**Short Communication**

# Future Map of Liver Transplantation

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**Abstract**

Liver transplantation (LT) is known to be the final solution for patients suffering from hepatic decompensation and its sequalae. There will be changing trend in liver transplant indications in the future. Non-Alcoholic Steatohepatitis (NASH) related cirrhosis will be the leading indication for LT in Europe, United State and in the Middle East. There will be change in the patient characteristics who are in need for liver transplantation. Liver transplant teams will encounter cases with NAFLD (Non- Alcoholic Fatty Liver Disease) and their linked comorbidity. There will be unmet need for expanding donor pool in the future. Direct-acting antivirals (DAAs) led to dramatic change in HCV treatment and have opened the road for using HCV positive organs as a trial to increase the donor pool. However, to generalize this concept in living donor liver transplant in Countries which had high volume of HCV cases who treated by DAAs as Egypt, this need consensus agreement between different liver transplant centers in the Country. There will be changing trend in NAFLD patient management pre and post liver transplant. There will be expanding role for bariatric surgery specially sleeve gastrectomy before or during LT surgery. Immunosuppression need to be modified and optimized to the patient metabolic risk profile. NAFLD associated comorbidities need specific management pre- and post-transplant. Multidisciplinary Teamwork will be the key for successful outcome of liver transplant operations.

**Key Words:** Liver Transplantation ; Changing Trend; NASH; Cirrhosis.

**1-Changing Map in Liver Transplantation indications:**

Liver transplantation (LT) is known to be the final solution for patients suffering from hepatic decompensation and its sequalae (1).

Several reports on LT indications have been published in different Western countries (2, 3, 4). However, few data on changing trend regarding LT indication in Eastern Countries, especially after the wide use of DAAs since 2014 (5). Before DAAs, the main indication for LT was HCV related hepatic decompensation without HCC (6).

DAAs led to dramatic change in HCV treatment, reduced HCV related liver cirrhosis and its index complications which need LT in those patients (7, 8). However, Non-Alcoholic Steatohepatitis (NASH) and ALD (Alcoholic Liver Disease) are increasing up to 28.1% and 37.7% of the total indications among LT candidates without HCC in 2019 in the United States. These percentages were considered to be much more than what was reported in 2002 (6).

HCC related to viral hepatitis or alcohol induced liver diseases are stationary. In contrast, HCC related to NAFLD/ NASH are increasing more than 7 folds (9).

The European LT Registry Annual Report in 2018 demonstrated a declining trend in viral hepatitis related cirrhosis as LT indication over 50 years, and the report highlighted that NASH related cirrhosis is the emerging indication for LT in the future (2).

Regarding Middle East, Alqahtani et al., (2021) in Saudi Arabia highlighted the difference in LT indications in two periods. The main LT indications were HCV (42%) and HBV (21%) in the era between 2001–2010. However, in the Era between 2011–2019, NASH was the main LT indications (30%) followed by HCV (24%)(10).

Also, Alqahtani et al., (2021) showed the difference in LT indications in relation to DAAs availability. Before DAAs, HCV (39%) followed by HBV (22%) were the most common indications for LT. However, post-DAAs, NASH emerged as the leading LT indication (30%), followed by HBV (23%)(10).

**2-Changing trend in patient characteristics:**

Patients with NASH when develop HCC are older with larger tumors (11) and they are discovered late (12). Only 15% of patients with NASH related HCC are diagnosed at early stage suitable for curative option (13).

**3-Changing trend in the contraindication of liver transplant:**

**3.1 Age of the recipients:**

Some experts stated that liver transplantation is contraindicated in older LT candidates due to associated comorbidities and they are prone to perioperative complications which decrease the long-term survival (14, 15).

One report showed that the patient and graft survival were similar in those transplanted in their 60s and 70s and they concluded that patient above 70 should not be prevented from transplant based mainly on age(16).

Other consider age more than 75 as a relative contraindication for LT( 17)

**3.2 Obesity in liver transplant candidates:**

Obesity in potential liver transplant candidates without another comorbidity is no longer contraindication for LT (18). Liver transplant candidates with body mass index (BMI) ≥40 kg/m2 is considered a relative contraindication for LT by two different guidelines (19, 20).

Obese patients who fails to achieve weight loss goal before liver transplant are candidates for combined LT surgery and bariatric surgery either before or during LT surgery (21).

Sleeve gastrectomy is better than Roux-en-Y gastric bypass surgery because it does not prolong transplant operation, preserves normal anatomy, and maintain normal absorption. Therefore, immunosuppression level can be easy optimized. In addition, biliary channels can be examined endoscopically in case of occurrence of biliary problems (22).

**4- Change in the discard and utilization of Hepatitis C – infected donor livers:**

**4.1 Changes in Discard Rate of Livers from HCV+ Donors:**

Before 2010, the discard rate of livers from HCV positive was 28% per year.

The discard rate declined over time reaching 22% in 2011, and 11% in 2015.

DDLT recipients who were HCV positive and received graft from HCV positive raised from 6.2% between 2005 - 2010 to 16.9% in 2015.

Despite the increase in utilization of HCV+ Donors, allograft survival remains equal between recipients of HCV positive or negative graft (23).

**4.2 Utilization of Hepatitis C – infected donor livers:**

DAA therapy decreased progressive liver disease posttransplant. Moreover, modern DAA therapy have opened the road for using HCV positive organs as trial to increase the donor pool and this concept will change the nature of solid organ transplantation (24).

**4.3 HCV-viremic organs could be considered in:**

- Patients with fulminant hepatitis, or HCC, or patients with low MELD score but had portal hypertension complications (25).
- Donors exposed to hepatitis C virus (HCV) can be used safely in HCV seronegative liver transplant candidates, provided that treatment is initiated early post LT (26).

**4.4 Concept Generalization regionally and globally:**

- To generalize this concept in living donor liver transplant in Countries which had high volume of HCV cases who treated by DAAs as Egypt, this need consensus agreement between different liver transplant centers.

**5- Changing trend in NAFLD patient management in the setting of liver transplantation (LT):**

**5.1 NAFLD pre and Post LT:**

NASH is the upcoming indication for LT in Western countries. Metabolic dysfunction associated fatty liver disease (MAFLD) is a new term which better characterize liver conditions with their associated metabolic dysfunction (27).

However, a debate has recently arisen in hepatology on this redefinition. Although strong evidence supports the new definition of MAFLD in clinical practice and research and this new definition has been endorsed by multiple stakeholders and societies, controversy still present (28). The American Association for the Study of Liver Diseases (AASLD) published Practice Guidance in 2023 using the traditional nonalcoholic fatty liver disease (NAFLD) nomenclature (29).

Different comorbidities as DM, morbid obesity, and CVD require different evaluation and management before transplant operation to minimize the risk of surgery and improve outcomes after liver transplantation. Patients with NASH are at increased risk of early post-transplant complications as infection and later, other as malignancy and cardiovascular complications may occur. In addition, patients with NAFLD/NASH are more prone to have metabolic sequalae after LT (30).

**5.2 Post-liver transplant management in NAFLD/MAFLD include (30):**

- Lifestyle modifications including weight loss, caloric restriction, and exercises.
- Modification of immunosuppressants.
- Treatment of metabolic syndrome as DM, Hypertension, and Dyslipidemia.

**5.3 Management of DM:**

In diabetic patients, steroids should be withdrawn early after LT and the tacrolimus dose should be minimized (30).

**5.4 Management of obesity:**

- Early introduction of Everolimus with use of lower dose tacrolimus should be considered (31).

**5.5 Management of hypertension and/or dyslipidaemia (32; 33):**

- Immunosuppressive minimization protocols are the role and Everolimus should be avoided.

**5.6 Tailored immunosuppression strategy:**

- mTORi or antimetabolites with reduced doses of tacrolimus, or tacrolimus withdrawal if possible, should be considered post LT for NASH cirrhosis to decrease the risk of metabolic complications (34).

**6. Conclusion:**

There is unmet need for expanding donor pool. The use of HCV positive treated donor is an option to increase donor pool. Consensus agreement in the future between different liver transplant centers for use of HCV positive treated donor is needed.

Older age and Obesity among liver transplant candidates are increasing and are no longer contraindication for LT. Sleeve gastrectomy before or during LT surgery can be done in selected morbidly obese LT candidates. NASH-related cirrhosis will be the main indication for LT within the next decade. The underlying metabolic conditions in cases of MAFLD are ongoing after LT. Therefore, important steps pre- and post-transplant are needed to improve outcomes in this category of LC. Lifestyle modifications, proper selection of potential LT candidates, as well as modification of immunosuppressants post LT are essential to improve the outcome and prevent recurrence of NAFLD/NASH after transplantation. Multidisciplinary Teamwork will be the key for successful outcome of liver transplant operations. Figure 1 shows the Future Map of Liver Transplantation.

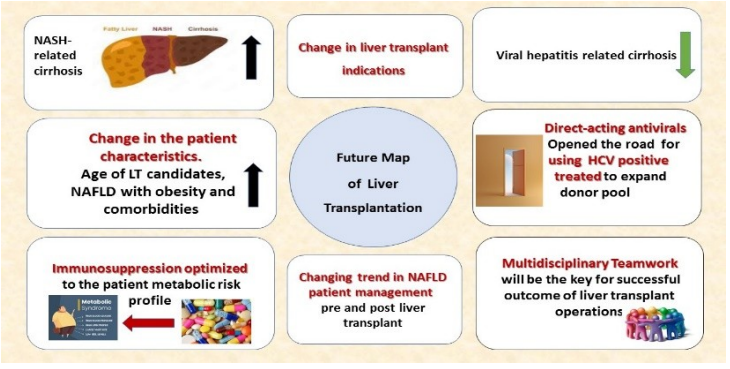


***Figure 1: Future Map of Liver Transplantation.***

**Declarations:** Nothing to declare

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