



## Editorial

# How to optimize the outcome of liver transplantation for non-alcoholic fatty liver disease

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Along with global epidemics of obesity and type 2 diabetes mellitus (T2DM), the prevalence of non-alcoholic fatty liver disease (NAFLD) is increasing worldwide. NAFLD is becoming one of the leading causes of liver transplantation (LT) both for end-stage liver disease (ESLD) and hepatocellular carcinoma.<sup>1,2</sup> NAFLD is commonly associated with metabolic risk factors such as obesity and T2DM and poses unique challenges when considering LT. Therefore, comprehensive cardiovascular risk assessment and proper management of comorbid conditions are crucial in the LT evaluation process and post-LT management to improve outcomes. Liver transplantation can cure ESLD but not the underlying metabolic risk factors associated with NAFLD. Thus, long-term strategies to address these comorbidities are of importance in patient management. Furthermore, the use of postoperative steroids and other immunosuppressive agents frequently aggravates metabolic derangement and fosters development of obesity, insulin resistance, T2DM, hypertension, and dyslipidemia.<sup>3</sup>

Because of the increasing prevalence of NAFLD and its im-

pact on LT, efforts should be made to improve liver-related outcomes and prevent the development of metabolic-related complications following LT.<sup>4</sup> However, present guidelines make no specific recommendation for LT recipients with NAFLD other than correction and optimal control of individual components of metabolic syndrome and cardiovascular risk factors.<sup>5,6</sup> The European Association for the Study of the Liver (EASL) recommends that metabolic comorbidities be assessed and controlled in pre- and post-transplant settings.<sup>5</sup> In the American Association for the Study of Liver Disease (AASLD) and American Society for Transplantation practice guidelines for LT, there are no NAFLD-specific directives other than that LT is an effective therapy for NAFLD cirrhosis.<sup>7</sup> This comprehensive review article focuses on indications of LT for NAFLD, pre-LT risk assessment, management of patients on the waiting list, optimal management of metabolic disorder, immunosuppressive agent use, prevention of recurrent non-alcoholic steatohepatitis/NAFLD, and short- and long-term outcomes after LT.<sup>8</sup>

Patients with NAFLD have a higher prevalence of cardiovascular disease with an increased risk of cardiovascular mortality than the general population because of common meta-

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bolic risk factors and shared pathogenic pathways.<sup>9,10</sup> Comprehensive cardiovascular risk assessment and testing are essential during the LT evaluation process, which warrants a multidisciplinary team approach, including cardiology, cardiac anesthesiology, and nutrition in addition to hepatology and transplant surgery, to appropriately stratify risk and optimize patient management.

Older age, higher Model for End-Stage Liver Disease score, and extreme body mass index, but not NAFLD itself, are risk factors for lower rate of survival after LT.<sup>11</sup> However, NAFLD recurrence is frequent after LT because of persistence of metabolic risk factors and immunosuppressive agent use.<sup>2</sup> Efforts should be made to achieve optimal control of metabolic comorbidities through a multidisciplinary team approach including nutrition, physical activity, and immunosuppressive agent modulation.

Unlike previous reviews, this study comprehensively describes research regarding association between post-LT outcomes and sarcopenia (pre-LT sarcopenia, post-LT sarcopenia, sarcopenic obesity, and changes in sarcopenic status). Sarcopenia has been increasingly reported to be associated with adverse outcome such as mortality, hospital stay, and infection after LT.<sup>12</sup> Thus, nutritional status and physical activity assessment should be considered as part of the standard care. Also, specific recommendations and practical advice on diet and physical activity would be useful and relevant from a clinical point of view and have been briefly covered by another review article.<sup>13</sup>

This review systematically describes management and therapeutic options to improve long-term outcomes with a particular emphasis on correction and control of metabolic comorbidities. Considering the growing impact of NAFLD on all aspects of LT, this review will provide useful information to optimize patient management in LT for NAFLD.

### Authors' contribution

Manuscript draft: Byeong Geun Song. Critical revision of manuscript: Dong Hyun Sinn.

### Conflicts of Interest

The authors have no conflicts to disclose.

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### Abbreviations:

Abbreviations: T2DM, type 2 diabetes mellitus; NAFLD, non-alcoholic fatty liver disease; LT, liver transplantation; ESLD, end-stage liver disease; AASLD, American Association for the Study of Liver Disease; EASL, European Association for the Study of the Liver

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