

Influence of cirrhosis in cardiac surgery outcomes

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Author contributions: Lopez-Delgado JC, Esteve F, Javierre C, Ventura JL and Mañez R wrote the paper; Farrero E, Torrado H, Rodríguez-Castro D and Carrio ML performed research; all authors approved the final version of the manuscript.

Conflict-of-interest: The authors declare no conflict of interest.

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Received: August 28, 2014

Peer-review started: August 29, 2014

First decision: October 14, 2014

Revised: November 10, 2014

Accepted: January 9, 2015

Article in press: January 12, 2015

Published online: April 18, 2015

cardiac surgery population. The presence of contributing factors for a poor outcome, such as coagulopathy, a poor nutritional status, an adaptive immune dysfunction, a degree of cirrhotic cardiomyopathy, and a degree of renal and pulmonary dysfunction, have to be taken into account for surgical evaluation when cardiac surgery is needed, together with the degree of liver disease and its primary complications. The associated pathophysiological characteristics that liver cirrhosis represents have a great influence in the development of complications during cardiac surgery and the postoperative course. Despite the population of cirrhotic patients who are referred for cardiac surgery is small and recommendations come from small series, since liver cirrhotic patients have increased their chance of survival in the last 20 years due to the advances in their medical care, which includes liver transplantation, they have been increasingly considered for cardiac surgery. Indeed, there is an expected rise of cirrhotic patients within the cardiac surgical population due to the increasing rates of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis, especially in western countries. In consequence, a more specific approach is needed in the assessment of care of these patients if we want to improve their management. In this article, we review the pathophysiology and outcome prediction of cirrhotic patients who underwent cardiac surgery.

Key words: Liver cirrhosis; Cardiac surgery; Outcomes; Coagulopathy; Nutritional status; Adaptive immune dysfunction; Cirrhotic cardiomyopathy

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Core tip: Cardiovascular risk factors are the same for the development of cardiomyopathy and chronic liver disease. Despite cirrhosis is not a recognized risk factor within the risk scores for cardiac surgery, it is well known that its pathophysiological characteristics have the potential for a higher surgical risk and poor prognosis in the perioperative course. In addition,

Abstract

Liver cirrhosis has evolved an important risk factor for cardiac surgery due to the higher morbidity and mortality that these patients may suffer compared with general

these types of patients are increasingly considered for cardiac surgery. Thus, there is a challenge in order to improve the outcome of these patients based on advances in procedures for cardiac surgeons and clinical perioperative management for physicians.

Lopez-Delgado JC, Esteve F, Javierre C, Ventura JL, Mañez R, Farrero E, Torrado H, Rodríguez-Castro D, Carrio ML. Influence of cirrhosis in cardiac surgery outcomes. *World J Hepatol* 2015; 7(5): 753-760 Available from: URL: <http://www.wjgnet.com/1948-5182/full/v7/i5/753.htm> DOI: <http://dx.doi.org/10.4254/wjh.v7.i5.753>

INTRODUCTION

Despite liver cirrhosis (LC) is not included within the most important cardiac surgery scores, such as European system for cardiac operative risk evaluation (EuroSCORE) or Parsonnet, it is considered a major preoperative risk factor in cardiac surgery (CS), and the outcome is strongly related to the severity of liver disease in those patients^[1]. The risk of mortality is higher compared with patients without cirrhosis, especially with advanced liver disease^[2,3].

The different anatomical and pathophysiological characteristics that cirrhosis represents have a significant influence in their perioperative course. Mortality has been widely studied among different series in the literature. It is recommended that CS can be done safely in patients with Child-Turcotte-Pugh (CTP) class B and C or with a higher model for end-stage liver disease score (MELD) with a cut-off ranging from 13 to 18^[1-5]. However, complications involving different features from the basis of different pathophysiological conditions are poorly described. Thus, further understanding is necessary to significantly modulate the current surgical results, and definitive recommendations and indications for CS in the cirrhotic population have to be reviewed. The understanding and evaluation of different score systems is also an area of interest to identify patients at risk. This review summarizes the influence of LC in CS based on current literature, including their clinical implications from a pathophysiological point of view. This is important since the advancement in the medical management and life expectancy of LC has led to the increased eligibility of those patients for CS in the past decades.

RESEARCH

Methods

The review of the indexed articles of series of patients with LC who underwent CS was performed by means of MEDLINE 1950 to March 2014 using the OVID interface. Only one manuscript was excluded from general LC analysis because it included patients from a past described series^[2]. The present review aim

to select manuscripts addressing outcome based on the degree of LC, such as MELD and/or CTP scores. Almost all the selected studies were retrospective, with only two of prospective profile^[5,6]. The selection of articles addressing the pathophysiology of cirrhotic patients and the implications in CS was done based on the importance, the latest publication and the citation of the manuscripts. Note that morbidities are not reported in detail in all the series and that the cause of death is reported in only approximately 60% of the dead patients.

Epidemiology of LC in CS

The frequency of LC patients who are referred for CS is low because of their compromised health status and poor expected survival. On the other hand, in recent years, increased longevity has contributed to the increased incidence of hepatocellular carcinoma and coronary artery disease in cirrhotic patients^[7].

Demographic characteristics of the series described in the literature and its aetiologies are showed in Tables 1 and 2. The aetiology of LC in those patients seems to be linked with the aetiology of LC in the general population and geographical differences: alcoholic LC is more frequent in western series while viral LC is more frequent in Asian series. One major problem is the absence of series from other countries or regions, such as Arabic countries or India.

The aetiology of LC is expected to change due to the global obesity epidemic, which is associated with the increasing prevalence of metabolic syndrome. In consequence, a large cohort of patients that will develop non-Alcoholic Steatohepatitis (NASH)/non-alcoholic fatty liver disease (NAFLD)-related LC is expected in CS^[8]. In future series, we would have to consider the emergence of this phenomenon, which have the same risk factors of cardiovascular disease.

Pathophysiological considerations of LC in CS

The estimation of liver functional reserve and the identification of coexisting pathophysiological disorders associated with LC are key issues in the evaluation of those patients before CS.

The occurrence of portal hypertension in LC leads to variceal bleeding, ascites and spontaneous bacterial peritonitis, and hepatic encephalopathy. Patients with LC are at higher risk of liver-related complications during the postoperative course of CS^[9]. In Tables 3 and 4 we show respectively the postoperative complications and the mortality causes of these patients. Morbidities are poorly studied in the majority of the series and LC predisposes to other complications in CS in addition to those liver-related complications. However, mortality is higher when liver-related complications occur.

Regarding the diagnosis of LC, despite liver biopsy remains the "gold standard", it is not imperative in clinical practice due to the advances in laboratory tests and imaging tools, such as abdominal ultrasound, computed tomography and magnetic resonance imaging^[10]. It

Table 1 Demographic characteristics of cirrhotic patients undergoing cardiac surgery

Ref.	Country	Age (yr)	Sex (male)	Liver cirrhosis aetiology					Mean MELD/ mean CTP
				Alcohol	Viral (Hep B/Hep C)	PBC/autoimmune	Congestive	Others	
Klemperer <i>et al</i> ^[48]	United States	65 ± 8.3	11 (84.6%)	10	2	1	-	-	NA
Suman <i>et al</i> ^[49]	United States	63.6 ± 12.6	27 (61.3%)	11	6 (3/3)	2	2	23	11.5 ± 4.2/6.29
Filsoofi <i>et al</i> ^[9]	United States	58 ± 10	20 (74%)	8	18 (5/13)	1	1	4	14.2 ± 4.2/NA
Lin <i>et al</i> ^[51]	China	56	14 (77.7%)	5	13	-	-	-	NA/NA
An <i>et al</i> ^[44]	China	53 ± 13	10 (41.6%)	1	15	-	7	1	NA/NA
Hayashida <i>et al</i> ^[50]	Japan	64 ± 12	11 (61.1%)	3	12	1	1	1	NA/NA
Murashita <i>et al</i> ^[52]	Japan	69.9 ± 9.4	5 (41.6%)	NA	NA	NA	NA	NA	NA/6.3
Morisaki <i>et al</i> ^[45]	Japan	69 ± 8.5	31 (73.8%)	5	27 (1/26)	2	7	7	11.8 ± 6/5.9 ± 1.6
Sugimura <i>et al</i> ^[55]	Japan	61.1 ± 11.2	11 (84.6%)	4	4 (0/4)	1	1	1	8.6 ± 2.5/6.7 ± 2
Morimoto <i>et al</i> ^[56]	Japan	69.8 ± 9.4	21 (65%)	7	25 (17/8)	-	-	-	11.5 ± 5.1/7.2 ± 1.9
Thielmann <i>et al</i> ^[1]	Germany	62 ± 10	38 (66.7%)	NA	NA	NA	NA	NA	13 ± 6/NA
Gundling <i>et al</i> ^[3]	Germany	65.4 ± 11.7	33 (70.2%)	25	6 (3/3)	1	1	14	NA/NA
Arif <i>et al</i> ^[54]	Germany	64 ± 10	82 (75.2%)	60	6	3	7	33	11.6 ± 5.1/6.4 ± 1.5
Bizouarn <i>et al</i> ^[6]	France	58.8 ± 13.9	8 (66.7%)	7	2	2	-	1	NA/NA
Vanhuyse <i>et al</i> ^[53]	France	65 ± 11	26 (76%)	20	11	2	-	1	12 ± 3.5/NA
Lopez-Delgado <i>et al</i> ^[5]	Spain	64.9 ± 11.6	10 (69%)	20	30 (4/26)	-	-	8	16 ± 5.4/NA

Hep: Hepatitis; PBC: Primary biliary cirrhosis; MELD: Model for end-stage liver disease; CTP: Child-Turcotte-Pugh; NA: Not available.

Table 2 Demographic characteristics of liver cirrhosis aetiologies by region

Region	LC etiology					Total
	Alcohol	Viral	PBC/autoimmune	Congestive	Others	
United States	29 (32.6%)	26 (29.2%)	4 (4.5%)	3 (3.4%)	27 (30.3%)	89
China	6 (14.3%)	28 (66.6%)	-	7 (16.8%)	1 (2.3%)	42
Japan	19 (17.4%)	68 (62.4%)	4 (3.6%)	9 (8.3%)	9 (8.3%)	109
Germany	75 (51%)	12 (8.2%)	4 (2.7%)	9 (6.1%)	47 (32%)	147
France	27 (60%)	13 (28.8%)	4 (9%)	-	1 (2.2%)	45
Spain	20 (34.5%)	30 (51.7%)	-	-	8 (13.8%)	58
Total (EU)	122 (48.8%)	55 (22%)	8 (3.2%)	9 (3.6%)	56 (22.4%)	250
Total (Asia)	25 (16.5%)	96 (63.5%)	4 (2.6%)	16 (10.8%)	10 (6.6%)	151

PBC: Primary biliary cirrhosis; LC: Liver cirrhosis.

Table 3 Postoperative complications of cirrhotic patients undergoing cardiac surgery

Ref.	Morbidities	RI-AKI	RRT needs	Sepsis	Pulmonary	Bleeding	Liver
Klemperer <i>et al</i> ^[48]	44% (7)	23% (3)	-	38% (5)	30% (4)	30% (4)	23% (3)
Suman <i>et al</i> ^[49]	-	13% (6)	-	11% (5)	-	-	27% (12)
Filsoofi <i>et al</i> ^[9]	52% (14)	15% (4)	15% (4)	18% (5)	22% (6)	7% (2)	15% (4)
Lin <i>et al</i> ^[51]	50% (9)	5% (1)	-	22% (4)	6% (1)	22% (4)	11% (2)
An <i>et al</i> ^[44]	75% (18)	29% (7)	-	17% (4)	29% (7)	25% (6)	12% (3)
Hayashida <i>et al</i> ^[50]	66.7% (12)	28% (5)	-	33% (6)	28% (5)	17% (3)	22% (4)
Murashita <i>et al</i> ^[52]	75% (9)	-	-	-	-	-	-
Morisaki <i>et al</i> ^[45]	31.7% (13)	-	-	-	-	-	-
Sugimura <i>et al</i> ^[55]	77% (10)	15% (2)	15% (2)	23% (3)	15% (2)	-	8% (1)
Morimoto <i>et al</i> ^[56]	53% (17)	9% (3)	-	9% (3)	29% (10)	26% (9)	11% (4)
Thielmann <i>et al</i> ^[1]	-	39% (22)	39% (22)	9% (5)	-	28% (16)	14% (8)
Arif <i>et al</i> ^[54]	> 50%	53% (58)	24% (26)	58% (63)	9% (10)	-	-
Bizouarn <i>et al</i> ^[6]	58% (7)	-	-	25% (3)	-	-	33% (4)
Vanhuyse <i>et al</i> ^[53]	-	21% (7)	-	50% (17)	9% (3)	18% (6)	12% (4)
Lopez-Delgado <i>et al</i> ^[5]	43.1% (25)	79% (46)	9% (5)	21% (12)	-	2% (1)	-
Ranges	31%-77%	5%-79%	9%-39%	11%-58%	6%-30%	2%-30%	8%-23%

RI-AKI: Renal insufficiency or acute kidney injury; RRT: Renal replacement therapies.

would be advisable to perform a preoperative evaluation of liver function in patients at risk with confirmed or suspected liver disease in order to stage the severity. The indocyanine green plasma disappearance rate (ICG-PDR)

is useful for assessing hepatic functional reserve and perfusion in the setting of CS. A lower preoperative ICG-PDR value (*e.g.*, below 8.2%/min) is an independent predictor for mortality after CS and a marker of

Table 4 Mortality¹ causes of cirrhotic patients undergoing cardiac surgery

Ref.	Liver	Sepsis	Bleeding	Cardiovascular	Other
Klemperer <i>et al</i> ^[48]	4				
Filsoofi <i>et al</i> ^[9]	3	2	1		1-Bowel ischaemia
Lin <i>et al</i> ^[51]	1				
An <i>et al</i> ^[44]		5	1		
Hayashida <i>et al</i> ^[50]	1	2			1
Sugimura <i>et al</i> ^[55]	1				
Morimoto <i>et al</i> ^[56]	1	2	2		2
Thielmann <i>et al</i> ^[11]	8	5	1	2	1-Bowel ischaemia
Gundling <i>et al</i> ^[3]	2	2		3	2
Bizouarn <i>et al</i> ^[6]	1				
Vanhuyse <i>et al</i> ^[53]	4	3			1; 1-Bowel ischaemia
Lopez-Delgado <i>et al</i> ^[5]	1	6			
Total	38.5% (27)	38.5% (27)	7.1% (5)	7.1% (5)	8.6% (6)

¹Thirty-day mortality or in-hospital mortality.

prolonged intensive care unit (ICU) treatment^[11,12].

Coagulopathy

Coagulopathy is a routine concern during CS, because the liver is the principal source of coagulation protein synthesis, including thrombopoietin, coagulation factors (II, V, VII, IX, X, XI, and XII), anticoagulation protein C, protein S, and antithrombin. In LC there is a decrease in both pro- and anti-coagulants. Thrombocytopenia due to poor nutritional status, hypersplenism and/or bleeding from varices may adversely influence bleeding problems. However, primary haemostasis may not be defective in LC and a low platelet count, if not severe, should not necessarily be considered as an automatic index of an increased risk of bleeding^[13].

Prothrombin time-derived international normalized ratio (PT-INR) is used to assess bleeding risk, prognosis in MELD score and to guide treatment of coagulation disturbances in clinical practice. The lack of improvement of PT-INR to the administration of vitamin K may reflect a poor hepatic reserve and a worse prognosis in CS of LC patients. Despite PT-INR provides a good measure of liver function, it only measures the activity of procoagulants. Thromboelastography provides better assessment of patient's degree of coagulopathy and offers information enabling immediate transfusion therapy, being useful in CS for guiding transfusion therapy^[14]. Thus, correction of severe thrombocytopenia and replenishment of vitamin K storages is mandatory before surgery, together with the assessment of coagulopathy status before and during surgery. Despite bleeding is a major concern during CS, it has shown an incidence of only 30% of significant postoperative bleeding and a low mortality in LC patients.

Immune dysfunction

Infections are an important cause of death in hospitalized cirrhotic patients, especially in the presence of advanced clinical stages of LC, and most of these are nosocomial infections^[15]. The presence of an innate and adaptive immune dysfunction in LC, the so called

cirrhosis-associated immune dysfunction syndrome, predisposes to an increased occurrence of systemic infections, having a simultaneous substantial impact on the development of liver dysfunction. Paradoxically, depression and overstimulation of immune system exist, resulting in an enhanced susceptibility to acute inflammatory processes. There is also a shift towards the persistence of inflammation leading to the progression of LC and the development of different complications, such as portal hypertension and hepatic encephalopathy^[16-18]. Sepsis is an important cause of mortality when is produced after CS leading to multi-system organ failure, especially impacting short-term outcome^[5]. In addition, the surgical invasiveness that cardiac surgery represents is an added risk factor for infections susceptibility, especially when cardiopulmonary bypass (CPB) is used^[19]. Septic problems range from 11% to 58% of the postoperative complications in these patients, being the main cause of known death together with liver-related repercussions.

Poor nutritional status

Nutritional status of LC is poor and the correct functioning of the immune and metabolic response systems is dependent on each other^[20]. As a result, LC patients do not have a sufficient nutritional reserve and may be functioning in a worse efficient metabolic state with an inadequate inflammatory and immune response to surgery. Preoperative serum albumin levels can be used to quantify nutritional status and underlying disease, with levels of albumin < 25 g/L being independently associated with an increased risk of reoperation for bleeding^[20]. Hypoalbuminaemia, a common condition in LC, also increased the risk of infection in CS patients^[21]. Sepsis is an important risk factor for mortality after CS, which produces a sepsis-induced cardiac dysfunction *per se*^[22]. Higher blood transfusion requirements after CS, which are associated with poor outcome, are also associated with an increased risk of infection at multiple sites, suggesting a system-wide immune response^[23]. The lack of response to the preoperative nutritional

support may be considered a surrogate marker of minimal hepatic reserve and poor prognosis in CS of LC patients.

Cardiac dysfunction

The evaluation of cardiovascular dysfunction in LC is crucial and it should be addressed preoperatively. The emergence of an underscoring NASH/NAFLD, especially in western countries, has the same risk factors for cardiovascular disease that other chronic liver disease^[24]. In addition, cardiovascular diseases are a common cause of mortality in LC because the severity of liver injury and inflammation is strongly associated with an increased cardiovascular risk and an atherogenic lipid profile^[25]. LC is associated with peripheral arterial vasodilatation, and activation of sodium and water retentive pathways which produces blood volume expansion and redistribution within the splanchnic bed. Thus, the resting hyperdynamic circulatory state with increased cardiac output is a response to splanchnic arterial vasodilatation. These changes increase with the progression of liver disease leading to cardiac failure. Cirrhotic cardiomyopathy develops a variety of progressive clinical manifestations being characterized by diastolic dysfunction along with impaired inotropic and chronotropic incompetence, leading to a suboptimal ventricular contractile response during stressful conditions, such as CS^[26]. Thus, hemodynamic postoperative management is crucial after CS and higher Central Venous Pressure is associated with worse short-term outcome^[5]. It seems that the assessment of preoperative cardiac function, even from a dynamic point of view with a dobutamine stress echocardiography, may play a role in the indication for CS and postoperative management in the setting of LC. Cirrhotic cardiomyopathy may also play a role in the pathogenesis of hepatorenal syndrome (HRS) or the development of acute kidney injury (AKI) in LC^[27].

If we exclude recurrent diseases, graft loss resulting from technical complications, and malignancies, cardiac complications are the most common cause of death after liver transplantation (LT). More than 50% of cirrhotic patients undergoing LT show a degree of cardiac dysfunction^[26]. There is a greater risk of cardiac deaths and ischemic events in LT patients as compared to age- and sex-matched population^[28]. A history of coronary artery disease, prior stroke, postoperative sepsis, and increased interventricular septal thickness are risk predictors after LT for early postoperative adverse cardiac events, such as myocardial infarction. These patients benefit from the use of perioperative β -blockers regardless of their risk profile^[29]. Theoretically, the same could be applied to cirrhotic patients who underwent CS, especially if we consider that those who underwent LT are patients with advanced cirrhosis. Cardiac dysfunction due to LC is poorly addressed after CS in those patients because the disease overlaps with other scenarios, such as low cardiac output syndrome.

AKI

Oliguria is a feature of AKI and renal dysfunction, a complication which is frequently present after CS and which has a strong influence on morbidity and mortality, even in long-term scenario^[30]. It leads to a positive fluid balance, resulting in vital organ edema^[31]. Having an appropriate renal function is closely related with a good cardiac output performance^[32]. LC leads to development of renal dysfunction and HRS which occurs in conjunction with microcirculatory dysfunction in other organs, including the heart and the peripheral vascular bed^[33]. Lower urine output in the first 24 h following surgery may be a valuable predictor of long-term outcome in patients with LC undergoing CS^[34]. It is difficult to compare AKI rates between series due to the differences in AKI definitions. However, assessment of preoperative renal function is of paramount importance due to the higher incidence of AKI after CS in those patients. AKI can be present in almost 80% of LC patients after CS and approximately 50% of them will need renal replacement therapies.

Pulmonary dysfunction

Ascites and fluid overload may cause or aggravate pulmonary function due to atelectasias and pulmonary edema. The end-expiratory lung volume can be decreased, leading to impairment in the mechanics of the respiratory system, lung and chest wall, as well as gas-exchange. Thus, initial use of moderate Positive End Expiratory Pressure is an advisable approach to improve oxygenation and compliance without causing adverse effects in the respiratory function^[35].

In advanced LC, hepatopulmonary syndrome, portopulmonary hypertension and hepatic hydrothorax are typical pulmonary complications. Whereas hepatopulmonary syndrome and portopulmonary hypertension represent pulmonary vascular diseases, the development of hepatic hydrothorax is associated with the presence of ascites and phrenic lesions. For severe hepatopulmonary syndrome and refractory hepatic hydrothorax, LT is the treatment of choice. In severe portopulmonary hypertension specific medical treatment is indicated. In selected patients, besides intravenous prostanooids, oral endothelin receptor antagonists and phosphodiesterase type-5 inhibitors are possible treatment options^[36,37]. These complications need to be screened in CS candidates, especially those with medical past history of respiratory failure and/or moderate or advanced LC patients because pulmonary complications can achieve an incidence of about 30%.

Pathophysiological considerations of CS

CS involves a systemic inflammatory response with the accumulation of both pro- and anti-inflammatory cytokines, which may be clinically irrelevant but may also lead to a worse outcome in many cases. Poor hepatosplanchnic perfusion affects intestinal mucosa, predisposing to endotoxemia, proinflammatory cytokine

Table 5 Operative characteristics of cirrhotic patients undergoing cardiac surgery

Ref.	Mean CPB (min)	Urgent-emergent	Type of surgery					
			CABG	Valve surgery	CABG + valve	Aortic	Other	Off pump (% mortality)
Klemperer <i>et al</i> ^[48]	102	9 (69.2%)	6	4	3	-	-	-
Suman <i>et al</i> ^[49]	114 ± 48	1 (2.3%)	16	16	10	-	2	-
Filsoufi <i>et al</i> ^[9]	142 ± 68	4 (15%)	8	12	-	3	4	5 (0%)
Lin <i>et al</i> ^[51]	138	-	4	13	1	-	-	2
An <i>et al</i> ^[44]	160 ± 53	7 (29.1%)	2	19	2	1	-	-
Hayashida <i>et al</i> ^[50]	151 ± 63	3 (16.7%)	6	9	1	1	1	3 (0%)
Murashita <i>et al</i> ^[52]	147 ± 41	0	3	9	-	-	-	2
Morisaki <i>et al</i> ^[45]	157 ± 50	7 (16.7%)	11	20	5	2	4	5
Sugimura <i>et al</i> ^[55]	242 ± 77	6 (46.1%)	1	7	1	3	1	3
Morimoto <i>et al</i> ^[56]	145 ± 98	7 (22%)	6	18	2	6	-	6
Thielmann <i>et al</i> ^[1]	125 ± 55	10 (18%)	24	11	19	-	3	2
Gundling <i>et al</i> ^[3]	101 ± 43	-	21	14	9	-	3	-
Arif <i>et al</i> ^[54]	-	23 (21%)	55	36	10	2	6	-
Bizouarn <i>et al</i> ^[6]	85	-	1	10	2	-	-	-
Vanhuyse <i>et al</i> ^[53]	100 ± 66	2 (6%)	13	20	-	-	-	1
Lopez-Delgado <i>et al</i> ^[5]	107 ± 37	3 (5.1%)	9	42	7	-	-	6 (0%)

CPB: Cardiopulmonary bypass; CABG: Coronary artery bypass graft.

release, and the systemic inflammatory response syndrome^[38]. Contact activation of factor XII by the extracorporeal circuit stimulates inflammation by the activation of the intrinsic coagulation pathway, kallikrein, and complement, worsening the coagulopathy status of LC^[39]. In addition, those physiologic risks associated with all major CS procedures (e.g., anesthesia, large volume transfusion) are amplified in the presence of LC due to the immunologic and metabolic higher demands that CPB imposes to the liver. The hemodynamics of CPB are non-physiological, with nonpulsatile flow and low cardiac output, leading to the ischemia-reperfusion hepatic injury. There is a decrease of the hepatic perfusion of approximately 20% and of the hepatic arterial blood flow of 20%-45% through vasoconstriction during CPB, resulting in an imbalanced oxygen supply^[40]. However, we should take into account that haemodilutional anaemia produced during CPB, even when below to a haematocrit of 20%, does not impair hepatic function and perfusion^[12]. In consequence, perioperative strategies that minimize or avoid, such as off-pump CS^[3], the duration of CPB and transfusion requirements together with higher perfusion flow rates (≥ 2.3 L/min), the addition of pulsatile perfusion, and more efficient circuits have a beneficial effect on hepatic function reducing injury and improving organ perfusion^[41,42]. Albumin, as priming solution for CPB, could have a more favourable profile in terms of bleeding in this scenario^[43]. Operative characteristics of cirrhotic patients undergoing CS described in the literature are shown in Table 5.

Predictors of outcome in LC patients undergoing CS

The survival and long-term outcomes of LC patients who underwent CS are related to the severity of their liver disease and also to the complications after cardiac surgery; especially those produced during ICU stay^[34]. Higher preoperative total plasma bilirubin, low

preoperative serum cholinesterase concentrations, prolonged CPB time, central venous pressure, preoperative and postoperative thrombocytopenia, operative time and age have all been identified as potential predictors of mortality after CS in LC patients^[5,44].

Although the European system for cardiac operative risk evaluation (EuroSCORE) is widely accepted in Europe as a valuable score in CS, in populations such as LC patients, do not have acceptable discriminatory ability. In addition, it does not take into account surgical prognosis factors such as CPB time^[45]. The development of local mortality risk scores corresponding to local epidemiological characteristics or a specific patient's population may improve the prediction of outcome and LC patients may benefit from it^[46]. Furthermore, the Parsonnet score does not consider specific liver variables. Because mortality in cirrhotic patients undergoing CS is associated with liver function, liver scores such as the MELD or CTP score are associated with outcome^[1]. MELD score most reliably identifies cirrhotic patients at high risk for CS. With regard to CTP class scores, mortality is higher in patients with a CTP score of class B and C^[1,5]. ICU scores such as simplified acute physiology score III provide an acceptable level of sensitivity and specificity, comparable with MELD results of other series, even in the long-term scenario^[1,5,47]. The postoperative long-term mortality rates reported in the literature are high for cirrhotic patients undergoing CS ranging from 40% to 70% at approximately six years. Comparing patients according to CTP score, mortality ranged from 45% to 80% in the Child A group and from 25% to approximately 50% in the Child B group. Mortality is extremely high in the Child C Group with a mean rate of 69.2%^[1-3,5]. In consequence, CS can be performed safely in CTP class A and in some class B patients or with a MELD cut-off ranging from 13 to 18^[1,3-5]. Regarding CTP class C patients, due to the higher mortality in these patients, liver function should be optimized prior to CS,

even performing LT.

CONCLUSION

There are physiological characteristics of LC and properties of CS itself that predispose to complications when LC patients undergo the surgical procedure. The occurrence of organ related dysfunctions is crucial for the development of post-CS complications and outcome, being closely related with preoperative status and the degree of surgical injury. Apart from the degree of liver disease, cardiovascular function, immune and nutritional status, renal function, degree of coagulopathy, and pulmonary function need to be also evaluated in order to perform an adequate prognosis, including postoperative management, and surgical approach. This is especially important in those patients with high risk profile, such as Child B and C, and/or high MELD. Since advanced LC represents a contraindication for CS, LT may be considered before CS in those patients.

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P- Reviewer: Li ZF, Velasco I S- Editor: Song XX
L- Editor: A E- Editor: Liu SQ





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