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Observational Study

Liver Transplantation for Hepatocellular Carcinoma in India - Are We Ready for 2040?

Liver Transplant for HCC in India

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Abstract

BACKGROUND

Liver transplantation (LT) for hepatocellular carcinoma (HCC) has been widely researched and is well established worldwide. The cornerstone of this treatment lies in the various criteria formulated by expert consensus and experience. The variations among the criteria are staggering, and the short- and long-term outcomes are controversial.

AIM

We aimed to study the differences in the current practices of LT for HCC at different centers in India and discuss their clinical implications in the future.

METHODS

We conducted a survey of major centers in India that performed LT in December 2022. A total of 23 responses were received. The centers were classified as high- and low-volume, and the current trend of care for patients undergoing LT for HCC was noted.

RESULTS

Of the 23 centers, 35% were high volume center (>500 Liver transplants) while 52% were high-volume centers that performed more than 50 transplants/year. Approximately 39% of centers had performed >50 LT for HCC while the percent distribution for HCC in LT patients was 5%–15% in approximately 73% of the patients. Barring a few, most centers were divided equally between University of California, San Francisco (UCSF) and center-specific criteria when choosing patients with HCC for LT, and most (65%) did not have separate transplant criteria for deceased donor LT (DDLT) and living donor LT (LDLT). Most centers (56%) preferred surgical resection over LT for a Child A cirrhosis patient with a resectable 4 cm HCC lesion. Positron-emission tomography-computed tomography (PET-CT) was the modality of choice for metastatic workup in the majority of centers (74%). Downstaging was the preferred

option for over 90% of the centers and included transarterial chemoembolization (TACE), transarterial radioembolization (TARE), stereotactic body radiotherapy (SBRT) and atezolizumab/bevacizumab with varied indications. The alpha-fetoprotein (AFP) cut-off was used by 74% of centers to decide on transplantation as well as to downstage tumors, even if they met the criteria. The criteria for successful downstaging varied, but most centers conformed to the UCSF or their center-specific criteria for LT, along with the AFP cutoff values. The wait time for LT from downstaging was at least 4–6 wk in all centers. Contrast-enhanced CT was the preferred imaging modality for post-LT surveillance in 52% of the centers. Approximately 65% of the centers preferred to start everolimus between 1 and 3 months post-LT.

CONCLUSION

The current predicted 5-year survival rate of HCC patients in India is less than 15%. The aim of transplantation is to achieve at least a 60% 5-year disease free survival rate, which will provide relief to the prediction of an HCC surge over the next 20 years. The current worldwide criteria (Milan/UCSF) may have a higher 5-year survival (>70%); however, the majority of patients still do not fit these criteria and are dependent on other suboptimal modes of treatment, with much lower survival rates.
To make predictions for 2040, we must prepare to arm ourselves with less stringent selection criteria to widen the pool of patients who may undergo transplantation and have a chance of a better outcome. With more advanced technology and better donor outcomes, LDLT will provide a cutting edge in the fight against liver cancer over the next two decades.

Key Words: HCC; Liver Transplant; India; Downstaging; Survey; Milan; UCSF; PVTT; Expanded Criteria

Pahari H, Raj A, Sawant A, Ahire DS, Rathod R, Rathi C, Sankalecha T, Palnitkar S, Raut V. Liver Transplantation for Hepatocellular Carcinoma in India - Are We Ready for 2040? *World J Transplant* 2023; In press

Core Tip: The current predicted 5-year survival rate of HCC patients in India is less that 15%. The aim of transplantation is to achieve at least a 60% 5-yr disease free survival which will truly provide a relief to the predictions of HCC surge over the next 20 years. The current worldwide criteria (Milan/UCSF) may have a higher 5-yr survival (>70%) but the majority of patients still do not fit these criteria and are dependent on other sub-optimal modes of treatment with much lower survival rates. In order to face predictions for 2040, we must prepare to arm ourselves with less stringent selection criteria to widen the pool of patients who may avail transplant and have a chance at a better outcome.

INTRODUCTION

Hepatocellular carcinoma (HCC) comprises for approximately 75%–80% of all liver cancer types in most countries. [1] HCC is the sixth most common cancer worldwide, comprising approximately 5% of the total cancer incidence, and causes approximately six deaths per 100,000 people annually. [2,3] In 2020, liver cancer was the third most common cause of cancer-related deaths worldwide (830,000). [4] There is a lack of statistical data from India, with the number of deaths estimated to be approximately 6.8 per 100,000 people, with a total of approximately 14,000 deaths annually in 2010. [5,6]

The burden of HCC has been increasing worldwide, and India is no exception. [7,8] Asian countries have reported the highest global liver cancer incidence (73%) and liver cancer deaths in 2020. [9] Between 1978 and 2012, there was a steady increase in the number of HCC cases in India. [10,11] In the USA, a recent study predicted a continued increase in HCC rates through 2030. [12] At present, India contributes to

approximately 18% of the incidence and 4% of the mortality. By 2040, the global burden of new cases and deaths from liver cancer may increase by up to 55% (an estimated 1.3 million cases and 1.4 million deaths). [13,14] However, India still has a low 5-year survival rate for HCC (<15%) despite the advancement of curative and palliative treatment options over the last two decades. [15,16]

Liver transplantation (LT) for HCC in patients with cirrhosis has been widely researched and is now well established worldwide. [17–19] The cornerstone of this treatment lies in the various criteria formulated by expert consensus and experience over the years. The Milan criteria was established by Mazzaferro *et al* in 1996 to improve the outcomes of LT for HCC in the initial aftermath of low survival and high recurrence rates. [20] Subsequent studies by Yao *et al* and Mazzaferro *et al* indicated the restrictive nature of these criteria, and slightly more liberal criteria, called the University of California, San Francisco (UCSF) criteria, were introduced in 2001. [21,22] These mainly included the number and size of HCC nodules, vascular invasion, and extrahepatic spread. Since then, several other criteria have been introduced, each with its own justification and outcomes. The variations among the criteria are staggering, and the short- and long-term outcomes are controversial. [19,23,24] Another factor is the evolution of living donor LT (LDLT) as a treatment option, which has led us to accept less stringent guidelines for LT in patients with HCC, as it does not affect the LT waitlist. However, the survival of HCC-LT recipients outside the standard criteria must be comparable to that of the expanded criteria to mitigate the additional risks to live donors. The incorporation of tumor markers into downstaging protocols has also contributed to improved outcomes and overall survival rates. We aimed to study the differences in the current practices of LT for HCC at different centers in India and discuss their clinical implications in the future.

MATERIALS AND METHODS

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