The Role of Liver Transplantation in the Treatment of Hepatocellular Carcinoma – a Single Center Experience from Budapest

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Background: Liver transplantation for hepatic tumours is known as a proven treatment opportunity. The outcome has improved over the past decades because of the appropriate recipient selection.

Materials and methods: In a single-institution study of 29 consecutive adult patients underwent orthotopic liver transplantation (OLT) between 1 January 2004 and 1 January 2011 in the Semmelweis University, Budapest with the indication of hepatocellular carcinoma (HCC).

Results: The 1-year survival was 85.7% and the 3-year survival was 71.7%.

Conclusions: Further investigations are needed on the field of histological and biological attributes of the hepatocellular carcinoma. Our aim is to find a better and individualized immunosuppressive protocol, which is also protective against malignant tumours.

Keywords: hepatocellular carcinoma, liver transplantation, mTOR-inhibitor

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Introduction

Liver transplantation (OLT) is a well-established and durable surgical therapy for all forms of end-stage liver disease and for certain malignancies. Over the years, the liver transplant survival rate improved. Adam R. et al. [1] described a 1- and 5-year survival of 83% and 75%, respectively. The success of such treatment has resulted in a progressively increasing claim for liver transplantation. At the same time, the organ donor shortage is rising. Several strategies have been established to increase the number of liver transplantation, such as harvesting organs from non-heart-beating donors and live donors, liver splitting and using organs from expanded criteria donors.

Liver transplantation is the best treatment option for patients with hepatocellular carcinoma and liver cirrhosis, unless they have excellent liver function and minimal portal hypertension [2]. Early experience of liver transplantation for patients with hepatocellular carcinoma was poor because tumoral recurrence was very frequent [3]. In 1996, Mazzaferro et al. [4] showed that a subgroup of patients with radiologic evidence of a single tumor ≤5 cm in diameter, or two to three tumors ≤3 cm in diameter had 5-year and recurrence-free survival rates of 75 and 83%, respectively. The Milan criteria were subsequently adopted by the United Network for Organ Sharing (UNOS) staging system for allocating organs for liver transplantation in the United States. However, recent data suggest that Milan criteria may be too conservative. Yao et al. [5] reported their results with a moderate expansion of these criteria (so-called University of California at San Francisco (UCSF) criteria). Patients selected with these expanded criteria had disease-free survival that was comparable to survival of patients selected with Milan criteria.

In Hungary the first liver transplantations were performed in 1995 in the Department of Transplantation and Surgery of the Semmelweis University, Budapest. In the case of hepatocellular carcinoma, from 2001 we started to adapt our policies to the Milan criteria, and our results are acceptable and comparable to the worldwide results. The 5-year survival after OLT for HCC is more than 50% comparing to the more than 80% 5-year survival rate after OLT for other indications [6]. In this review the author analyzes the survival results of an ongoing study of liver transplantation for hepatocellular carcinoma between 1 January 2004 and 1 January 2011. Our aim is to find the possible ways to improve patient survival by refining recipient selection and tailoring individual immunosuppressive therapy.

Material and method

A single-institution study of 29 consecutive adult patients undergoing orthotopic liver transplantation between 1 January 2004 and 1 January 2011 with the indication of hepatocellular carcinoma. Survival was calculated with Kaplan-Meyer log rank analysis. Mean age at time of transplantation was 50.8 years (28–63). The median follow-up was 1236.3 days (89–2266). 55.17% of the recipients were male (n = 16) and 44.82% were female (n = 13). All surgeons used similar “cross-clamp” technique (recipient hepatectomy including vena cava segment). The histological examinations are under investigation regarding tumour
Liver transplantation for HCC in the adult population

Discussion

While patients with early resectable HCC and preserved hepatic function should undergo surgical resection, in those with unresectable disease due to underlying liver dysfunction, orthotopic liver transplantation offers the best chance for cure. Liver transplantation for hepatic tumours is known as a proven treatment opportunity. The first chance for cure. Liver transplantation for hepatic tumours function, orthotopic liver transplantation offers the best for those with unresectable disease due to underlying liver dysfunction.

size, grade, vessel invasion and extrahepatic propagation. The average intraoperative demand for blood transfusion was 5.8 units (0–26). All of the liver transplant recipients received a maintenance immunosuppressive therapy combination of tacrolimus or cyclosporine A, mycophenolate-mofetil (MMF) and corticosteroids. In the case of tumour recurrence, the immunosuppression was converted into an mTOR-inhibitor (sirolimus or everolimus).

Results

Survival was calculated with Kaplan-Meyer log rank analysis (Figure 1). Nine of our patients died in the late postoperative period (31.0%). The main cause of death was HCC recurrence, in 6 cases: 3 in the liver, 1 in the lung, 1 in the cardia and 1 in the femur were observed. 2 patients died because of HCV recurrence and 1 with liver angiosarcoma. The 1-year survival was 85.7% and the 3-year survival was 71.7%. According to the histology fifteen patients were within the Milan criteria and 14 exceeded the criteria.

Our results with the 1- and 3- year survival rates – 85.7% and 71.7% respectively – are comparable to other’s in the literature. Herrero et al. [14] reported a 1-, 3-, 5-, 7-, and 10-year survival rates of their 73 transplanted HCC patients were 86%, 74%, 70%, 61%, and 50%, respectively. Similarly their patients exceeding Milan criteria had a higher dropout rate due to tumoral progression. According to a large multicenter study by Mazaferro et al. [15] for those transplanted outside the Milan criteria, 5-year overall survival was 53.6% compared with 73.3% for those that met the criteria.

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Another very important issue is the effective immunosuppression therapy by using drugs that help to decrease HCC recurrence. Introduction of mTOR-inhibitors to the immunosuppressive therapy protocols guided to lower tumour incidence among transplant patients in general.
hibitor could be effective in patients with posttransplant HCC recurrence not suitable for radical therapy, but the toxicity and efficacy need to be further evaluated [17]. In our department we are trying to find mTOR activity in the HCC, normal and cirrhotic liver biopsies to evaluate the potential efficacy of our immunosuppressive strategy. Asian transplant centers have significantly modified the previous restrictions with the use of biomarker des-carboxy-prothrombin [18]. These strategies should help to improve better outcomes of liver transplantation for malignancies in the future.

Conclusion

Further investigations are needed on the field of histological and biological attributes of the hepatocellular carcinoma. Our aim is to find a better and individualized immunosuppressive protocol, which is not only protective against acute rejection of the transplanted organ, but also protective against recurrence or de novo manifestation of malignancy. Moreover it is important to expand the liver donor pool by developing the living donor liver transplant program.

References