Long-Term Management of the Successful Adult Liver Transplant: A Patient-Friendly Summary of the 2012 AASLD and AST Practice Guideline

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This article will summarize the practice guidelines put forth by the American Association for the Study of Liver Diseases (AASLD) and the American Society of Transplantation (AST) on long-term management of liver transplant recipients in an easy-to-read format for patients and their caregivers. The purpose of the summary is to help patients and their caregivers better understand this condition. However, this summary should not replace expert medical care provided by the transplant center. A link to the full document is available at: https://www.aasld.org/sites/default/files/2019-06/2013PracticeGuidelineLongTermManagementofSuccessfulLT.pdf.

LIVER TRANSPLANTATION

Liver transplantation (LT) is a lifesaving surgery for end-stage liver disease, which involves replacing a patient’s existing liver with a donor liver. Most patients do well after LT and survive for several years. However, the new transplanted liver requires close monitoring and immunosuppressive medications to prevent complications.

Monitoring Liver Tests

Recommendations:
- The frequency of monitoring with liver tests should be individualized by the transplant center according to the time from LT, the complications from LT, the stability of serial test results, and the underlying cause.
- Depending on the pattern of liver tests, magnetic resonance imaging (MRI), computed tomography (CT), endoscopic retrograde cholangiopancreatography, and sonography may be appropriate.

Abbreviations: AASLD, American Association for the Study of Liver Diseases; AST, American Society of Transplantation; BMD, bone mineral density; CT, computed tomography; LT, liver transplantation; MRI, magnetic resonance imaging; SPF, sun protection factor.

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Liver histology should be obtained when parenchymal injury is suspected as the cause of abnormal liver tests.

**Patient summary:** LT recipients need close monitoring in the first year after transplantation, with very frequent blood work to make sure the new liver is working well. The frequency of blood work is often very high in the first year after transplant, with the highest frequency during the first 3 months. The reason for frequent blood work is to catch and correct any problems that may arise with the new liver’s function. Problems that could arise in the new liver include issues with blood supply to the liver, complications with bile flow out of the liver, or rejection of the new liver where the patient’s immune system attacks the new liver. If the liver blood tests are abnormal, your doctors may pursue additional testing, which often includes a liver biopsy, additional blood tests, and imaging studies such as MRI, CT, or ultrasound. These additional tests will often help guide the doctors in pursuing the best available treatment strategies to protect the new liver and extend its long-term functionality.

**Key point:** Rejection of a new liver requires a liver biopsy for confirmation (Fig. 1).

### Immunosuppression

**Recommendations:** Immunosuppressive drugs for LT recipients should be prescribed and monitored only by those with knowledge and expertise in that area. The choice of agents will depend on many factors, and no one regimen can be recommended for any patient. Every patient’s immunosuppressive regimen should be reviewed at least every 6 months and modified as required with the goal of minimizing long-term toxicities.

**Patient summary:** The new liver placed in a patient after transplantation is seen as a foreign entity by the patient’s immune system. If left unchecked, the patient’s immune system will start attacking the new liver, which could lead to rejection (inflammation) of the new liver and may potentially lead to liver failure. Therefore, all LT patients require a combination of antirejection (immunosuppressant) medications to protect the new liver. The choice of antirejection medications (tacrolimus, cyclosporine, mycophenolate mofetil, everolimus, sirolimus, or prednisone) is dependent on multiple factors, such as the reason for liver transplant, existing medical conditions, and kidney function, to name just a few. These medications require fine-tuning for optimal drug levels, have potential side effects, and may interact with other medications. Therefore, they require very close monitoring with frequent blood draws and should be managed only by doctors with special training in transplant medicine.

**Key point:** Antirejection medications should be adjusted only by your transplant team.

### SYSTEMIC DISEASES

After LT, the patient’s body goes through several changes. The addition of new antirejection medications may cause some of these changes and separately affect multiple different aspects of the patient’s health. Therefore, specific monitoring is required for different aspects of the body, and we will go through these systems in parts as described in the following subsections (Fig. 2).

#### Bone Health and Kidney Disease

**Recommendations:**
- In the first 5 years after transplantation, screening by bone mineral density (BMD) should be done yearly for patients with osteopenia and every 2 to 3 years for patients with normal BMD; thereafter, screening depends on the progression of BMD and on risk factors (grade 2, level B).
- Monitoring of renal function in LT recipients for the detection and management of chronic kidney disease should use an estimating equation to evaluate the glomerular filtration rate. The reduction or withdrawal of calcineurin inhibitor–associated immunosuppression is an appropriate response to the development of chronic kidney disease in LT recipients.

**Patient summary:** All LT patients undergo significant bone loss in the initial few months, most likely because of the high intensity of antirejection medication in these months. Patients are therefore susceptible to unexpected fractures and should be closely monitored with regular BMD scans, and if needed, they should be treated for osteoporosis. You should discuss vitamin D supplementation with your transplant center or primary care doctor. Chronic kidney disease is the most common complication in long-term survivors of LT and occurs because of several reasons, with antirejection medication playing another key role here. Your transplant doctors will frequently monitor the levels for the antirejection medication and will adjust these...
FIG 1  (A) Potential causes of liver injury after LT. (B) Recommendations for follow-up to protect the liver and potential tests that may be required if liver injury is suspected. Figure was created with “Biological illustration” (http://smart.servier.com) by Servier, used under the Creative Commons Attributions 3.0 Unported License, and modified by Akshay Shetty.
medications in such a combination as to help protect your kidneys’ long-term health.

Metabolic Syndrome

Recommendations:
• The treatment of diabetes mellitus after LT should aim for a hemoglobin A1c target goal of <7.0% with a combination of lifestyle modifications and pharmacological agents as appropriate.
• The treatment of hypertension should aim for a target goal of 130/80 mm Hg with a combination of lifestyle modifications and pharmacological agents as appropriate.
• The measurement of blood lipids after a 14-hour fast is recommended annually for healthy LT recipients. An elevated low-density lipoprotein cholesterol level >100 mg/dL, with or without hypertriglyceridemia, requires therapy.
• All LT patients require ongoing dietary counseling to avoid obesity.

Patient summary: As the body starts recovering, weight gain occurs rapidly among LT patients, usually starting around the fourth month from the transplant. This places all patients at risk for developing metabolic syndrome and its complications, such as diabetes, high blood pressure, and high blood cholesterol levels. In patients who already have diabetes or develop new diabetes after LT, tight control of their blood sugars is recommended with a goal hemoglobin A1c of less than 7.0%. Patients may often need insulin therapy and should see a specialist (endocrinology) to treat their diabetes. Similarly, close control of high blood pressure, cholesterol, and triglycerides is recommended by initially modifying lifestyle; then this may be followed by initiation of medications if the above conditions remain abnormal. Control of these diseases is important to decrease the risk of a future heart attack and to prevent new onset or recurrence of fatty liver.

Reproductive Health

Recommendations:
• For female LT recipients of a childbearing age, preconception counseling about contraception and the risks and outcomes of pregnancy should start in the pretransplant period and should be reinforced after transplantation.
Pregnancy in an LT recipient should be managed by a high-risk obstetrician in coordination with the transplant hepatologist.

Pregnancy should be delayed for 1 year after LT and occur at a time with good, stable allograft function, with maintenance immunosuppression, and with good control of any medical complications, such as hypertension and diabetes.

Patient summary: All females of childbearing age who are undergoing LT should discuss contraception options with their transplant physicians, because some antirejection medications carry significant risks to a fetus. Most female patients have recovery of their normal menstruation and fertility by the end of the first year; however, if appropriate contraceptives are not used, female patients remain at risk for pregnancy. When a pregnancy is desired, early discussions should be held with the transplant physicians and a high-risk obstetrician. For best outcomes, a pregnancy should be pursued after the first year of LT, when the new liver is working well without any recent issues, such as rejection, and the antirejection medications remain on stable doses. Although pregnancy in LT patients carries some risk to both the mother and the fetus, successful outcomes are possible with early planning.

**PROMOTING HEALTH AFTER LT**

**Recommendations:**

- Frequent handwashing reduces the risk for infection with pathogens acquired by direct contact, including *Clostridium difficile*, community-acquired viral infections, and pathogens found in soil.

- Shoes, socks, long-sleeve shirts, and long pants should be worn for activities that will involve soil exposure and tick exposure and also to avoid unnecessary sun exposure.

- During periods of maximal immunosuppression, LT recipients should avoid crowds to minimize exposures to respiratory illnesses.

- Work in high-risk areas, such as construction, animal care settings, gardening, landscaping, and farming, should be reviewed with the transplant team to develop appropriate strategies for the prevention of high-risk exposures.

- LT recipients should avoid the consumption of water from lakes and rivers.

- LT recipients should avoid unpasteurized milk products and raw and undercooked eggs and meats (particularly uncooked pork, poultry, fish, and seafood).

- LT recipients should avoid high-risk pets, which include rodents, reptiles, chicks, ducklings, and birds.

- Travel by LT recipients, especially to developing countries, should be reviewed with the transplant team a minimum of 2 months before departure to determine optimal strategies for the reduction of travel-related risks.

- LT recipients should take precautions to prevent vector (including mosquito)-borne diseases. These include avoiding going out during peak mosquito feeding times (dawn and dusk) and using N,N-diethyl-meta-toluamide—containing insect repellants.
• LT recipients should undertake a thorough review of hobbies to assess potential infectious disease risks, particularly those associated with outdoor hobbies.
• All LT recipients should be educated about the importance of sun avoidance and sun protection through the use of a sunblock with a sun protection factor (SPF) of at least 15 and protective clothing. They should be encouraged to examine their skin on a regular basis and report any suspicious or concerning lesions to their physicians.
• Because of the strong association of lung, head, and neck cancers with smoking, the sustained cessation of smoking is the most important preventive intervention.

**Patient summary:** As a LT patient, the addition of antirejection medications changes how your immune system interacts with the everyday routine activities you used to complete before your transplant. Therefore, several precautions are recommended to protect your health and to add to your well-being. These recommendations are summarized in Table 1. In addition to this, when traveling outside of the country, especially if traveling to developing countries where sanitation may be a potential issue, please discuss precautions with your transplant team so you can better prepare for the travel. Travel to certain countries may require you to take some preventive medications, while in others, special precautions are required when drinking water and eating foods. Discussions should be held a minimum of 2 months before scheduled travel so appropriate planning may be carried out (Fig. 3).

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**FIG 3** Various precautions that are required to promote a patient’s health after LT.