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Review Article

Cardiovascular Considerations in Liver TransplantationA Review of Risks, Diagnostics, and Management

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Abstract
This comprehensive review article delves into the critical role of cardiovascular disorders in liver transplantation (LT) candidates, focusing on coronary artery disease (CAD), cirrhotic cardiomyopathy (CCM), and structural heart disease. It examines the prevalence and implications of these conditions on LT outcomes, emphasizing the necessity of a thorough preoperative cardiac evaluation and risk stratification. The article explores various aspects of cardiac risk in LT, including CAD, CCM, and coexisting structural heart diseases. It highlights the importance of diagnostic techniques such as echocardiography, stress testing, cardiac catheterization, and CMR in the evaluation process. The review aligns with current guidelines from major cardiac societies and discusses the implications of CCM and structural heart disease on LT. It also assesses the role of cardiac biomarkers in predicting postoperative outcomes and explores functional cardiopulmonary assessment tools. Finally, the article considers the intraoperative and postoperative cardiac risks associated with LT, concluding with the significant impact of cardiovascular management in improving LT outcomes.

2. Introduction

Liver transplantation (LT) has emerged as a pivotal treatment modality for end-stage liver disease and certain liver cancers. The success of LT, however, is intricately linked to the cardiovascular health of candidates. Cardiovascular disorders, prevalent in LT candidates, play a critical role in shaping preoperative evaluation and perioperative management strategies. This review delves into the complex interplay between LT and cardiovascular conditions, highlighting the significance of thorough cardiac evaluation and risk stratification in enhancing patient outcomes and optimizing transplant resource utilization.

2. Prevalence and Impact of Cardiovascular Conditions in LT Candidates

Cardiovascular disorders in LT candidates, encompassing coronary artery disease (CAD), cirrhotic cardiomyopathy (CCM), and structural heart disease, present unique risks and challenges. CAD's prevalence in LT populations is notable, often associated with demographic factors such as older age and comorbidities, critically influencing postoperative complications and mortality [1-3]. CCM, characterized by a spectrum of cardiovascular aberrations in patients with end-stage liver disease (ESLD), includes diastolic dysfunction and stress-induced systolic dysfunction, posing significant management challenges during LT [4-7]. Additionally, structural heart diseases, often coexisting with liver conditions, can profoundly impact perioperative outcomes, with conditions like ventricular failure and severe valvular disease contributing to early postoperative mortality [8-11]. The identification and management of these conditions are therefore pivotal in the LT process.

3. Cardiovascular Risk Assessment in LT Candidates

The cardiovascular risk assessment in LT candidates is complex, requiring a comprehensive and multidisciplinary approach. This process involves evaluating hemodynamic perturbations, coagulation abnormalities, and other complications that could have fatal implications for patients with underlying cardiac illness [14,15]. Diagnostic techniques play an essential role in this assessment, with echocardiography being crucial for identifying structural heart diseases and assessing cardiac function [12]. Non-invasive stress testing, although limited in predictive value, especially in patients with non-alcoholic ESLD, helps in identifying significant CAD [16]. Cardiac catheterization becomes critical when non-invasive tests are inconclusive or indicate significant disease [15]. Additionally, Cardiac Magnetic Resonance (CMR) offers valuable insights into myocardial viability and function in complex cases [17]. Adhering to guidelines and recommendations from authoritative bodies like the American College of Cardiology/American Heart Association (ACC/AHA) and the European Society of Cardiology/European Society of Anaesthesiology (ESC/ESA) is crucial in this process. These guidelines underscore the importance of a comprehensive cardiac evaluation, with specific recommendations tailored to the risk profiles of LT candidates [18,19]. Consequently, the assessment significantly influences LT candidacy and outcomes.

4. Cirrhotic Cardiomyopathy (CCM) in LT

Cirrhotic Cardiomyopathy (CCM) represents a unique cardiac risk in LT candidates, characterized by a range of cardiovascular aberrations in patients with end-stage liver disease (ESLD). Clinically, CCM encompasses manifestations such as diastolic dysfunction and stress-induced systolic dysfunction, with the potential to evolve into heart failure indicative of decompensated CCM. This condition also includes electrophysiological abnormalities and structural changes like left-ventricular hypertrophy and biatrial enlargement [4-7]. The pathophysiology of CCM involves complex interactions between the liver, heart, and kidneys, characterized by systemic inflammation, autonomic dysfunction, and activation of vasodilatory factors, resulting in a hyperdynamic circulation with high cardiac output and low peripheral vascular resistance [22-24]. The impact of CCM on LT is significant, especially in the perioperative period, with associated complications predisposing patients to cardiovascular complications during and after LT [25,26]. Up to 21% of deaths following LT are attributed to heart failure, often related to underlying cardiovascular disease [27,28]. Accordingly, careful preoperative cardiac assessment and perioperative management are vital to managing CCM-related risks in LT candidates.

5. Structural Heart Disease in LT Candidates

Structural heart diseases in LT candidates, such as CAD and pulmonary hypertension (PH), significantly influence transplantation outcomes. The prevalence of CAD ranges from 20% to 28%, while PH varies from 5% to 10% among these patients, with shared risk factors like alcohol use and non-alcoholic fatty liver disease (NAFLD) contributing to their development [15]. Preoperative screening is essential for assessing risk and planning management, with echocardiography playing a central role in grading valvular lesions and determining right ventricular systolic pressure (RVSP). In cases where RVSP exceeds 45 mm Hg, right heart catheterization may be required [29]. The presence and severity of structural heart diseases can significantly impact intraoperative and postoperative recovery, with CAD patients exhibiting a 1-year mortality rate of 40% post-LT [30]. Stress echocardiography has been useful in excluding patients with significant disease [15].

6. Predictive Tools and Techniques

Predicting perioperative cardiac risk in LT is challenging due to the complexity of variables involved. Risk factor analysis has correlated preoperative cardiac risk factors with postoperative cardiac events, with key risk factors including age, diabetes, known cardiac disease, and NASH. For example, studies of LT patients over three years found these factors predictive of post-transplant cardiac events [32,33]. Advanced cardiac disease history was also predictive of early post-transplant mortality in high-MELD LT patients [34]. Dobutamine Stress Echocardiography (DSE) is used to detect occult CAD and predict postoperative cardiac outcomes. A normal DSE predicts a low risk for postoperative cardiac events [35]. Echocardiography-based studies indicate that left ventricular hypertrophy (LVH) and diastolic dysfunction are predictive of postoperative mortality, graft failure, and heart failure [37, 38]. Cardiac biomarkers such as Troponin T (TnT), Troponin I (TnI), and Brain Natriuretic Peptide (BNP) play a pivotal role in assessing myocardial injury and heart failure in LT candidates. Their preoperative levels have shown predictive value for major cardiac events and postoperative mortality [39-41]. Functional cardiopulmonary assessments, including the 6-minute walk test and cardiopulmonary exercise testing (CPET), are critical for evaluating cardiopulmonary reserve in LT candidates, with their results providing insights into pre-transplant survival and postoperative outcomes [42,43].

7. Intraoperative and Postoperative Cardiac Risks

Liver transplantation (LT) is a procedure that imposes significant intraoperative cardiac risks due to its complex nature, involving substantial blood loss, fluid shifts, and critical events such as organ reperfusion. These challenges can precipitate prolonged hypotension and severe post-reperfusion syndrome, both of which are critical in determining post-transplant outcomes [45, 46]. Studies have shown that variables like intraoperative mean arterial pressure (MAP) are predictive of adverse outcomes, including post-transplant mortality and graft failure, emphasizing the importance of maintaining stable hemodynamic during surgery [6].

The management of postoperative cardiac events is a crucial aspect of LT care. Postoperative cardiac complications, including myocardial injury following non-cardiac surgery (MINS), pose significant risks. Elevated postoperative troponin levels, for instance, have been linked to higher mortality rates [47]. The prevalence of MINS in LT patients is notable, correlating with higher rates of cardiovascular and all-cause mortality, primarily influenced by severe ESLD and hemodynamic instability during surgery [48]. The importance of continuous monitoring and intervention strategies cannot be overstated. These include regular cardiac biomarker assessments and vigilant monitoring

of hemodynamic parameters. Such strategies are instrumental in early detection and management of cardiac complications, thereby reducing the risk of postoperative mortality and improving overall patient outcomes.

8. Conclusions and Future Directions

This review has underscored the complex and significant role of cardiovascular risks in liver transplantation. The prevalence and impact of conditions like CAD, CCM, and structural heart disease highlight the necessity of comprehensive cardiovascular care in LT. The challenges in preoperative cardiac evaluation, coupled with the predictive value of cardiac biomarkers and functional assessments, emphasize the need for meticulous preoperative planning and perioperative management. However, gaps in current research point to the need for further studies, particularly in refining risk assessment tools and management protocols. Future research should focus on enhancing predictive models for cardiovascular complications in LT, developing more effective preoperative assessment techniques, and optimizing perioperative management strategies. The evolving nature of cardiovascular care in LT underscores the importance of multidisciplinary collaboration and adherence to continuously updating guidelines. As advancements in medical technology and research continue to emerge, the field of LT is poised to benefit from improved cardiovascular risk management, leading to better patient outcomes and more effective use of transplant resources.

References

1. CAREY, W. D., DUMOT, J. A., PIMENTEL, R. R., BARNES, D. S., HOBBS, R. E., HENDERSON, J. M., ... & EASLEY, K. A. (1995). The prevalence of coronary artery disease in liver transplant candidates over age 50. *Transplantation, 59*(6), 859-863.
2. VanWagner, L. B., Harinstein, M. E., Runo, J. R., Darling, C., Serper, M., Hall, S., ... & Hammel, L. L. (2018). Multidisciplinary approach to cardiac and pulmonary vascular disease risk assessment in liver transplantation: an evaluation of the evidence and consensus recommendations. *American Journal of Transplantation, 18*(1), 30-42.
3. Kwon, H. M., Moon, Y. J., Kim, K. S., Shin, W. J., Huh, I. Y., Jun, I. G., ... & Hwang, G. S. (2021). Prognostic Value of B-Type Natriuretic Peptide in Liver Transplant Patients: Implication in Posttransplant Mortality. *Hepatology, 74*(1), 336-350.
4. Lee RF, Glenn TK, Lee. (2007). *SSCardiac Dysfunction in Cirrhosis.*
5. Wray, (2017). CLLiver Transplantation in Patients With Cardiac Disease.
6. Barjaktarevic, I., Lopez, R. C., Steadman, R., Wray, C., Qadir, N., Chang, S. Y., & Wang, T. (2018, October). Perioperative considerations in liver transplantation. *In Seminars in Respiratory and Critical Care Medicine* (Vol. 39, No. 05, pp. 609-624). Thieme Medical Publishers.
7. Dowsley, T. F., Bayne, D. B., Langnas, A. N., Dumitru, I., Windle, J. R., Porter, T. R., & Raichlin, E. (2012). Diastolic dysfunction in patients with end-stage liver disease is associated with development of heart failure early after liver transplantation. *Transplantation, 94*(6), 646-651.
8. Josefsson, A., Fu, M., Allayhari, P., Björnsson, E., Castedal, M., Olausson, M., & Kalaitzakis, E. (2012). Impact of peri-transplant heart failure & left-ventricular diastolic dysfunction on outcomes following liver transplantation. *Liver International, 32*(8), 1262-1269.
9. Ruíz-del-Árbol, L., Achécar, L., Serradilla, R., Rodríguez-Gandía, M. Á., Rivero, M., Garrido, E., & Natcher, J. J. (2013). Diastolic dysfunction is a predictor of poor outcomes in patients with cirrhosis, portal hypertension, and a normal creatinine. *Hepatology, 58*(5), 1732-1741.
10. Krowka, M. J., Plevak, D. J., Findlay, J. Y., Rosen, C. B., Wiesner, R. H., & Krom, R. A. (2000). Pulmonary hemodynamics and perioperative cardiopulmonary-related mortality in patients with portopulmonary hypertension undergoing liver transplantation. *Liver Transplantation, 6*(4), 443-450.
11. Leithead, J. A., Kandiah, K., Steed, H., Gunson, B. K., Steeds, R. P., & Ferguson, J. W. (2014). Tricuspid regurgitation on echocardiography may not be a predictor of patient survival after liver transplantation. *American Journal of Transplantation, 14*(9), 2192-2193.
12. Bradley, S. M., Soine, L. A., Caldwell, J. H., & Goldberg, S. L. (2010). Screening stress myocardial perfusion imaging and eligibility for liver transplantation. *The American journal of cardiology, 105*(7), 1010-1013.
13. VanWagner, L. B., Lapin, B., Levitsky, J., Wilkins, J. T., Abecassis, M. M., Skaro, A. I., & Lloyd-Jones, D. M. (2014). High early cardiovascular mortality after liver transplantation. *Liver transplantation, 20*(11), 1306-1316.
14. Jha, A. K., & Lata, S. (2020). Liver transplantation and cardiac illness: Current evidences and future directions. *Journal of Hepato-Biliary-Pancreatic Sciences, 27*(5), 225-241.
15. Brusich, K. T., Acan, I., Filipcic, N. V., & Gustin, D. (2013). Liver transplantation: An adventure for the anaesthesiologist. *OA Anaesthetics, 1*(2), 11.
16. Bazoukis, G., Papadatos, S. S., Michelongona, A., Lampropoulos, K., Farmakis, D., & Vassiliou, V. (2021). Contemporary role of cardiac magnetic resonance in the management of patients with suspected or known coronary artery disease. *Medicina, 57*(7), 649.
17. Arnett DK, Blumenthal RS, Albert MA, et. al.ACC/AHA Arnett, D. K., Blumenthal, R. S., Albert, M. A., Buroker, A. B., Goldberger, Z. D., Hahn, E. J., ... & Ziaeian, B. (2019). 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation, 140*(11), e563-e595. 2019.
18. Kristensen, S. L., Ahlehoff, O., Lindhardsen, J., Erichsen, R., Lamberts, M., Khalid, U., ... & Hansen, P. R. (2014). Inflammatory bowel disease is associated with an increased risk of hospitalization for heart failure: a Danish Nationwide Cohort study. *Circulation: Heart Failure, 7*(5), 717-722.
19. Liu H, (2017). Jayakumar STraboulsi M, Lee SSCirrhotic CardiomyopathyImplications for Liver Transplantation .
20. Baik SK, Fouad TR, Lee. (2007). SSCirrhotic Cardiomyopathy.
21. Chancharoenthana, W., & Leelahavanichkul, A. (2019).

Acute kidney injury spectrum in patients with chronic liver disease: Where do we stand?. *World journal of gastroenterology, 25*(28), 3684.
22. Møller, S., Hove, J. D., Dixen, U., & Bendtsen, F. (2013). New insights into cirrhotic cardiomyopathy. *International journal of cardiology, 167*(4), 1101-1108.
23. García-Estañ, J., Ortiz, M. C., & Lee, S. S. (2002). Nitric oxide and renal and cardiac dysfunction in cirrhosis. *Clinical Science, 102*(2), 213-222.
24. Eimer, M. J., Wright, J. M., Wang, E. C., Kulik, L., Blei, A., Flamm, S., ... & Gheorghiade, M. (2008). Frequency and significance of acute heart failure following liver transplantation. *The American journal of cardiology, 101*(2), 242-244.
25. Rachwan, R. J., Kutkut, I., Hathaway, T. J., Timsina, L. R., Kubal, C. A., Lacerda, M. A., ... & Mangus, R. S. (2020). Postoperative atrial fibrillation and flutter in liver transplantation: an important predictor of early and late morbidity and mortality. *Liver Transplantation, 26*(1), 34-44.
26. Zardi, E. M., Zardi, D. M., Chin, D., Sonnino, C., Dobrina, A., & Abbate, A. (2016). Cirrhotic cardiomyopathy in the pre-and post-liver transplantation phase. *Journal of Cardiology, 67*(2), 125-130.
27. Marella, H., Yedlapati, N., Kothadia, J. P., Mupparaju, V. K., Marella, S., & Nair, S. (2021). Impact of left ventricular diastolic dysfunction on liver transplantation outcomes based on the latest American Society of Echocardiography/ European Association of Cardiovascular Imaging recommendations. *Clinical and Experimental Hepatology, 7*(4), 390-395.
28. Cotton, C. L., Gandhi, S., Vaitkus, P. T., Massad, M. G., Benedetti, E., Mrtek, R. G., & Wiley, T. E. (2002). Role of echocardiography in detecting portopulmonary hypertension in liver transplant candidates. *Liver Transplantation, 8*(11), 1051-1054.
29. Hawkins, R. B., Young, B. A. C., Mehaffey, J. H., Speir, A. M., Quader, M. A., Rich, J. B., ... & Investigators for the Virginia Cardiac Services Quality Initiative. (2019). Model for end-stage liver disease score independently predicts mortality in cardiac surgery. *The Annals of thoracic surgery, 107*(6), 1713-1719.
30. Nicolau-Raducu, R., Gitman, M., Ganier, D., Loss, G. E., Cohen, A. J., Patel, H., ... & Nossaman, B. (2015). Adverse cardiac events after orthotopic liver transplantation: a cross-sectional study in 389 consecutive patients. *Liver Transplantation, 21*(1), 13-21.
31. Petrowsky, H., Rana, A., Kaldas, F. M., Sharma, A., Hong, J. C., Agopian, V. G., ... & Busuttil, R. W. (2014). Liver transplantation in highest acuity recipients: identifying factors to avoid futility. *Annals of surgery, 259*(6), 1186-1194.
32. Nguyen, P., Plotkin, J., Fishbein, T. M., Laurin, J. M., Satoskar, R., Shetty, K., & Taylor, A. J. (2013). Dobutamine stress echocardiography in patients undergoing orthotopic liver transplantation: a pooled analysis of accuracy, perioperative and long term cardiovascular prognosis. *The International Journal of Cardiovascular Imaging, 29,* 1741-1748.
33. Umphrey, L. G., Hurst, R. T., Eleid, M. F., Lee, K. S., Reuss, C. S., Hentz, J. G., ... & Appleton, C. P. (2008). Preoperative dobutamine stress echocardiographic findings and subsequent short-term adverse cardiac events after orthotopic liver transplantation. *Liver transplantation, 14*(6), 886-892.
34. Darstein, F., König, C., Hoppe-Lotichius, M., Grimm, D., Knapstein, J., Mittler, J., ... & Zimmermann, T. (2014). Preoperative left ventricular hypertrophy is associated with reduced patient survival after liver transplantation. *Clinical Transplantation, 28*(2), 236-242.
35. Kwon, H. M., & Hwang, G. S. (2018). Cardiovascular dysfunction and liver transplantation. *Korean journal of anesthesiology, 71*(2), 85-91.
36. Kim, Y. K., Shin, W. J., Song, J. G., Kim, Y., Kim, W. J., Kim, S. H., & Hwang, G. S. (2011, June). Evaluation of intraoperative brain natriuretic peptide as a predictor of 1-year mortality after liver transplantation. In Transplantation proceedings (Vol. 43, No. 5, pp. 1684-1690). Elsevier.
37. Watt, K. D., Coss, E., Pedersen, R. A., Dierkhising, R., Heimbach, J. K., & Charlton, M. R. (2010). Pretransplant serum troponin levels are highly predictive of patient and graft survival following liver transplantation. *Liver transplantation, 16*(8), 990-998.
38. Park, J., Lee, S. H., Han, S., Jee, H. S., Lee, S. K., Choi, G. S., & Kim, G. S. (2017). Preoperative cardiac troponin level is associated with all-cause mortality of liver transplantation recipients. *PLoS One, 12*(5), e0177838.
39. Carey, E. J., Steidley, D. E., Aqel, B. A., Byrne, T. J., Mekeel, K. L., Rakela, J., ... & Douglas, D. D. (2010). Six-minute walk distance predicts mortality in liver transplant candidates. *Liver Transplantation, 16*(12), 1373-1378.
40. Prentis, J. M., Manas, D. M., Trenell, M. I., Hudson, M., Jones, D. J., & Snowden, C. P. (2012). Submaximal cardiopulmonary exercise testing predicts 90-day survival after liver transplantation. *Liver transplantation, 18*(2), 152-159.
41. Duarte-Rojo, A., Ruiz-Margáin, A., Montaño-Loza, A. J., Macías-Rodríguez, R. U., Ferrando, A., & Kim, W. R. (2018). Exercise and physical activity for patients with end-stage liver disease: improving functional status and sarcopenia while on the transplant waiting list. *Liver Transplantation, 24*(1), 122-139.
42. Huang, C. J., Cheng, K. W., Chen, C. L., Wu, S. C., Shih, T. H., Yang, S. C., ... & Wang, C. H. (2017). Clinical beneficial effects of using crystalloid only in recipients of living donor liver transplantation. *International journal of environmental research and public health, 14*(11), 1418.
43. Fu, H., Sun, K., Li, J., Gong, W., Agopian, V., Yan, M., ... & Xia, V. W. (2018). Preoperative beta blockade and severe intraoperative bradycardia in liver transplantation. *Clinical transplantation, 32*(12), e13422.
44. Ruetzler, K., Smilowitz, N. R., Berger, J. S., Devereaux, P. J., Maron, B. A., Newby, L. K., ... & American Heart Association Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation; Council on Clinical Cardiology; and Council on Cardiovascular Surgery and Anesthesia. (2021). Diagnosis and management of patients with myocardial injury after noncardiac surgery: a

scientific statement from the American Heart Association. *Circulation, 144*(19), e287-e305.

45. Snipelisky, D., Donovan, S., Levy, M., Satyanarayana, R., & Shapiro, B. (2013). Cardiac troponin elevation predicts mortality in patients undergoing orthotopic liver transplantation. Journal of Transplantation, 2013.