Influence of cirrhosis in cardiac surgery outcomes

Juan C Lopez-Delgado, Francisco Esteve, Casimiro Javierre, Josep L Ventura, Rafael Mañez, Elisabet Farrero, Herminia Torrado, David Rodríguez-Castro, Maria L Carrio

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 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

© The Author(s) 2015. Published by Baishideng Publishing Group Inc. All rights reserved.
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, Estève 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[4-5]. 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 pathophysiologic 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[7-9].

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[10]. 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
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 RI-AKI: Renal insufficiency or acute kidney injury; RRT: Renal replacement therapies.

### Table 1
Postoperative complications of cirrhotic patients undergoing cardiac surgery

| Ref.                | Morbidities | RI-AKI | RRT needs | Sepsis | Pulmonary | Bleeding | Liver |
|---------------------|-------------|--------|-----------|--------|-----------|----------|-------|
| Klempner et al.     | 44% (7)     | 23% (3) | -         | 38% (5) | 30% (4)   | 30% (4)  | 23% (5) |
| Suman et al.        | 13% (6)     | -      | -         | 11% (5) | -         | -        | 27% (12) |
|Filisoufi et al.     | 52% (14)    | 15% (4) | -         | 18% (5) | 22% (6)   | 7% (2)   | 15% (4) |
| Lin et al.          | 50% (9)     | 5% (1)  | -         | 22% (4) | 6% (1)    | 22% (4)  | 11% (2) |
| An et al.           | 75% (18)    | 29% (7) | -         | 17% (4) | 29% (7)   | 25% (6)  | 12% (5) |
| Hayashida et al.    | 66.7% (12)  | 28% (5) | -         | 33% (6) | 28% (5)   | 17% (3)  | 22% (4) |
| Murashita et al.    | 75% (9)     | -      | -         | -      | -         | -        | -     |
| Morisaki et al.     | 31.7% (13)  | -      | -         | -      | -         | -        | -     |
| Sugimura et al.     | 77% (10)    | 15% (2) | -         | 23% (3) | 15% (2)   | -        | 8% (1) |
| Morimoto et al.     | 53% (17)    | 9% (3)  | -         | 9% (3)  | 29% (10)  | 26% (9)  | 11% (4) |
| Thielmann et al.    | -           | 39% (22)| 39% (22)  | 9% (5)  | -         | 28% (16) | 14% (8) |
| Arif et al.         | > 50%       | 53% (58)| 24% (26)  | 58% (63)| 9% (10)   | -        | -     |
| Bizouarn et al.     | 58% (7)     | -      | -         | 25% (3) | -         | -        | 33% (4) |
| Vanhuyse et al.     | -           | 21% (7) | -         | 50% (17)| 9% (3)    | 18% (6)  | 12% (4) |
| Lopez-Delgado et al.| 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.
Table 4  Mortality\(^1\) causes of cirrhotic patients undergoing cardiac surgery

| Ref. | Liver | Sepsis | Bleeding | Cardiovascular | Other |
|------|-------|--------|----------|----------------|-------|
| Klempner et al\(^{[21]}\) | 4     |        |          |                |       |
| Filsoufi et al\(^{[8]}\) | 3     | 2      | 1        |                | 1-Bowel ischaemia |
| Lin et al\(^{[22]}\) | 1     |        |          |                |       |
| An et al\(^{[23]}\) | 5     | 1      |          |                |       |
| Hayashida et al\(^{[8]}\) | 1     | 2      |          |                |       |
| Sugimura et al\(^{[8]}\) | 1     |        |          |                |       |
| Morimoto et al\(^{[24]}\) | 1     | 2      | 2        |                |       |
| Thielmann et al\(^{[8]}\) | 8     | 5      | 1        | 2              | 1-Bowel ischaemia |
| Gundling et al\(^{[8]}\) | 2     | 2      |          | 3              | 2     |
| Bizzoarn et al\(^{[8]}\) | 1     |        |          |                |       |
| Vanhuysse et al\(^{[8]}\) | 4     | 3      |          |                | 1-Bowel ischaemia |
| Lopez-Delgado et al\(^{[8]}\) | 1     | 6      |          |                |       |
| Total | 38.5% (27) | 38.5% (27) | 7.1% (5) | 7.1% (5) | 8.6% (6) |

\(^1\)Thirty-day mortality or in-hospital mortality.

**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\(^{[19]}\). 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\(^{[20]}\). Hypoaalbuminaemia, 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 underscored 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\(^27\). 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
release, and the systemic inflammatory response syndrome. 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. 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 imbalance of oxygen supply. 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. In consequence, perioperative strategies that minimize or avoid, such as off-pump CS, 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. Albumin, as priming solution for CPB, could have a more favourable profile in terms of bleeding in this scenario. 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. 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. 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. 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. 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. The 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. 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. 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%. 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. Regarding CTP class C patients, due to the higher mortality in these patients, liver function should be optimized prior to CS.

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 et al. | 102 | 9 (69.2%) | 6 | 4 | 3 | - | - | - |
| Sumar et al. | 114 ± 48 | 1 (2.3%) | 16 | 16 | 10 | - | - | 2 |
| Filsoufi et al. | 142 ± 68 | 4 (15%) | 8 | 12 | - | 3 | 4 | 5 (0%) |
| Lin et al. | 158 | - | 4 | 13 | 1 | - | - | 2 |
| An et al. | 160 ± 53 | 7 (29.1%) | 2 | 19 | 2 | - | - | - |
| Hayashi et al. | 151 ± 63 | 3 (16.7%) | 6 | 21 | 1 | - | 1 | 3 (0%) |
| Murakawa et al. | 147 ± 41 | 0 | 3 | 1 | - | - | - | - |
| Morisaki et al. | 157 ± 50 | 7 (16.7%) | 11 | 20 | 5 | 2 | 4 | 5 |
| Sugimura et al. | 242 ± 77 | 6 (46.1%) | 1 | 7 | 1 | 3 | 1 | 3 |
| Morimoto et al. | 145 ± 98 | 7 (22%) | 6 | 18 | 2 | 6 | - | 6 |
| Thielmann et al. | 125 ± 55 | 10 (18%) | 21 | 14 | 9 | - | 3 | - |
| Gundling et al. | 101 ± 43 | - | 21 | 14 | 9 | - | 3 | - |
| Able et al. | 23 (21%) | 55 | 36 | 10 | - | 2 | 6 | - |
| Bizouarn et al. | 85 | - | 1 | 10 | 2 | - | - | - |
| Vanhuyse et al. | 100 ± 66 | 2 (6%) | 13 | 20 | - | - | 1 | - |
| Lopez-Delgado et al. | 107 ± 37 | 3 (5.1%) | 9 | 42 | 7 | - | - | 6 (0%) |

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

REFERENCES

1. Thielmann M, Mechmet A, Neuhäuser M, Wendt D, Tossios P, Canbay A, Massoudy P, Jakob H. Risk prediction and outcomes in patients with liver cirrhosis undergoing open-heart surgery. Eur J Cardiothorac Surg 2010; 38: 592-599 [PMID: 20413316 DOI: 10.1016/j.ejcts.2010.02.042]
2. Macaron C, Hanouna IA, Suman A, Lopez R, Johnston D, Carey WW. Safety of cardiac surgery for patients with cirrhosis and Child-Pugh scores less than 8. Clin Gastroenterol Hepatol 2012; 10: 535-539 [PMID: 22210437 DOI: 10.1016/j.cgh.2011.12.030]
3. Gundling F, Seidl H, Gansera L, Schuster T, Hoffmann E, Kemkes BM, Eichinger B, Gansera B, Schepp W, Schmidt F. Early and late outcomes of cardiac operations in patients with cirrhosis: a retrospective survival-rate analysis of 47 patients over 8 years. Eur J Gastroenterol Hepatol 2010; 22: 1466-1473 [PMID: 21346421 DOI: 10.1097/MEG.0b013e32834f59be]
4. Modl A, Vohra HA, Barlow CW. Do patients with liver cirrhosis undergoing cardiac surgery have acceptable outcomes? Interact Cardiovasc Thorac Surg 2010; 11: 630-634 [PMID: 20739405 DOI: 10.1510/ictvs.2010.241190]
5. Lopez-Delgado JC, Esteve F, Javierre C, Perez X, Torrado H, Carrio ML, Rodriguez-Castro D, Farrero E, Ventura JL. Short-term independent mortality risk factors in patients with cirrhosis undergoing cardiac surgery. Interact Cardiovasc Thorac Surg 2013; 16: 332-338 [PMID: 2324034 DOI: 10.1093/ictvs/ivs051]
6. Bizouar P, Ausseur A, Desseigne P, Le Teurnier Y, Nougarede B, Train M, Michaud JL. Early and late outcome after elective cardiac surgery in patients with cirrhosis. Ann Thorac Surg 1999; 67: 1334-1338 [PMID: 10355407]
7. Shaheen AA, Kaplan GG, Hubbard JN, Myers RP. Morbidity and mortality following coronary artery bypass graft surgery in patients with cirrhosis: a population-based study. Liver Int 2009; 29: 1141-1151 [PMID: 19515218 DOI: 10.1111/j.1478-2753.2009.02053.x]
8. Wong RJ, Ahmed A. Obesity and non-alcoholic fatty liver disease: Disparate associations among Asian populations. World J Hepatol 2014; 6: 263-273 [PMID: 24868320 DOI: 10.4245/wjg.v6.i5.263]
9. Filsouf F, Salzberg SP, Rahmanian PB, Schiano TD, Elesai H, Squire A, Adams DH. Early and late outcome of cardiac surgery in patients with liver cirrhosis. Liver Transpl 2007; 13: 990-995 [PMID: 17427174]
10. Nathangtsho IL, Brunt EM. Role of liver biopsy in nonalcoholic fatty liver disease. World J Gastroenterol 2014; 20: 9026-9037 [PMID: 25083076 DOI: 10.3748/wjg.v20.i27.9026]
11. Weis F, Kilger E, Beiras-Fernandez A, Hinske CL, Nassau K, Adnan L, Vicol C, Kur F, Möhlne P. Indocyanine green clearance as an outcome prediction tool in cardiac surgery: a prospective study. J Crit Care 2014; 29: 224-229 [PMID: 24332990 DOI: 10.1016/j.jcrc.2013.10.023]
12. Sander M, Spies CD, Berger K, Schröder T, Grubitzsch H, Wernecke KD, von Heymann C. Perioperative indocyanine green clearance is predictive for prolonged intensive care unit stay after coronary artery bypass grafting—an observational study. Crit Care 2009; 13: R149 [PMID: 19747406 DOI: 10.1186/cc8405]
13. Violi F, Basili S, Raparelli V, Chowdary P, Gatt A, Burroughs AK. Patients with liver cirrhosis suffer from primary haemostatic defects? Fact or fiction? J Hepatol 2011; 55: 1415-1427 [PMID: 21718688 DOI: 10.1016/j.jhep.2011.06.008]
14. Tripodi A, Caldwell SH, Hoffman M, Trotter JF, Sanyal AJ. Review article: the prothrombin time test as a measure of bleeding risk and prognosis in liver disease. Aliment Pharmacol Ther 2007; 26: 141-148 [PMID: 17593061]
15. Bajaj JS, O’Leary JG, Wong F, Reddy KR, Kamath PS. Bacterial infections in end-stage liver disease: current challenges and future directions. Gut 2012; 61: 1219-1225 [PMID: 22661495 DOI: 10.1136/gutjnl-2012-302339]
16. Bonnel AR, Bouchonvillatuck C, Reddy KR. Immune dysfunction and infections in patients with cirrhosis. Clin Gastroenterol Hepatol 2011; 9: 727-738 [PMID: 21397731 DOI: 10.1016/j.cgh.2011.02.031]
17. Duddempudi AT. Immunology in alcoholic liver disease. Clin Liver Dis 2012; 16: 687-698 [PMID: 23101977 DOI: 10.1016/j.cld.2012.08.003]
18. Sipeki N, Antal-Szalmas P, Lakatos PL, Papp M. Immune dysfunction in cirrhosis. World J Gastroenterol 2014; 20: 2564-2577 [PMID: 24627592 DOI: 10.3748/wjg.v20.i10.2564]
19. Raja SG, Berg GA. Impact of off-pump coronary artery bypass surgery on systemic inflammation: current best available evidence. J Card Surg 2007; 22: 445-455 [PMID: 17803591]
20. Engelman DT, Adams DH, Byrne JG, Aranki SF, Collins JJ, Couper GS, Alfreid EN, Cohn LH, Rizzo RJ. Impact of body mass index and albumin on morbidity and mortality after cardiac surgery. J Thorac Cardiovasc Surg 1999; 118: 866-873 [PMID: 10534602]
21. Rapp-Kesek D, Stähle E, Karlsson TT. Body mass index and albumin in the preoperative evaluation of cardiac surgery patients. Clin Nutr 2004; 23: 1398-1404 [PMID: 15556262]
22. McGuinness J, Boucher-Hayes D, Redmond JM. Understanding the inflammatory response to cardiac surgery. Surgeon 2008b; 6: 162-171 [PMID: 18581753]
23. Oliver E, Carrio ML, Rodriguez-Castro D, Javierre C, Farrero E, Torrado H, Castells E, Ventura JL. Relationships among haemoglobin level, packed red cell transfusion and clinical outcomes in patients after cardiac surgery. Intensive Care Med 2009; 35: 1548-1555 [PMID: 19547956 DOI: 10.1007/s00134-009-1526-0]
24. Vernon G, Baranova A, Younossi ZM. Systematic review: the epidemiology and natural history of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in adults. Aliment Pharmacol Ther 2011; 34: 274-285 [PMID: 21623852 DOI: 10.1111/j.1365-2036.2011.04724.x]
25. Alkhouri N, Tammini TA, Yerian L, Lopez R, Zein NN, Feldstein AE. The inflamed liver and atherosclerosis: a link between histologic severity of nonalcoholic fatty liver disease and increased cardiovascular risk. Dig Dis Sci 2010; 55: 2644-2650 [PMID: 19966252 DOI: 10.1007/s10620-009-0737-y]
26. Zardi EM, Abbate A, Zardi DM, Dobrina A, Margiotta D, Van Tassell BW, Afeltra A, Sanyal AJ. Cirrhotic cardiomyopathy. J Am Coll Cardiol 2010; 56: 539-549 [PMID: 20668208 DOI: 10.1016/j.jacc.2009.12.075]
27. Theocharidou E, Krag A, Bendsen F, Møller S, Burroughs AK. Cardiac dysfunction in cirrhosis - does adrenal function play a role? A hypothesis. Liver Int 2012; 32: 1327-1332 [PMID: 22292920 DOI: 10.1111/j.1478-3231.2011.02751.x]
28. Johnston SD, Morris JK, Cramb R, Gunson BK, Neuberger J. Cardiovascular morbidity and mortality after orthotopic liver transplantation. Transplantation 2002; 73: 901-906 [PMID: 12048657]
Lopez-Delgado JC et al. Cirrhosis influence in cardiac surgery

on coagulation and inflammatory response when used as priming solutions for cardiopulmonary bypass. Minerva Anestesiol 2010; 76: 584-591 [PMID: 20661198]

An Y, Xiao YB, Zhong QJ. Open-heart surgery in patients with liver cirrhosis: indications, risk factors, and clinical outcomes. Eur Surg Res 2007; 39: 67-74 [PMID: 17283429]

Morisaki A, Hosono M, Sasaki Y, Kubo S, Hirai H, Suehiro S, Shibata T. Risk factor analysis in patients with liver cirrhosis undergoing cardiovascular operations. Ann Thorac Surg 2010; 89: 811-817 [PMID: 20172135 DOI: 10.1016/j.athoracsur.2009.12.021]

Tournoupsik IK, Anagnostopoulos CE, Swistel DG, DeRose JJ. Does EuroSCORE predict length of stay and specific postoperative complications after cardiac surgery? Eur J Cardiothorac Surg 2005; 27: 128-133 [PMID: 15621484]

Sadeghi MM, Arasteh M, Gharipour M, Nilforough P, Sham-solktetabi H, Etseampour A, Sadeghi FM, Kiani A, Sadeghi PM, Farahmand N. Evaluation of accuracy of Euroscore risk model in prediction of perioperative mortality after coronary bypass graft surgery in Isfahan. J Res Med Sci 2011; 16: 787-792 [PMID: 22091308]

Klempner JD, Ko W, Krieger KH, Connolly M, Rosengart TK, Altorki NK, Lang S, Isom OW. Cardiac operations in patients with cirrhosis. Ann Thorac Surg 1998; 65: 85-97 [PMID: 9456100]

Suman A, Barnes DS, Zein NN, Levinthin GN, Connor JT, Carey WD. Predicting outcome after cardiac surgery in patients with cirrhosis: a comparison of Child-Pugh and MELD scores. Clin Gastroenterol Hepatol 2004; 2: 719-723 [PMID: 15290666]

Hayashida N, Shoujima T, Teshima H, Yokokura Y, Takagi K, Tomoeda H, Aoyagi S. Clinical outcome after cardiac operations in patients with cirrhosis. Ann Thorac Surg 2004; 77: 500-505 [PMID: 14759426]

Lin CH, Lin FY, Wang SS, Yu HY, Hsu RB. Cardiac surgery in patients with liver cirrhosis. Ann Thorac Surg 2005; 79: 1551-1554 [PMID: 15854932]

Murashita T, Komiy T, Tamura N, Sakaguchi G, Kobayashi T, Furukawa T, Matushita A, Sunagawa G. Preoperative evaluation of patients with liver cirrhosis undergoing open heart surgery. Gen Thorac Cardiovasc Surg 2009; 57: 293-297 [PMID: 19533274 DOI: 10.1007/s11748-008-0374-0]

Vanhuysse F, Maureira P, Portocarrero E, Laurent N, Lekelah M, Carteaux JP, Vilemop JC. Cardiac surgery in cirrhotic patients: results and evaluation of risk factors. Eur J Cardiothorac Surg 2012; 42: 293-299 [PMID: 22590226 DOI: 10.1093/ejcts/ezr320]

Arif R, Seppelt P, Schwills S, Kojic D, Ghodsizad A, Ruhparwar A, Karck M, Kallebesch K. Predictive risk factors for patients with cirrhosis undergoing heart surgery. Ann Thorac Surg 2012; 94: 1947-1952 [PMID: 22921237 DOI: 10.1016/j.athoracsur.2012.06.0 57]

Sugimura Y, Toyama M, Katoh M, Kato Y, Hisamoto K. Analysis of open heart surgery in patients with liver cirrhosis. Asian Cardiovasc Thorac Ann 2012; 20: 263-268 [PMID: 22718713 DOI: 10.1177/1055676612453393]

Morimoto N, Okada K, Okita Y. The model for end-stage liver disease (MELD) predicts early and late outcomes of cardiovascular operations in patients with liver cirrhosis. Ann Thorac Surg 2013; 96: 1672-1678 [PMID: 23987897 DOI: 10.1016/j.athoracsur.2013.06.007]

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