values, the absence of clinical signs of portal hypertension (platelet count, splenomegaly and esophageal varices), only tumor diameter < 5 cm (without vascular invasion), asymptomatic and MELD < 8[107,133,134]. Hyperbilirubinemia, portal hypertension and clinical deterioration criteria are considered signs of poor postoperative course, despite the tumor resectability[135].

Analyzing the issue of remnant liver volume after partial hepatectomy, the functional quality of paren-chyma should not be ignored. In obtaining the computed tomography images, it enables the calculation of the future liver remnant (FLR), in patients with normal liver function, it must be greater than 25% of the liver total volume, corresponding to 0.5 of the patient weight. In patients with cirrhosis, prolonged exposure to chemotherapy and biliary obstruction, this value is 40%, corresponding to 0.7 of the patient weight[136]. The occlusion of a branch of the portal vein can be performed in order to minimize the occurrence of hepatic insuf-ficiency after major resections. This procedure makes possible the treatment of tumors previously classified as unresectable, providing contralateral liver hypertrophy, thereby increasing the FLR[137,138]. In some situations resectability only occurs when performing two sequential hepatectomies associated with portal ligation for mani-pulation of the FLR, the two-stage hepatectomy[139].

FINAL CONSIDERATIONS

In the context of liver resections, the risk assessment of postoperative AKI requires the analysis of multiple variables involved in this complex universe, but probably there are main factors which significantly influence these patients for the occurrence of AKI: The massive blood loss during operation with or without an increased renal susceptibility to ischemia, and the occurrence of PLF. Certainly, the key interventions for preventing postoperative AKI after partial hepatectomy would be an appropriate preoperative work up, careful patient selection for surgery and rigorous perioperative control of the patient hemodynamic status by the surgical team.

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