Review

Cardiovascular manifestation of end-stage liver disease and perioperative echocardiography for liver transplantation: anesthesiologist's view

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Liver transplantation (LT) is the curative therapy for decompensated cirrhosis. However, anesthesiologists can find it challenging to manage patients undergoing LT due to the underlying pathologic conditions of patients with end-stage liver disease and the high invasiveness of the procedure, which is frequently accompanied by massive blood loss. Echocardiography is a non-invasive or semi-invasive imaging tool that provides real-time information about the structural and functional status of the heart and is considered to be able to improve outcomes by enabling accurate and detailed assessments. This article reviews the pathophysiologic changes of the heart accompanied by cirrhosis that mainly affect hemodynamics. We also present a comparative review of the diagnostic criteria for cirrhotic cardiomyopathy published by the World Congress of Gastroenterology in 2005 and the Cirrhotic Cardiomyopathy Consortium in 2019. This article discusses the conditions that could affect hemodynamic stability and postoperative outcomes, such as coronary artery disease, left ventricular outflow tract obstruction, portopulmonary hypertension, hepatopulmonary syndrome, pericardial effusion, cardiac tamponade, patent foramen ovale, and ascites. Finally, we cover a number of intraoperative factors that should be considered, including intraoperative blood loss, rapid reaccumulation of ascites, manipulation of the inferior vena cava, post-reperfusion syndrome, and adverse effects of excessive fluid infusion and transfusion. This article aimed to summarize the cardiovascular manifestations of cirrhosis that can affect hemodynamics and can be evaluated using perioperative echocardiography. We hope that this article will provide information about the hemodynamic characteristics of LT recipients and stimulate more active use of perioperative echocardiography.

Keywords: Cardiomyopathies; Cirrhosis; Echocardiography; Liver transplantation.

INTRODUCTION

Liver transplantation (LT) is considered the only definitive therapy for decompensated cirrhosis or severe acute liver failure that can improve the expected lifespan and quality of life [1]. Despite improvements in hemodynamic monitoring devices and anesthetic techniques, LT remains an extremely challenging procedure for anesthesiologists. Not only does the procedure itself pose a high risk of massive blood loss [2], but patients with end-stage liver disease (ESLD) are fre-

quently accompanied by many conditions that contribute to hemodynamic instability, such as cirrhotic cardiomyopathy (CCM), pericardial effusion, coronary artery disease (CAD), portopulmonary hypertension (PoPH), electrolyte derangements, and large amounts of ascites [3–5].

Echocardiography is a powerful tool that directly visualizes the structural and functional status of the heart in real-time at the bedside [5]. Transthoracic echocardiography (TTE) is a non-invasive cardiac investigation technique that obtains images from the surface of the body through four acoustic windows: parasternal, apical, subcostal, and suprasternal notch [6]. Transesophageal echocardiography (TEE) is a semi-invasive imaging tool in which the probe is inserted into the esophagus, and images are obtained through the esophagus and stomach [7]. Moreover, echocardiography provides more reliable measures than traditional pressure-based indicators such as pulmonary artery occlusion pressure and central venous pressure. It also has a high diagnostic value for detecting systolic or diastolic dysfunction, wall motion abnormalities, valvular dysfunction, hypovolemia, volume overload, left ventricular outflow tract obstruction (LVOTO), pericardial abnormalities, intracardiac air, and thrombus [5,8]. Echocardiography is gaining popularity and is becoming more broadly adopted due to these advantages. TTE is recommended for all LT candidates by the American Association for the Study of Liver Diseases (AASLD) [1]. According to the American Society of Echocardiography (ASE) guidelines, the usefulness of intraoperative TEE during LT is supported by a grade B2 level of evidence [9], and TEE has already been widely utilized during LT in the United States [10]. In contrast, the use of pulmonary artery catheterization has decreased even though it is still recommended and useful [11].

Although anesthesiologists cannot fully play the role of cardiologists, perioperative echocardiography is still a feasible and useful option, considering that it provides additional accurate and detailed assessments that could affect patient management strategies with minimal or no risk to the patient. Perioperative echocardiography by anesthesiologists is especially helpful when performing emergency operations because the ability to complete a comprehensive preoperative evaluation of patients is unlikely [12,13]. As the majority of liver transplants are from deceased donors worldwide, most are likely to be emergency cases. Therefore, perioperative echocardiography by anesthesiologists seems a useful tool. Although in Korea, 75.2% of the LT were performed with livers from living donors in 2019, deceased donor LT

still accounted for 24.8% of the cases, which is not a negligible number [14].

PATHOPHYSIOLOGIC CHANGES OF CIRRHOSIS AND EFFECTS ON CARDIAC FUNCTION

Cirrhosis results from hepatic inflammation, fibrogenesis, angiogenesis, and loss of parenchymal cells. Structural and functional abnormalities of the liver lead to increased hepatic resistance and portal hypertension, which underlie most of the complications and mortality in patients with cirrhosis [15]. Subsequently, systemic vasodilation occurs mainly in the splanchnic vasculature bed because of increased circulating endothelial vasodilators from enhanced release and impaired degradation [16]. Decreased peripheral vascular resistance is initially compensated for by increased cardiac output, forming a characteristic circulatory status in patients with ESLD known as hyperdynamic circulation [17]. Relative arterial underfilling also stimulates baroreceptors and causes expansion of plasma volume with activation of the neurohumoral axis, including the renin-angiotensin-aldosterone system (RAAS), sympathetic nerve system (SNS), and arginine vasopressin [18]. Prolonged alterations in hemodynamic status and subsequent structural and functional changes in the heart could contribute to the development of CCM [19].

Structural change of heart

Structural remodeling of the heart has been reported in cirrhotic patients, including left ventricular hypertrophy, especially in the interventricular septum, and increased left ventricular end-systolic diameter, end-diastolic diameter, and volume of the left atrium. However, the degree of change seems modest [20–23].

Systolic dysfunction

In cirrhotic patients, systolic dysfunction is related to mortality and severe complications, such as hepatorenal syndrome (HRS) [24]. Some of the suspected causes of dysfunction are diminished β-adrenergic signaling, altered membrane current, and upregulation of endogenous cannabinoids and cardio-depressant substances [25–27]. Many cirrhotic patients are asymptomatic at rest and show normal or enhanced systolic function due to hyperkinetic circulatory

abnormalities [28]. However, when physically or pharmacologically challenged, they are unable to increase or even show decreased contractility, revealing dysfunction masked by hyperdynamic status [29–31]. This could be a plausible explanation for the deterioration of subclinical systolic dysfunction to overt heart failure under surgical stress or normalized pulmonary vascular resistance after LT [32,33].

The left ventricular ejection fraction (LVEF) is the most frequently used parameter to assess systolic function. However, it is limited in that it can be strongly affected by the loading condition, which may mask systolic dysfunction when afterload is severely decreased, as in cirrhotic patients [34]. Global longitudinal strain (GLS) is an emerging parameter for systolic function evaluation that indicates the percentage of systolic myocardial shortening in the longitudinal direction derived from automated speckle tracking echocardiography. GLS has been shown to be superior in detecting subclinical systolic dysfunction when LVEF is still within the normal range [35,36].

Diastolic dysfunction

Diastolic dysfunction is quite common in cirrhotic patients, with a reported prevalence ranging from 25.7% to 81.4% [37]. However, it is associated with adverse outcomes such as higher allograft rejection, graft failure, and mortality [38]. Diverse mechanisms have been suggested, including hypertrophy of the myocardium, cardiomyocyte edema, and patchy fibrosis, and consequently, increased stiffness of the myocardial wall [25,39]. Sodium retention may also contribute to diastolic dysfunction in patients [40]. Enhanced RAAS seems to play a role in fibrotic changes in the heart [41].

Diastolic function can be easily assessed using Doppler echocardiographic parameters. Deceleration time, isovolumetric relaxation time, and the ratio of early and late transmitral flow velocities (E/A) were included as diagnostic criteria for diastolic dysfunction in the 2005 Montreal guideline for CCM. The 2016 American Society of Echocardiography and European Association of Cardiovascular Imaging (ASE/EACVI) guidelines for diastolic dysfunction exploit the following parameters, which are also adopted in the updated diagnostic criteria for CCM by the Cirrhotic Cardiomyopathy Consortium (CCC): septal or lateral early diastolic mitral annular velocity (e'), E/e' ratio, tricuspid regurgitation (TR) velocity, and left atrial volume index (LAVI) [42,43].

Rhythm disturbance

There are two main abnormalities in rhythm disturbance: autonomic dysfunction and conduction abnormalities. Autonomic dysfunction is associated with increased SNS activity, reduced heart rate variability, baroreflex sensitivity, and chronotropic incompetence. Impaired autonomous nervous systems are thought to contribute to hemodynamic dysregulation in patients with cirrhosis [44]. Impaired function of the autonomous nervous system can be explained by altered lipid metabolism and disturbed nerve integrity, the influence of vasodilating substances, and inhibition of vagal function by increased angiotensin II [45,46]. Chronotropic incompetence refers to the inability to respond appropriately to physiological or pharmacological stimulation with an increased heart rate or contractility. Enhanced SNS activity and the resultant increased levels of circulating catecholamines and downregulation of β-adrenergic receptors are thought to be responsible for autonomic dysfunction. This is supported by evidence that abnormal cardiac distribution of sympathetic activity was observed in a study using meta-iodobenzylguanidine (mIBG), an analog of noradrenaline [44]. The prevalence is reported as high as 50% in cirrhotic patients, and the presence of chronotropic incompetence is related to adverse outcomes. Umphrey et al. [47] showed that cirrhotic patients who failed to achieve 82% of the maximum predicted heart rate on dobutamine stress echocardiography (DSE) were associated with increased perioperative complications after LT.

Prolonged QT interval is the most commonly observed conduction abnormality in patients with cirrhosis. The prevalence in cirrhotic patients is reported to be 30–60% when a rate-corrected QT (QTc) interval > 440 ms is applied as the cut-off value [48]. The degree of prolongation seems to be affected by the severity of liver disease, as seen in the correlation between the QT interval and Child-Pugh score [49]. The suspected mechanism for the abnormality includes potassium ion channel dysfunction, which can deteriorate by cytokine release during infection or bleeding [23,50]. QT prolongation has been associated with lethal ventricular arrhythmia, especially the type known as "torsades de pointes." Some studies have demonstrated an association between QT prolongation and an increased risk of sudden death or reduced survival. However, sudden cardiac death is rare in cirrhotic patients, and the clinical significance of prolonged QT intervals in cirrhotic patients remains unclear [48,51]. Atrial fibrillation is frequently encountered in pa-

tients with cirrhosis. The model for end-stage liver disease (MELD) has been shown to be a risk factor for new-onset atrial fibrillation. Autonomic dysfunction, inflammatory mediators, cytokines, vasoactive substances, and fibrotic pathways seem to play a role [52]. Electromechanical uncoupling, asynchrony of electrical and mechanical activation, is another example of a conduction abnormality reported in cirrhosis [53].

Right heart dysfunction

Reddy et al. [54] demonstrated that a high output state in cirrhotic patients and increased preload could elevate left ventricular filling pressure and, subsequently, pulmonary artery pressure. A chronically sustained hyperdynamic state may cause enlargement of the right heart and even heart failure [43]. Underlying PoPH may also contribute to the occurrence of right heart failure [8].

CIRRHOTIC CARDIOMYOPATHY: UPDATED CRITERIA IN 2019

These cardiovascular abnormalities, typically accompanied by cirrhosis, can be diagnosed as cirrhotic cardiomyopathy when they are severe enough to meet certain criteria. CCM refers to a pathological cardiac condition in patients with ESLD in the absence of prior heart disease [43]. Initially

believed to be the result of direct cardiac toxicity of alcohol in the 1950s, it was named for the first time in 1989 as 'cirrhotic cardiomyopathy' and started to be perceived as a syndrome of cardiac dysfunction in ESLD patients [55,56]. It was more clearly defined at the Montreal 2005 World Congress of Gastroenterology as an impaired contractile response to stress and/or diastolic dysfunction with electrophysiological abnormalities. In addition, diagnostic criteria for CCM have been proposed [40]. Recently, updated criteria with modern concepts of heart failure were proposed by a multidisciplinary expert group called the CCC in 2019 (Table 1) [43].

Heart failure is an important cause of death, accounting for 7–21% of post-LT mortality. Heart failure is also one of the leading causes of hospital admissions, accounting for 24% of admissions within 90 days of LT in the United States [57]. CCM is quite common and is believed to be present in approximately half of cirrhotic patients without symptoms at rest [58]. However, under conditions that impose physiological or pharmacological stress on the heart with CCM, such as infections, transjugular intrahepatic portosystemic shunt, and surgical stimuli during LT, cardiac dysfunction may be unmasked and progress to overt heart failure. Normalization of peripheral vasodilation in the post-LT period could also be a stressor in the heart with increased afterload and cause post-LT heart failure [32,33]. Moreover, the association between CCM and other conditions such as HRS and increased mortality and/or morbidity after therapeutic procedures has

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Table 1. Comparison of the Diagnostic Criteria for Cirrhotic Cardiomyopathy

Type of dysfunction	2005 Montreal criteria	2019 CCC criteria	Note
Systolic dysfunction	Any of the following is met: - LV ejection fraction < 55% - Blunted contractile response on stress testing	Any of the following is met: - LV ejection fraction < 50% - Absolute GLS < 18% or > 22%	More sensitive for detecting subclinical systolic dysfunction Validity of the adjusted cut-off value for LV ejection fraction has been questioned
Diastolic dysfunction	Any of the following is met: - Deceleration time > 200 ms - Isovolumetric relaxation time > 80 ms - E/A < 1	≥ 3 of the following is met:* - Septal e' velocity < 7 cm/s - E/e' ratio ≥ 15 - LAVI > 34 ml/m^2 - TR velocity > 2.8 m/s†	Updated to detect advanced diastolic dysfunction with increased specificity Concern exists about the prevalence of advanced diagnostic dysfunction being too low
Supportive criteria Or Area for future research	Abnormal chronotropic response	Abnormal chronotropic/inotropic response	Considered as potential additional markers, not diagnostic
	Electrophysiological abnormalities	Electrocardiographic changes	Prolonged QTc is no longer diagnostic
	Prolonged QTc interval	Electromechanical uncoupling	New potential serum biomarkers included (i.e., galectin-3)
	Enlarged left atrium	Serum biomarkers	CMRI is included for detecting subclinical myocardial dysfunction
	Increased myocardial mass	Chamber enlargement	
	Increased BNP, proBNP, troponin I	CMRI	

CCC: Cirrhotic Cardiomyopathy Consortium, LV: left ventricle, GLS: global longitudinal strain, E: early transmitral flow velocity, A: late transmitral flow velocity, e:' early diastolic mitral annular velocity, LAVI: left atrial volume index, TR: tricuspid regurgitation, BNP: brain natriuretic peptide, proBNP: prohormone of BNP, CMRI: cardiac magnetic resonance imaging. *Diagnosed with advanced (grade II or III) diastolic dysfunction. †Primary pulmonary hypertension or portopulmonary hypertension should be ruled out.

been observed in several studies [51]. Considering its high prevalence and harmful effects, it is a noteworthy complication that should be investigated prior to LT surgery.

The diagnostic criteria for CCM consist of three categories: systolic dysfunction, diastolic dysfunction, and other supportive criteria. In the 2005 Montreal criteria, systolic dysfunction was diagnosed when any of the following criteria were met: blunted contractile response on stress testing or LVEF < 55%. However, the usefulness of these criteria has been questioned for several reasons. First, there is no universally accepted definition of blunted contractile response. Second, stress testing is often limited or possibly confounded by factors such as the common use of β-adrenergic antagonists and the inability to perform exercise stress tests. Third, subclinical systolic dysfunction can be masked by decreased afterload due to the vasodilatory state of patients with cirrhosis. Fourth, together with the reasons mentioned above, additional parameters other than LVEF have been used to evaluate cardiac functional reserve. Considering these, the 2019 CCC guideline re-defined systolic dysfunction as when any of the following is present: LVEF ≤ 50%, absolute GLS < 18%, or > 22% [43]. GLS was included as it seems to be a more sensitive parameter of systolic function and a superior predictor of cardiac events and mortality than LVEF. In addition, it is relatively less dependent on loading conditions than LVEF [59,60]. Although there are limitations in that GLS is affected by age, sex, and loading condition, and only limited and conflicting evidence for the use of GLS in detecting CCM with normal LVEF is present, it is still believed to play a role in detecting subclinical systolic dysfunction in cirrhotic patients. Downward adjustment of the LVEF cut-off value from 55% to 50% was made without any detailed description in the article but was seemingly done to reflect normal values in the general population [43]. However, some researchers have questioned the validity of adjusted LVEF cut-off values based on post-LT mortality [61].

According to the 2005 Montreal criteria, diastolic dysfunction was diagnosed when any of the following criteria were met: deceleration time > 200 ms, isovolumetric relaxation time > 80 ms, or E/A < 1. However, these parameters can be affected by loading conditions and heart rate. In addition, a U-shaped relationship with the degree of diastolic dysfunction renders it difficult to distinguish between advanced and normal function [43]. Relatively new guidelines for the assessment of diastolic dysfunction were issued in 2016 by the ASE/EACVI. These guidelines have two different algorithms for screening and grading. To screen for diastolic dysfunc-

tion, the guidelines recommend four parameters: septal e,' the ratio of E to e' of the medial wall or average, TR velocity, and LAVI. For grading, E/A was used instead of septal e' velocity [42]. To simplify and integrate the two algorithms, Oh et al. [62] proposed a revised unified version that was adopted in the 2019 CCC criteria. In the 2019 CCC criteria, patients who met more than three of the following criteria were diagnosed as having advanced (grade II or III) diastolic dysfunction: septal e' velocity < 7 cm/s, E/e' ratio ≥ 15, LAVI > 34 ml/m^2 and TR velocity > 2.8 m/s. Notably, primary pulmonary hypertension or PoPH should be ruled out before applying the TR velocity criterion [43]. Compared to previous guidelines, the 2016 ASE/EACVI is considered simpler and more specific, with a significantly lower prevalence of diastolic dysfunction. However, there is a concern about the possibility that updated guidelines can only detect advanced cases [63]. The increased specificity of the 2016 ASE/EACVI guidelines was also observed in cirrhotic patients undergoing LT [64].

A number of features not included in both the systolic and diastolic function sections were classified as supportive criteria in the 2005 Montreal criteria. In the 2019 CCC criteria, the supportive criteria section was replaced by 'Area for Future Research Which Requires Further Validation.' Although the names and classifications of features have changed, they seem to include roughly similar content, except for several updates. The blunted contractile response has moved from the systolic dysfunction section to an area for future research, which requires further validation because of the limitations mentioned above. Electrophysiological abnormalities, including prolonged QTc interval, are no longer considered to have significant diagnostic value for CCM, with prevalence as high as 50% in cirrhosis and suspicious predictive power for poor outcomes. Serum biomarkers are recommended to be helpful when used in conjunction with imaging studies. A variety of biomarkers, such as nitric oxide, endothelin, copeptin, endocannabinoids, interleukins, and galectin-3, have been proposed as potentially useful parameters in the future. However, further studies are required to confirm their clinical application. In addition, previously recommended biomarkers, brain natriuretic peptide, pro-peptide N-terminal prohormone of BNP, and

T- and I-troponin, are still recognized for their clinical importance with their ability to reflect the severity of cirrhosis and cardiac dysfunction and predict morbidity and mortality. Cardiac magnetic resonance imaging is newly included in the criteria because it appears to have diagnostic value for

subclinical myocardial dysfunction and provides a comprehensive evaluation [43].

Studies on CCM reported its prevalence to be 46–63% in cirrhosis patients when the 2005 Montreal criteria were applied. Razpotnik et al. [58] conducted a study to compare the prevalence of CCM in 122 patients with cirrhosis using different criteria. They found that the overall prevalence was slightly higher with the 2005 Montreal criteria than the 2019 CCC criteria. However, the results differed remarkably between the two criteria when systolic and diastolic dysfunctions were analyzed separately. When the 2019 CCC criteria were applied, the prevalence of systolic dysfunction was higher (16.4% vs. 53.3%), while diagnostic dysfunction was lower (64.8% vs. 6.4%), reflecting the increased specificity of 2016 ASE/EACVI guidelines for diastolic dysfunction and more sensitive detection of subclinical systolic dysfunction by the implementation of GLS [58].

OTHER CLINICAL CONSIDERATIONS IN CIRRHOTIC PATIENTS

There are many pathological conditions accompanied by cirrhosis that can harmfully affect hemodynamic stability, as well as typical cardiovascular abnormalities, including CCM.

Coronary artery disease

The risk of ischemic heart disease is higher in patients with cirrhosis. Tiukinhoy-Laing et al. [65] evaluated the prevalence of CAD in LT candidates without known CAD and found that 26% of the patients had moderate to severe degree coronary stenosis. This result is consistent with another study that used multidetector computed tomographic angiography and found that only 9.2% of LT candidates showed normal coronary arteries, and 33.8% had moderate to severe stenosis [66]. Moreover, cirrhotic patients with non-alcoholic steatohepatitis, independent of traditional cardiac risk factors, have an increased perioperative risk of cardiovascular complications after LT [67,68]. Thus, it is not surprising that the incidence of ischemic events and cardiovascular mortality is as high as 2.5–3 times compared to the general population matched for cardiac risk factors [69]. However, the appropriate evaluation of CAD in patients with cirrhosis is limited for various reasons. Stress echocardiography, both exercise and pharmacological, is often limited because of physical constraints, chronotropic incompetence, common use of β-adrenergic antagonists, and a chronic state of vasodilation [8,70]. These limitations may contribute to the limited capability of DSE in LT patients. DSE in cirrhotic patients undergoing LT showed low sensitivity and moderate specificity for detecting CAD [71,72]. Invasive coronary angiography (CAG) is the gold standard for diagnosis and is recommended for patients at a high risk of CAD [73]. However, the invasiveness and risk of contrast-induced nephropathy have been concerns for CAG. Compared to CAG, coronary computed tomography angiography can be considered an acceptable non-invasive alternative with high sensitivity and negative predictive value [74]. Additional information about prognosis can be acquired with simple exercise testing, such as the 6-minute walk test, when available [75].

Dynamic left ventricular outflow tract obstruction

LVOTO is defined as a peak Doppler pressure gradient equal to or greater than 30 mmHg and is considered hemodynamically significant when the pressure gradient exceeds 50 mmHg [76]. Although typically related to hypertrophic cardiomyopathy or acute myocardial infarction, LVOTO can also occur under conditions such as decreased preload, afterload, increased heart rate, and contractility, which is similar to the pathophysiologic changes in cirrhotic patients. Substantial intraoperative blood loss, decrease in systemic vascular resistance during the reperfusion period, activation of the sympathetic nervous system by surgical stress, and intraoperative use of inotropic agents can induce LVOTO [77–79]. In some patients, LVOTO demonstrated during DSE was related to the occurrence of intraoperative hypotension [80]. Intraoperative TEE is useful for helping clinicians comprehend structural and functional abnormalities from real-time images and to guide the appropriate use of fluid and vasopressors [81].

Pulmonary vascular complications: portopulmonary hypertension and hepatopulmonary syndrome

Pulmonary vascular complications of cirrhosis occur mostly in two forms: PoPH and hepatopulmonary syndrome (HPS). PoPH is defined as pulmonary artery hypertension that occurs in association with portal hypertension irrespective of underlying liver cirrhosis [82]. It is related to increased mortality and morbidity, with a reported five-year survival of 14% when not treated and may lead to right heart failure if severe [83]. It is also associated with significant perioperative

KSTA

morbidity and mortality [84]. The current diagnostic criteria for PoPH include identified portal hypertension with or without cirrhosis, mean pulmonary artery pressure > 25 mmHg, pulmonary artery occlusion pressure ≤ 15 mmHg, and pulmonary vascular resistance > 240 dyn·s·cm^{-5} or 3 Wood units [85]. The prevalence of PoPH was recently reported to be 6.3–8.5% in LT candidates and showed no association with MELD scores [86,87]. The proposed underlying mechanism for PoPH is that increased CO imposes shear stress on the pulmonary vascular wall and stimulates the release of vasoactive proliferative mediators. Moreover, the entrance of unfiltered vasoactive substances, bacteria, and endotoxins from the splanchnic circulation into the pulmonary circulation via the portosystemic shunt contributes to the pathologic change [85]. Echocardiography is considered the best screening tool for PoPH [88]. The right ventricular systolic pressure can be calculated from the measured peak TR velocity using the Bernoulli equation and used to estimate the pulmonary artery pressure. Different cut-off values are used depending on the purpose. A cut-off value of 30 mmHg is highly sensitive (97%) and adequate for screening PoPH, whereas a cut-off value of 50 mmHg can be used to detect moderate to severe PoPH that should proceed to right heart catheterization for diagnosis and further evaluation [89,90]. Medical treatments for PoPH include phosphodiesterase type-5 inhibitors, prostacyclins, and endothelial receptor antagonists [88]. Although severe PoPH is considered a contraindication for LT, PoPH that responds appropriately to medical therapy is indicated for LT, and postoperative reversal of PoPH has been reported [91]. Maintaining hemodynamic stability is a challenge in patients with PoPH. Physiological disturbances such as hypoxia, hypercarbia, hypothermia, and acidosis should be avoided because they can lead to the deterioration of pulmonary hypertension. Judicious fluid infusion is also required because hypovolemia and fluid overload can lead to right ventricular dysfunction. When right heart function is compromised, several inotropic agents or pulmonary vasodilators should be considered [84].

Hepatopulmonary syndrome is characterized by intrapulmonary vascular dilatation (IPVD) and resultant arterial hypoxia in patients with cirrhosis [92]. Excessive IPVD leads to ventilation/perfusion mismatch, insufficient transit time for the oxygenation of red blood cells, intrapulmonary shunting, and consequent arterial hypoxia [93]. Contrast-enhanced echocardiography can also be used to diagnose HPS. Microbubbles that appear in the left heart between 4–6 beats after their appearance in the right heart are considered evidence of IPVD [92]. The prevalence of HPS has been reported to be 15–30% in LT candidates, depending on the study population [94]. Cirrhotic patients with HPS show increased mortality and morbidity compared to non-HPS patients. However, HPS does not appear to be a direct cause of death. Rather, the progression of cirrhosis and associated complications are related to adverse outcomes [93]. LT is the only curative therapy available for HPS. Although perioperative mortality was increased compared to non-HPS patients, Arguedas et al. showed that most patients who survived surgery showed improvements or resolution of the abnormalities within six to 12 months after LT [95]. HPS can manifest as intraoperative and postoperative hypoxia in the perioperative period and frequently requires prolonged postoperative mechanical ventilation. However, an analysis of recent studies showed that perioperative mortality, which occurred as a direct consequence of HPS, did not increase [92].

Pericardial effusion and cardiac tamponade

Pericardial effusion is reported to be common in cirrhotic patients, with a prevalence of 4–10% and up to 63% in decompensated cirrhosis. The pathophysiology of cirrhosis, including fluid retention, seems to play a role, and effusion is reported to resolve after LT [96,97]. The estimated size of effusion and presence of hemodynamic compromise should be evaluated using echocardiography [98]. Hemodynamic compromise can be assessed by chamber collapse and characteristic alterations of mitral and tricuspid flow according to respiration [99]. Preemptive drainage can be considered when a large amount of effusion with a possible risk of hemodynamic compromise is identified [100]. Rarely, tense ascites can also compress the heart, causing hemodynamic compromise with a constrictive pathology [101].

Patent foramen ovale

Patent foramen ovale (PFO) is quite common in the general population, with a prevalence of PFO from autopsy studies of around 26% [102]. PFO has been associated with cryptogenic stroke, although its clinical significance and need for extensive closure are controversial [103]. The risk of paradoxical embolism in LT recipients is expected to increase further because remarkable hemodynamic changes and large fluid shifts might change intracardiac flow dynamics, and air emboli can be formed during surgery. Despite the theoretical possibility of paradoxical embolism and the

presence of several reported cases, data on perioperative stroke in cirrhotic patients with PFO is too rare to evaluate the incidence [104]. Furthermore, several studies have reported no increased adverse outcomes in patients with PFO following LT [105,106]. Hence, it is advised not to close the PFO in patients without a previous history of stroke before LT [104].

Ascites

Removal of large-volume ascites results in the faster reaccumulation of ascites and hypotension in patients with cirrhosis. Although not yet fully understood, suspected pathophysiology includes simple fluid shifting and, more importantly, mechanical decompression followed by a decrease in systemic vascular resistance in response to increased perfusion and shear stress [4,107]. Drainage of large-volume ascites is believed to contribute to fluid shift and intraoperative hypovolemia during the preanhepatic phase of LT [108].

CLINICAL CONSIDERATIONS FOR INTRAOPERATIVE RISK OF LIVER TRANSPLANTATION

Intraoperative hemodynamic instability during LT is associated with various contributing factors. Intraoperative blood loss is one of the most common and important risk factors. LT frequently results in massive blood loss. A recent study investigated 108 LT patients with an average intraoperative blood loss of 1,505.8 ml. Blood loss of more than 1,000 ml was observed in 72.2% of cases and more than 2,000 ml in 14.8% [109]. Although several possible predictors have been suggested, massive blood loss is still considered unpredictable with conflicting and inconsistent results. Therefore, sufficient intravenous access and blood products should be prepared before surgery [110]. The aforementioned abdominal decompression by drainage of ascites and opening of the abdomen may also contribute to decreased preload with vasodilation and reaccumulation of ascites [4,107]. Intraoperative manipulation of the inferior vena cava (IVC), including clamping of the IVC during the anhepatic phase and release for reperfusion, is another major contributor to abrupt changes in the preload during surgery. During clamping of the IVC, the significantly decreased preload should be replaced with fluid resuscitation to maintain hemodynamic stability. However, a decrease in preload is transient, and excessive fluid infusion may result in worsened hemodynamic

instability, especially in the setting of right ventricular dysfunction [111]. Fluid overload is strongly associated with postoperative pulmonary complications [112]. In addition to fluid infusion, the transfusion of blood products is associated with pulmonary complications through transfusion-associated circulatory overload and transfusion-related acute lung injury [113]. Therefore, judicious fluid infusion and transfusion are required, and intraoperative TEE can be useful for guiding fluid infusion and transfusion when used in conjunction with hemodynamic parameters [114,115]. The reperfusion phase, which starts with unclamping of the IVC, is considered the most critical stage of LT in which major hemodynamic events are frequently encountered. Post-reperfusion syndrome (PRS) refers to an event that presents as severe hypotension, bradycardia, and low systemic vascular resistance within 5 min after unclamping. Cold, acidic, hyperkalemic blood that contains vasoactive inflammatory substances from ischemic grafts is thought to be responsible for PRS [116]. The relationship between PRS and CCM is not yet clear, with insufficient and inconsistent data. However, one study demonstrated a correlation between diastolic dysfunction and PRS, indicating a possible association [117]. These intraoperative hemodynamic instabilities and metabolic changes impose remarkable stress on the recipient's heart. As shown by the association mentioned above between cardiac dysfunction and adverse outcomes, cirrhotic patients with cardiac dysfunction may be more vulnerable to such stress. Unfortunately, there is no reliable method for identifying LT candidates with a high risk of perioperative cardiac complications.

CONCLUSIONS

Cardiovascular abnormalities are frequently observed in patients with ESLD. Although LT is the only definitive therapy for ESLD, LT imposes remarkable stress on the heart, such as rapid hemodynamic changes and metabolic disturbances. As a result of underlying pathological conditions and acute stressful stimuli, cardiovascular complications account for a considerable portion of perioperative morbidity and mortality in LT recipients. Echocardiography is a powerful non- or semi-invasive tool that directly visualizes the structural and functional state of the heart, such as chamber sizes, systolic and diastolic function, valvular function, and pulmonary artery pressure. It can be used to evaluate the heart condition prior to surgery and intraoperatively to assess hemodynamic status. The usefulness of echocardiogra-

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phy can be inferred from the fact that the AASLD recommends the preoperative use of TTE for all candidates, and the ASE recommends intraoperative TEE with a grade B level of evidence. We recommend the use of preoperative TTE and intraoperative TEE for LT, if not contraindicated. CAG or coronary computed tomography angiography should be considered in patients with a high risk of CAD, as stress echocardiography is often limited. Broader application of echocardiography and further research would be able to improve LT outcomes in the future.

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CONFLICTS OF INTEREST

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AUTHOR CONTRIBUTIONS

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REFERENCES

1. Martin P, DiMartini A, Feng S, Brown R Jr, Fallon M. Evaluation for liver transplantation in adults: 2013 practice guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. Hepatology 2014; 59: 1144-65.

2. Bang SR, Ahn HJ, Kim GS, Yang M, Gwak MS, Ko JS, et al. Predictors of high intraoperative blood loss derived by simple and objective method in adult living donor liver transplantation. Transplant Proc 2010; 42: 4148-50.

3. Adelmann D, Kronish K, Ramsay MA. Anesthesia for liver transplantation. Anesthesiol Clin 2017; 35: 491-508.

4. Lindsay AJ, Burton J, Ray CE Jr. Paracentesis-induced circulatory dysfunction: a primer for the interventional radiologist. Semin Intervent Radiol 2014; 31: 276-8.

5. Rudnick MR, Marchi LD, Plotkin JS. Hemodynamic monitoring during liver transplantation: a state of the art review. World J Hepatol 2015; 7: 1302-11.

6. Mitchell C, Rahko PS, Blauwet LA, Canaday B, Finstuen JA, Foster MC, et al. Guidelines for performing a comprehensive transthoracic echocardiographic examination in adults: recommendations from the American Society of Echocardiography. J Am Soc Echocardiogr 2019; 32: 1-64.

7. Prabhu M, Raju D, Pauli H. Transesophageal echocardiography: instrumentation and system controls. Ann Card Anaesth 2012; 15: 144-55.

8. VanWagner LB, Harinstein ME, Runo JR, Darling C, Serper M, Hall S, et al. Multidisciplinary approach to cardiac and pulmonary vascular disease risk assessment in liver transplantation: an evaluation of the evidence and consensus recommendations. Am J Transplant 2018; 18: 30-42.

9. Porter TR, Shillcutt SK, Adams MS, Desjardins G, Glas KE, Olson JJ, et al. Guidelines for the use of echocardiography as a monitor for therapeutic intervention in adults: a report from the American Society of Echocardiography. J Am Soc Echocardiogr 2015; 28: 40-56.

10. Soong W, Sherwani SS, Ault ML, Baudo AM, Herborn JC, De Wolf AM. United States practice patterns in the use of transesophageal echocardiography during adult liver transplantation. J Cardiothorac Vasc Anesth 2014; 28: 635-9.

11. Hofer RE, Vogt MNP, Taner T, Findlay JY. Influence of intraoperative transesophageal echocardiography and pulmonary artery catheter monitoring on outcomes in liver transplantation. Transplant Direct 2020; 6: e525.

12. Canty DJ, Royse CF. Audit of anaesthetist-performed echocardiography on perioperative management decisions for non-car-

diac surgery. Br J Anaesth 2009; 103: 352-8.

13. Kobal SL, Trento L, Baharami S, Tolstrup K, Naqvi TZ, Cercek B, et al. Comparison of effectiveness of hand-carried ultrasound to bedside cardiovascular physical examination. Am J Cardiol 2005; 96: 1002-6.

14. Korean Network for Organ Sharing. Annual report of the transplant 2019. Seoul: Korean Network for Organ Sharing; 2020 Aug. Report No.: 11-1352159-001434-10. 262 p.

15. Tsochatzis EA, Bosch J, Burroughs AK. Liver cirrhosis. Lancet 2014; 383: 1749-61.

16. Kontos HA, Shapiro W, Mauck HP, Patterson JL Jr. General and regional circulatory alterations in cirrhosis of the liver. Am J Med 1964; 37: 526-35.

17. Abraldes JG, Iwakiri Y, Loureiro-Silva M, Haq O, Sessa WC, Groszmann RJ. Mild increases in portal pressure upregulate vascular endothelial growth factor and endothelial nitric oxide synthase in the intestinal microcirculatory bed, leading to a hyperdynamic state. Am J Physiol Gastrointest Liver Physiol 2006; 290: G980-7.

18. Schrier RW. Water and sodium retention in edematous disorders: role of vasopressin and aldosterone. Am J Med 2006; 119(7 Suppl 1): S47-53.

19. Dourakis SP, Geladari E, Geladari C, Vallianou N. Cirrhotic cardiomyopathy: the interplay between liver and cardiac muscle. How does the cardiovascular system react when the liver is diseased? Curr Cardiol Rev 2021; 17: 78-84.

20. Li X, Yu S, Li L, Han D, Dai S, Gao Y. Cirrhosis-related changes in left ventricular function and correlation with the model for end-stage liver disease score. Int J Clin Exp Med 2014; 7: 5751-7.

21. Rector WG Jr, Adair O, Hossack KF, Rainguet S. Atrial volume in cirrhosis: relationship to blood volume and plasma concentration of atrial natriuretic factor. Gastroenterology 1990; 99: 766-70.

22. Møller S, Søndergaard L, Møgelvang J, Henriksen O, Henriksen JH. Decreased right heart blood volume determined by magnetic resonance imaging: evidence of central underfilling in cirrhosis. Hepatology 1995; 22: 472-8.

23. Møller S, Hove JD, Dixen U, Bendtsen F. New insights into cirrhotic cardiomyopathy. Int J Cardiol 2013; 167: 1101-8.

24. Krag A, Bendtsen F, Henriksen JH, Møller S. Low cardiac output predicts development of hepatorenal syndrome and survival in patients with cirrhosis and ascites. Gut 2010; 59: 105-10.

25. Ma Z, Lee SS. Cirrhotic cardiomyopathy: getting to the heart of the matter. Hepatology 1996; 24: 451-9.

26. Møller S, Henriksen JH. Cirrhotic cardiomyopathy: a pathophysiological review of circulatory dysfunction in liver disease. Heart 2002; 87: 9-15.

27. Baldassarre M, Giannone FA, Napoli L, Tovoli A, Ricci CS, Tufoni M, et al. The endocannabinoid system in advanced liver cirrhosis: pathophysiological implication and future perspectives. Liver Int 2013; 33: 1298-308.

28. Gould L, Shariff M, Zahir M, Di Lieto M. Cardiac hemodynamics in alcoholic patients with chronic liver disease and a presystolic gallop. J Clin Invest 1969; 48: 860-8.

29. Wong F, Girgrah N, Graba J, Allidina Y, Liu P, Blendis L. The cardiac response to exercise in cirrhosis. Gut 2001; 49: 268-75.

30. Kelbaek H, Eriksen J, Brynjolf I, Raboel A, Lund JO, Munck O, et al. Cardiac performance in patients with asymptomatic alcoholic cirrhosis of the liver. Am J Cardiol 1984; 54: 852-5.

31. Liu H, Lee SS. Cardiopulmonary dysfunction in cirrhosis. J Gastroenterol Hepatol 1999; 14: 600-8.

32. Zardi EM, Abbate A, Zardi DM, Dobrina A, Margiotta D, Van Tassell BW, et al. Cirrhotic cardiomyopathy. J Am Coll Cardiol 2010;56:539-49. Erratum in: J Am Coll Cardiol 2010; 56: 1000.

33. Sampathkumar P, Lerman A, Kim BY, Narr BJ, Poterucha JJ, Torsher LC, et al. Post-liver transplantation myocardial dysfunction. Liver Transpl Surg 1998; 4: 399-403.

34. Monge García MI, Jian Z, Settels JJ, Hunley C, Cecconi M, Hatib F, et al. Determinants of left ventricular ejection fraction and a novel method to improve its assessment of myocardial contractility. Ann Intensive Care 2019; 9: 48.

35. Flachskampf FA, Blankstein R, Grayburn PA, Kramer CM, Kwong RYK, Marwick TH, et al. Global longitudinal shortening: a positive step towards reducing confusion surrounding global longitudinal strain. JACC Cardiovasc Imaging 2019; 12(8 Pt 1): 1566-7.

36. Russo C, Jin Z, Elkind MS, Rundek T, Homma S, Sacco RL, et al. Prevalence and prognostic value of subclinical left ventricular systolic dysfunction by global longitudinal strain in a community-based cohort. Eur J Heart Fail 2014; 16: 1301-9.

37. Stundiene I, Sarnelyte J, Norkute A, Aidietiene S, Liakina V, Masalaite L, et al. Liver cirrhosis and left ventricle diastolic dysfunction: systematic review. World J Gastroenterol 2019; 25: 4779-95.

38. Mittal C, Qureshi W, Singla S, Ahmad U, Huang MA. Pre-transplant left ventricular diastolic dysfunction is associated with post transplant acute graft rejection and graft failure. Dig Dis Sci 2014; 59: 674-80.

39. Møller S, Henriksen JH. Cirrhotic cardiomyopathy. J Hepatol 2010; 53: 179-90.

40. Møller S, Henriksen JH. Cardiovascular complications of cirrhosis. Gut 2008; 57: 268-78.

41. AlQudah M, Hale TM, Czubryt MP. Targeting the renin-angiotensin-aldosterone system in fibrosis. Matrix Biol 2020; 91-92:

92-108.

42. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF 3rd, Dokainish H, Edvardsen T, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2016; 29: 277-314.

43. Izzy M, VanWagner LB, Lin G, Altieri M, Findlay JY, Oh JK, et al. Cirrhotic Cardiomyopathy Consortium. Redefining cirrhotic cardiomyopathy for the modern era. Hepatology 2020; 71: 334-45.

44. Møller S, Mortensen C, Bendtsen F, Jensen LT, Gøtze JP, Madsen JL. Cardiac sympathetic imaging with mIBG in cirrhosis and portal hypertension: relation to autonomic and cardiac function. Am J Physiol Gastrointest Liver Physiol 2012; 303: G1228-35.

45. Ates F, Topal E, Kosar F, Karincaoglu M, Yildirim B, Aksoy Y, et al. The relationship of heart rate variability with severity and prognosis of cirrhosis. Dig Dis Sci 2006; 51: 1614-8.

46. Newton JL, Allen J, Kerr S, Jones DE. Reduced heart rate variability and baroreflex sensitivity in primary biliary cirrhosis. Liver Int 2006; 26: 197-202.

47. Umphrey LG, Hurst RT, Eleid MF, Lee KS, Reuss CS, Hentz JG, et al. Preoperative dobutamine stress echocardiographic findings and subsequent short-term adverse cardiac events after orthotopic liver transplantation. Liver Transpl 2008; 14: 886-92.

48. Baik SK, Fouad TR, Lee SS. Cirrhotic cardiomyopathy. Orphanet J Rare Dis 2007; 2: 15.

49. Bernardi M, Calandra S, Colantoni A, Trevisani F, Raimondo ML, Sica G, et al. Q-T interval prolongation in cirrhosis: prevalence, relationship with severity, and etiology of the disease and possible pathogenetic factors. Hepatology 1998; 27: 28-34.

50. Ward CA, Ma Z, Lee SS, Giles WR. Potassium currents in atrial and ventricular myocytes from a rat model of cirrhosis. Am J Physiol 1997; 273(2 Pt 1): G537-44.

51. Wiese S, Hove JD, Bendtsen F, Møller S. Cirrhotic cardiomyopathy: pathogenesis and clinical relevance. Nat Rev Gastroenterol Hepatol 2014; 11: 177-86.

52. Huang WA, Dunipace EA, Sorg JM, Vaseghi M. Liver disease as a predictor of new-onset atrial fibrillation. J Am Heart Assoc 2018; 7: e008703.

53. Wong F. Cirrhotic cardiomyopathy. Hepatol Int 2009; 3: 294-304.

54. Reddy YNV, Melenovsky V, Redfield MM, Nishimura RA, Borlaug BA. High-output heart failure: a 15-year experience. J Am Coll Cardiol 2016; 68: 473-82.

55. Lee SS. Cardiac abnormalities in liver cirrhosis. West J Med 1989; 151: 530-5.

56. Timoh T, Protano MA, Wagman G, Bloom M, Vittorio TJ. A perspective on cirrhotic cardiomyopathy. Transplant Proc 2011; 43: 1649-53.

57. VanWagner LB, Serper M, Kang R, Levitsky J, Hohmann S, Abecassis M, et al. Factors associated with major adverse cardiovascular events after liver transplantation among a national sample. Am J Transplant 2016; 16: 2684-94.

58. Razpotnik M, Bota S, Wimmer P, Hackl M, Lesnik G, Alber H, et al. The prevalence of cirrhotic cardiomyopathy according to different diagnostic criteria. Liver Int 2021; 41: 1058-69.

59. Namazi F, van der Bijl P, Hirasawa K, Kamperidis V, van Wijngaarden SE, Mertens B, et al. Prognostic value of left ventricular global longitudinal strain in patients with secondary mitral regurgitation. J Am Coll Cardiol 2020; 75: 750-8.

60. Krishnasamy R, Isbel NM, Hawley CM, Pascoe EM, Burrage M, Leano R, et al. Left ventricular global longitudinal strain (GLS) is a superior predictor of all-cause and cardiovascular mortality when compared to ejection fraction in advanced chronic kidney disease. PLoS One 2015; 10: e0127044.

61. Kwon HM, Moon YJ, Jung KW, Park YS, Kim KS, Jun IG, et al. Appraisal of cardiac ejection fraction with liver disease severity: implication in post-liver transplantation mortality. Hepatology 2020; 71: 1364-80.

62. Oh JK, Miranda WR, Bird JG, Kane GC, Nagueh SF. The 2016 diastolic function guideline: is it already time to revisit or revise them? JACC Cardiovasc Imaging 2020; 13(1 Pt 2): 327-35.

63. Almeida JG, Fontes-Carvalho R, Sampaio F, Ribeiro J, Bettencourt P, Flachskampf FA, et al. Impact of the 2016 ASE/EACVI recommendations on the prevalence of diastolic dysfunction in the general population. Eur Heart J Cardiovasc Imaging 2018; 19: 380-6.

64. Park J, Lee J, Kwon A, Choi HJ, Chung HS, Hong SH, et al. The 2016 ASE/EACVI recommendations may be able to more accurately identify patients at risk for diastolic dysfunction in living donor liver transplantation. PLoS One 2019; 14: e0215603.

65. Tiukinhoy-Laing SD, Rossi JS, Bayram M, De Luca L, Gafoor S, Blei A, et al. Cardiac hemodynamic and coronary angiographic characteristics of patients being evaluated for liver transplantation. Am J Cardiol 2006; 98: 178-81.

66. Keeling AN, Flaherty JD, Davarpanah AH, Ambrosy A, Farrelly CT, Harinstein ME, et al. Coronary multidetector computed tomographic angiography to evaluate coronary artery disease in liver transplant candidates: methods, feasibility and initial experience. J Cardiovasc Med (Hagerstown) 2011; 12: 460-8.

67. Vanwagner LB, Bhave M, Te HS, Feinglass J, Alvarez L, Rinella ME. Patients transplanted for nonalcoholic steatohepatitis are at increased risk for postoperative cardiovascular events. Hepa-

tology 2012; 56: 1741-50.

68. Targher G, Day CP, Bonora E. Risk of cardiovascular disease in patients with nonalcoholic fatty liver disease. N Engl J Med 2010; 363: 1341-50.

69. Johnston SD, Morris JK, Cramb R, Gunson BK, Neuberger J. Cardiovascular morbidity and mortality after orthotopic liver transplantation. Transplantation 2002; 73: 901-6.

70. Davidson CJ, Gheorghiade M, Flaherty JD, Elliot MD, Reddy SP, Wang NC, et al. Predictive value of stress myocardial perfusion imaging in liver transplant candidates. Am J Cardiol 2002; 89: 359-60.

71. Nguyen P, Plotkin J, Fishbein TM, Laurin JM, Satoskar R, Shetty K, et al. Dobutamine stress echocardiography in patients undergoing orthotopic liver transplantation: a pooled analysis of accuracy, perioperative and long term cardiovascular prognosis. Int J Cardiovasc Imaging 2013; 29: 1741-8.

72. Snipelisky D, Levy M, Shapiro B. Utility of dobutamine stress echocardiography as part of the pre-liver transplant evaluation: an evaluation of its efficacy. Clin Cardiol 2014; 37: 468-72.

73. Møller S, Bernardi M. Interactions of the heart and the liver. Eur Heart J 2013; 34: 2804-11.

74. Blankstein R, Di Carli MF. Integration of coronary anatomy and myocardial perfusion imaging. Nat Rev Cardiol 2010; 7: 226-36.

75. Carey EJ, Steidley DE, Aqel BA, Byrne TJ, Mekeel KL, Rakela J, et al. Six-minute walk distance predicts mortality in liver transplant candidates. Liver Transpl 2010; 16: 1373-8.

76. Gatzoulis MA, Webb GD, Daubeney PEF. Diagnosis and management of adult congenital heart disease. 3rd ed. Philadelphia (PA), Elsevier. 2018, pp 615-21.

77. Slama M, Tribouilloy C, Maizel J. Left ventricular outflow tract obstruction in ICU patients. Curr Opin Crit Care 2016; 22: 260-6.

78. Yang JH, Park SW, Yang JH, Cho SW, Kim HS, Choi KA, et al. Dynamic left ventricular outflow tract obstruction without basal septal hypertrophy, caused by catecholamine therapy and volume depletion. Korean J Intern Med 2008; 23: 106-9.

79. Hioki H, Izawa A, Miura T, Motoki H, Aizawa K, Koshikawa M, et al. Dynamic left ventricular outflow tract obstruction due to anemia in a 71-year-old patient with sigmoid septum. J Cardiol Cases 2010; 1: e144-6.

80. Maraj S, Jacobs LE, Maraj R, Contreras R, Rerkpattanapipat P, Malik TA, et al. Inducible left ventricular outflow tract gradient during dobutamine stress echocardiography: an association with intraoperative hypotension but not a contraindication to liver transplantation. Echocardiography 2004; 21: 681-5.

81. Robertson A. Intraoperative management of liver transplantation in patients with hypertrophic cardiomyopathy: a review.

Transplant Proc 2010; 42: 1721-3.

82. Savale L, O'Callaghan DS, Magnier R, Le Pavec J, Hervé P, Jaïs X, et al. Current management approaches to portopulmonary hypertension. Int J Clin Pract Suppl 2011; 169: 11-8.

83. Swanson KL, Wiesner RH, Nyberg SL, Rosen CB, Krowka MJ. Survival in portopulmonary hypertension: Mayo Clinic experience categorized by treatment subgroups. Am J Transplant 2008; 8: 2445-53.

84. Gordon C, Collard CD, Pan W. Intraoperative management of pulmonary hypertension and associated right heart failure. Curr Opin Anaesthesiol 2010; 23: 49-56.

85. Porres-Aguilar M, Zuckerman MJ, Figueroa-Casas JB, Krowka MJ. Portopulmonary hypertension: state of the art. Ann Hepatol 2008; 7: 321-30.

86. Kawut SM, Krowka MJ, Trotter JF, Roberts KE, Benza RL, Badesch DB, et al. Pulmonary Vascular Complications of Liver Disease Study Group. Clinical risk factors for portopulmonary hypertension. Hepatology 2008; 48: 196-203.

87. Ramsay MA, Simpson BR, Nguyen AT, Ramsay KJ, East C, Klintmalm GB. Severe pulmonary hypertension in liver transplant candidates. Liver Transpl Surg 1997; 3: 494-500.

88. Galiè N, Hoeper MM, Humbert M, Torbicki A, Vachiery JL, Barbera JA, et al. ESC Committee for Practice Guidelines (CPG). Guidelines for the diagnosis and treatment of pulmonary hypertension: the Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS), endorsed by the International Society of Heart and Lung Transplantation (ISHLT). Eur Heart J 2009; 30: 2493-537. Erratum in: Eur Heart J 2011; 32: 926.

89. Colle IO, Moreau R, Godinho E, Belghiti J, Ettori F, Cohen-Solal A, et al. Diagnosis of portopulmonary hypertension in candidates for liver transplantation: a prospective study. Hepatology 2003; 37: 401-9.

90. Kim WR, Krowka MJ, Plevak DJ, Lee J, Rettke SR, Frantz RP, et al. Accuracy of Doppler echocardiography in the assessment of pulmonary hypertension in liver transplant candidates. Liver Transpl 2000; 6: 453-8.

91. Bozbas SS, Bozbas H. Portopulmonary hypertension in liver transplant candidates. World J Gastroenterol 2016; 22: 2024-9.

92. Fauconnet P, Klopfenstein CE, Schiffer E. Hepatopulmonary syndrome: the anaesthetic considerations. Eur J Anaesthesiol 2013; 30: 721-30.

93. Porres-Aguilar M, Altamirano JT, Torre-Delgadillo A, Charlton MR, Duarte-Rojo A. Portopulmonary hypertension and hepatopulmonary syndrome: a clinician-oriented overview. Eur Respir Rev 2012; 21: 223-33.

KSTA

94. Arguedas MR, Singh H, Faulk DK, Fallon MB. Utility of pulse oximetry screening for hepatopulmonary syndrome. Clin Gastroenterol Hepatol 2007; 5: 749-54.

95. Arguedas MR, Abrams GA, Krowka MJ, Fallon MB. Prospective evaluation of outcomes and predictors of mortality in patients with hepatopulmonary syndrome undergoing liver transplantation. Hepatology 2003; 37: 192-7.

96. Muralimohan R, Delu A, Ma T. Pericardial effusion of obscure origin. Dig Dis Sci 2014; 59: 2909-12.

97. Naschitz JE, Slobodin G, Lewis RJ, Zuckerman E, Yeshurun D. Heart diseases affecting the liver and liver diseases affecting the heart. Am Heart J 2000; 140: 111-20.

98. Garg A, Armstrong WF. Echocardiography in liver transplant candidates. JACC Cardiovasc Imaging 2013; 6: 105-19.

99. Sagristà-Sauleda J, Mercé AS, Soler-Soler J. Diagnosis and management of pericardial effusion. World J Cardiol 2011; 3: 135-43.

100. Park J, Lee M, Kim J, Choi HJ, Kwon A, Chung HS, et al. Intraoperative management to prevent cardiac collapse in a patient with a recurrent, large-volume pericardial effusion and paroxysmal atrial fibrillation during liver transplantation: a case report. Transplant Proc 2019; 51: 568-74.

101. Apple SJ, Lee J, Freeze M, Rizk D, Trimmingham A, McFarlane SI. Tense ascites causing extracardiac compression: a case report and literature review. Am J Med Case Rep 2021; 9: 402-6.

102. Homma S, Sacco RL. Patent foramen ovale and stroke. Circulation 2005; 112: 1063-72.

103. Falanga G, Carerj S, Oreto G, Khandheria B, Zito C. How to understand patent foramen ovale clinical significance - part II: therapeutic strategies in cryptogenic stroke. J Cardiovasc Echogr 2015; 25: 46-53.

104. Harinstein ME, Iyer S, Mathier MA, Flaherty JD, Fontes P, Planinsic RM, et al. Role of baseline echocardiography in the preoperative management of liver transplant candidates. Am J Cardiol 2012; 110: 1852-5.

105. Alba AC, Verocai Flaman F, Granton J, Delgado DH. Patent foramen ovale does not have a negative impact on early outcomes in patients undergoing liver transplantation. Clin Transplant 2011; 25: 151-5.

106. Werlang ME, Palmer WC, Boyd EA, Cangemi DJ, Harnois DM, Taner CB, et al. Patent foramen ovale in liver transplant recipients does not negatively impact short-term outcomes. Clin Transplant 2016; 30: 26-32.

107. Cabrera J, Falcón L, Gorriz E, Pardo MD, Granados R, Quinones A, et al. Abdominal decompression plays a major role in early postparacentesis haemodynamic changes in cirrhotic patients with tense ascites. Gut 2001; 48: 384-9.

108. Kang Y, Elia E. Anesthesia management of liver transplantation. In: Contemporary liver transplantation: the successful liver transplant program. Edited by Doria C: Cham, Springer. 2017, pp 143-87.

109. Kornberg A, Witt U, Kornberg J, Ceyhan GO, Mueller K, Friess H, et al. Prognostic impact of intraoperative blood loss in liver transplant patients with advanced hepatocellular carcinoma. Anticancer Res 2016; 36: 5355-64.

110. Jawan B, Wang CH, Chen CL, Huang CJ, Cheng KW, Wu SC, et al. Review of anesthesia in liver transplantation. Acta Anaesthesiol Taiwan 2014; 52: 185-96.

111. Krishnan S, Schmidt GA. Acute right ventricular dysfunction: real-time management with echocardiography. Chest 2015; 147: 835-46.

112. Feltracco P, Carollo C, Barbieri S, Pettenuzzo T, Ori C. Early respiratory complications after liver transplantation. World J Gastroenterol 2013; 19: 9271-81.

113. Smith NK, Kim S, Hill B, Goldberg A, DeMaria S, Zerillo J. Transfusion-related acute lung injury (TRALI) and transfusion-associated circulatory overload (TACO) in liver transplantation: a case report and focused review. Semin Cardiothorac Vasc Anesth 2018; 22: 180-90.

114. Brezeanu LN, Brezeanu RC, Diculescu M, Droc G. Anaesthesia for liver transplantation: an update. J Crit Care Med (Targu Mures) 2020; 6: 91-100.

115. Gouveia V, Marcelino P, Reuter DA. The role of transesophageal echocardiography in the intraoperative period. Curr Cardiol Rev 2011; 7: 184-96.

116. Manning MW, Kumar PA, Maheshwari K, Arora H. Post-reperfusion syndrome in liver transplantation-an overview. J Cardiothorac Vasc Anesth 2020; 34: 501-11.

117. Xu ZD, Xu HT, Yuan HB, Zhang H, Ji RH, Zou Z, et al. Post-reperfusion syndrome during orthotopic liver transplantation: a single-center experience. Hepatobiliary Pancreat Dis Int 2012; 11: 34-9.