Orthotopic liver transplantation for primary hepatic cancer*☆

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Abstract

BACKGROUND: The affected liver can be completely removed by liver transplantation, long-term efficacy is superior to liver resection, the 5-year survival rate reaches 70% H1. In addition, liver transplantation can avoid a serious risk for incomplete liver function caused by hepatic resection in the case of liver dysfunction.
OBJECTIVE: To retrospectively analyze the treatment effects and importance of orthotopic liver transplantation for primary hepatic cancer patients.
METHODS: A total of 75 patients with primary hepatic cancer treated by orthotopic liver transplantation in Department of Hepatobiliary Surgery, Fuzhou General Hospital of Nanjing Military Area Command of Chinese PLA from March 1980 to December 2008 were involved in the analysis for the postoperative survival rates and recurrence of tumors.
RESULTS AND CONCLUSION: For all the patients, the total postoperative survival rate in the 1st, 2nd and 3rd year was 86.6%, 66.7% and 53.3% respectively, the disease free survival rate was 65.2%, 53.9%, 34.1%. Their mean survival time is 25 months. For the patients in line with Milan standard, the postoperative survival rate in the 1st, 2nd and 3rd year was 88.4%, 72.5% and 57.9% respectively, the disease free survival rate was 77.6%, 62.3%, 51.8%. Their mean survival time is 39 months. Tumor recurrence occurred within one year in all six patients who were beyond Milan standard. Two patients died in one year after operation, the survival rate at postoperative one year was 66.7% and the remanent four patients all died in the 2nd year after operation. Orthotopic liver transplantation was one of the effective treatments for primary hepatic cancer patients. The patients which were measured up to Milan standard would have the best curative effects.

INTRODUCTION

It is well-known that early diagnosis and treatment are difficult for primary hepatic cancer patients, these can result in the poor prognosis. Although hepatectomy is regarded as the preferred treatments for hepatic cancer patients, it is regrettable that most of the patients can not endure this operation because of the poor liver function caused by concomitant liver cirrhosis or polycentric cancers. Even the hepatectomy could be performed in these patients, tumor still may reoccur in three years after operation. These all result in the curative effects for hepatic cancers by routine therapy. Clinical liver transplantation brings a delightful new therapeutic method for liver cancer patients. In this operation, the total morbid liver, local lymph nodes and possible corrosive local vessels would be totally resected. By this method, not only the cancer could be resected but also the portal hypertension caused by liver cirrhosis could be resolved radically. Then we could get new livers with normal structure and function[1]. It reveals more predominance than routine therapies for hepatic cancers. In this article, seventy-five hepatic cancer patients treated by liver transplantations in Department of Hepatobiliary Surgery, Fuzhou General Hospital of Nanjing Military Area Command of Chinese PLA from March 1980 to December 2008 would be analyzed.

SUBJECTS AND METHODS

Design

Case analysis.

Time and setting

The experiment was implemented in Department of Hepatobiliary Surgery, Fuzhou General Hospital of Nanjing Military Area Command of Chinese PLA from March 1980 to December 2008.

Subjects

Seventy-five hepatic cancer patients treated by liver transplantations in our hospital from March 1980 to December 2008 were analyzed (Male 59 cases, Female 16 cases). Among these patients, sixty-nine patients met a criterion of Milan and six patients were below standard of Milan. Their age was from 25 to 72 years (average 46.87 years). The follow-up time was from 1 to 44 months (average 19.25 months). The follow-up rate was 100%. The liver functions of the patients were 58 cases with Child grade A, 15 cases with Child grade B, 2 cases with Child grade C. Seventy-one patients had traditional orthotopic liver transplantations and four patients had piggy back liver transplantations.

Tumors

The size, amount, vessels and proliferative area of tumors were ascertained by B ultrasound, CT or MRI before operation and pathology after operation. Sixty-nine cancer patients were measured up to Milan standard and six patients were not (Three cases had only one liver cancer node without proliferation but the diameter of the cancer node was more than 10 centimeters. Two patients had diffuse small cancer nodes in the liver without outside proliferation. One patient had a 2-centimeter large and 3-centimeter large cancer node in liver with hepatic portal lymph node metastasis).

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Statistic analysis

The total survival rate and disease free survival rate of all involved patients were determined. Tumor reoccurrence rate and survival time in 1, 2 and 3 years after operation for these hepatic cancer patients were analyzed respectively. Data were imported into Systat software (SPSS 11.0 software package for statistical computations and graphing). One-way analysis of variance, independent-samples *t*-test and Chi-Square tests were used to evaluate the differences between groups. A level of $P < 0.05$ was considered a significant difference.

RESULTS

For 1, 2 and 3 years after operation, the total survival rates and disease-free survival rates for all the forty-five patients were 86.6%, 66.7%, 53.3% and 65.2%, 53.9%, 34.1% respectively. The survive time ranged from 3 days to 45 months (average 25 months). There were ten, fifteen and ten patients died in the first, second and third years after operations. Forty patients lived more than three years. Tumor reoccurrence time ranged from 2 months to 39 months (average 25 months).

For 1, 2 and 3 years after operation, the total survival rates and disease-free rates for patients measured up to Milan Standard were 88.4%, 72.5%, 57.9% and 77.6%, 62.3%, 51.8% respectively. The average survive time was 39 months. Tumor recrudescence occurred in the six patients who were not measured up to Milan Standard in the first year after operation. Two patients died in the first year after operation and the one-year survival rate was 66.7%. The other four patients died in the second year after operation and the average live time was 14 months. For the survival rate and tumor recrudescence rate in the 1, 2 and 3 years after operation, there were significant differences between the two groups ($P < 0.05$).

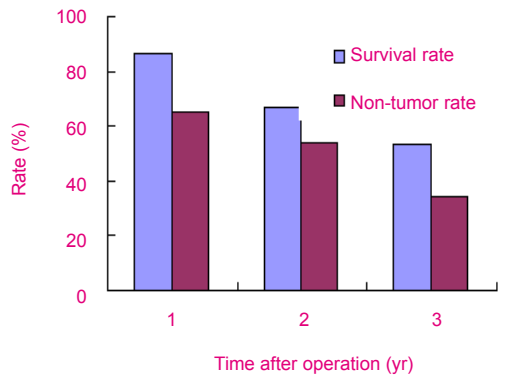

Figure 1 Postoperative survival rate and disease-free survival rate for 75 hepatic cancer patients treated by liver transplantation

DISCUSSION

Choice of indication for liver transplantations in hepatic cancer patients

Milan Standard is regarded as the routine indication for liver transplantations in hepatic cancer patients nowadays. This standard means a single tumor with diameter's not larger than 5 centimeters or less than three tumors with diameters' not larger than 3 centimeters, with no vessels infiltrate in the liver and no metastasis outside the liver[1]. It has reported that for hepatic cancer patients keep to Milan standard and not, the four-year survival rate of the former group was much higher than the latter[1-2]. In our center, seventy-five hepatic cancer patients were treated by liver transplantations from March 1980 to December 2008. In these patients, sixty-nine cases measured up to the Milan standard, and they had much better prognosis than those who did not measure up to Milan standard. We also found that forty cases of these patients lived longer than three years after transplantation. For those patients who did not measure up to Milan standard, the one-year recrudescence rate after operation was 100% and the long term prognosis was much poorer.

Recrudescence risks of hepatic cancers patients after liver transplantations

Many factors could induce the cancer recrudescence for patients after liver transplantation, such as surgical indications, surgical processes and the choice of postoperative immunosuppressant therapy[3]. Could the primary hepatic cancer especially the progressive cancer be regarded as indications for liver transplantation? The estimation should base on the tumor size and amount or the envelope of tumors, as well as the vessel infiltration and the lymph node metastasis. The biological and pathological characteristics of tumors, hepatocirrhosis and hepatitis virus infections also should be analyzed before transplantations[4]. Generally speaking, small liver cancer (diameter smaller than 5 centimeters) with hepatocirrhosis, no vessel infiltration and outside metastasis are the accepted indication for liver transplantation[5]. But for many patients with progressive cancers, the very small metastasis could not be found before transplantations, these made the cancer recrudescence easily occurred after liver transplantation. If the manipulations during the operation were not appropriate, the tumor cells' strewment also easily occurred, therefore causing the cancer recrudescence after operation[6]. Then it was very important for us to pay more attention to the manipulations during the operation to avoid the tumor cells' strewment. At the same time, postoperative immunosuppressant therapy restrained the anti-tumor immunoreaction of patients, these also made the cancer recrudescence easily occurred[7].

Prevention of liver cancer recurrence after liver transplantations

Prevention of cancer recurrence is the most important thing for those liver cancer patients treated by transplantations. Appropriate choice of indication for liver transplantations in hepatic cancer patients maybe directly affects the prognosis for these patients. Small liver cancer with liver cirrhosis is commonly regarded as the ideal indication for liver transplantation nowadays, but whether the exhibition period liver cancer could be regarded as the indication for transplantation still has debates[8-10]. Because the liver

cancer could grow larger and metastasis to other sites in the patients waiting for transplantations, then the antiblastic treatment for cancers before transplantations becomes helpful to prevent the cancer cell metastasis and post-operative recurrence[11-12]. Take the transcatheter hepatic arterial chemoembolization for an example, PEI and peri-operative chemotherapy all could be used in the operation waiting period[13-15]. Excessive use of immunosuppressant after transplantation could cause cancer recurrence and post-operative infections, but deficient use also induces post-operative repulsion. Then appropriate use of immunosuppressant is very important for these transplantation patients[17-19]. With the development of living donor liver transplantations, waiting time for donors becomes markedly shorter than before[20-21]. This also is helpful to prevent post-operative cancer recurrence[22-24]. Generally speaking, post-transplantation cancer recurrence is still a hotspot in clinical transplantations[25-29]. We all hope that the prevention for post-transplantation cancer recurrence might become consummated by our unremitting research.

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原位肝移植治疗原发性肝癌*☆

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摘要

背景：肝移植可完整切除病肝，远期疗效优于肝切除，其5年存活率可达70%H1。此外，肝移植还可避免在肝功能不良的情况下肝切除带来的术后肝功能不全的严重风险。

目的：回顾性分析原发性肝癌原位肝移植治疗效果及意义。

方法：对解放军南京军区福州总医院肝胆外科1980-03/2008-12因原发性肝癌行原位肝移植术患者75例术后生存及肿瘤复发情况进行总结分析。

结果与结论：75例患者术后1, 2, 3年的总体生存率及无瘤生存率分别为：86.6%, 66.7%, 53.3%及65.2%, 53.9%, 34.1%, 平均生存时间25个月。其中符合Milan标准的手术患者术后1, 2, 3年的总体生存率及无瘤生存率分别为：88.4%, 72.5%, 57.9%及77.6%, 62.3%, 51.8%, 平均生存时间39个月。超出Milan标准的6例患者均在术后1年内出现肿瘤的复发，有2例患者在术后1年内死亡，术后1年生存率为66.7%。其余4例患者于术后2年内相继死亡。平均生存时间14个月。提示原位肝移植是原发性肝癌的有效治疗方法之一，选择符合Milan标准的原发性肝癌患者行肝移植手术治疗将会取得最佳疗效。

关键词：原发性，肝癌；肝移植；原位；Milan标准
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课题的意义：肝移植是治疗肝癌的一个有效手段，特别适合于伴有肝功能障碍的早期肝癌，对于大肝癌伴或不伴有门静脉分支癌栓的肝癌患者，在无远处转移情况下，肝移植也是一个较好的选择。

提供临床借鉴的价值：肝移植对于门静脉主干有癌栓者，肝移植应列为禁忌。此外肝癌肝移植术后应重视免疫抑制剂的应用调整，这对于防止肝癌术后复发有一定的意义。

外国专家修饰的医学英语句型：本刊英文部

中文	修饰前	修饰后
早晨抽取空腹静脉血	Following admission (within 3 days), at 6, 12, and 30 days subsequent to disease attack, 3 mL venous blood was **taken from each patient before morning mean, followed by 10-minute centrifugation at 3 000 r/min.**	Following admission (within three days), at days 6, 12, and 30 days subsequent to disease attack, 3 mL venous blood was **taken from each patient before the morning meal,** and were centrifuged at 3 000 r/min for 10 minutes.
预后良好 预后不良	Basic recovery, marked improvement, and improvement were regarded **as good prognosis**, and no changes and deterioration were considered **poor prognosis**.	Basic recovery, marked improvement, and improvement were regarded **being signs of good prognosis,** and no change and deterioration **were considered signs of poor prognosis.**
长度超过…… 甚至…… longer than …., with… even…	In the NGF group, neurites were apparently presented, and the length of neurite in some adult neurons could reach **over** 100 μm, **even** 200 μm.	In the NGF group, neurites were present, and the length of neurites in some adult neurons was **longer than** 100 μm, **with some even** reaching 200 μm.