

学 位 論 文 の 要 約

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主論文の題名

Hypertension and HCV infection are strong risk factors for developing late renal dysfunction after living donor liver transplantation: significance of renal biopsy

(高血圧と HCV 感染は生体肝移植後における晚期腎機能障害の危険因子である
- 腎生検の意義について -)

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主論文の要約

Introduction

Among various comorbidities and morbidities influencing long-term outcome after liver transplantation, renal dysfunction (RD) is known to be one of the most important factors.

Background

There have been a few studies on the development of LRD after living donor liver transplantation (LDLT), in which the factors different from deceased donor liver transplantation (DDLT) such as small-for-size graft should be included.

Early diagnosis of LRD during the long-term follow-up after LDLT, is very important to provide proper treatment as early as possible according to its etiology.

Objectives

The aim of the present study was to analyze the risk factors for LRD after LDLT by using simple criteria of LRD, paying special attention to the significance of renal biopsy.

Methods

Among the 98 recipients undergoing LDLT between March 2002 and June 2008, 77 surviving more than one year were the subject of this study by excluding 21 who died within one year or had been followed at the other institutions. LRD was defined as the condition that serum creatinine level showed 1.5 mg/ml or more at any point in time after one year undergoing LDLT. Regardless of serum creatinine level, renal biopsy was indicated when the patient developed the following conditions: unexplained acute or rapidly progressive renal failure, nephrotic syndrome and significant non-nephrotic proteinuria, persistent glomerular hematuria, and systemic diseases with renal involvement.

Results

LRD was found in 22 patients (28.6%). Comparing various risk factors between 22 patients with LRD (LRD group) and 55 without LRD (non-LRD group), univariate analysis revealed recipient's age, generation, hypertension, HCV antibody positive, pre-transplant serum creatinine level and graft-to-recipient weight ratio (GRWR) as significant risk factors for LRD. By multivariate analysis of the factors influencing LRD, HCV and hypertension were selected as independent risk factors.

Renal biopsy was performed in 4 HCV positive patients, of whom 3 had concomitant hypertension and 2 had concomitant DM. As the result of histological and/or electron micrographic examination, however, only one patient was diagnosed as HCV-related membranous proliferative nephritis, one as diabetic nephropathy and two as drug (tacrolimus)-induced renal dysfunction.

Cumulative survival rate in LRD group was significantly lower than that of non-LRD group ($P=0.040$).

Consideration

In the present study, the univariate analysis of risk factors for LRD after LDLT revealed almost the same factors as those after DDLT, except for GRWR.

Multivariate analysis, however, revealed that HCV and hypertension were selected as independent risk factors. CYP3A5 and ACE genotypes did not differ between non-LRD and LRD groups.

We performed renal biopsy in the 4 patients who developed clinical manifestations regardless of serum creatinine levels. Because all of these patients were HCV positive, we suspected that the etiology of RD was nephritis related to HCV. However, the renal biopsy disclosed that only one patient was diagnosed as HCV-related membranous proliferative nephritis, one as diabetic nephropathy and two as drug (tacrolimus)-induced renal dysfunction.

In LRD group, long-term prognosis was significantly poor than in non-LRD group. The causes of death in both groups did not differ, and actually there was no death directly related to LRD. According to the multivariate analysis, HCV and hypertension were the independent risk factor for LRD, and it was therefore considered that these two factors adversely affected prognosis.

Conclusion

Although HCV and hypertension were determined as independent risk factors for LRD after LDLT, renal biopsy should be performed when clinical symptoms develop regardless of creatinine levels in order to provide appropriate treatment.