

## The Clinical Outcome of HBsAg(+) Renal Allograft Recipients

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=국문초록=

### B형 간염 항원(HBsAg) 양성인 말기 신부전증 환자에서 신이식 후의 임상 경과에 관한 연구

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HBsAg 양성인 신이식 후의 임상 경과에 미치는 영향에 대해서는 아직 논란이 많은 실정이다. HBsAg 양성인 환자에서 신이식 후 간부전과 감염 등으로 인한 사망률이 높다는 연구 보고가 있는 반면에, 이러한 차이를 발견하지 못하였다는 보고도 있다. 그러나 지금까지의 연구 보고는 사체신이식을 포함하고 있었으며, 신이식 전에 간조직 검사를 시행하지 않았던 경우가 대부분이었다. 이에 저자 등은 HBsAg 양성인 신수혜자에서 B형 간염 바이러스가 생체신이식 후의 임상 경과에 미치는 영향을 알아보고자, 1979년 4월부터 1994년 12월 사이에 연세의료원에서 신이식을 받은 환자 1259예 중 생체신 이식을 받고, 면역억제제로 cyclosporine A를 사용한, anti-HCV 음성인 1102예를 대상으로 HBsAg 양성군과 음성군으로 나누어 각 군의 임상 경과를 비교하여 다음과 같은 결과를 얻었다.

1) HBsAg 양성군 환자는 34예(3.1%)로 남녀비는 3.3 : 1, 평균 연령은 32.5세이었다. 이식전 간조직 검사는 33예에서 시행하였으며, 14예에서는 정상 간조직 소견(이하 carrier), 18예에서는 만성 지속성 간염(chronic persistent hepatitis, 이하 CPH), 그리고 1예에서는 만성 활동성 간염(chronic active hepatitis) 소견을 보였다.

2) HBsAg 양성군에서는 음성군에 비해 신이식 후 간부전으로 인한 사망(50.0% vs. 5.4%,  $p < 0.05$ ), 만성 간염(41.2% vs. 1.1%,  $p < 0.05$ ), 그리고 간외 감염(20.6% vs. 9.1%,  $p < 0.05$ )이 유의있게 많았으나, 급성 거부반응은 양군 사이에 의미있는 차이가 없었다.

3) 5년 이식신 및 환자 생존율은 HBsAg 양성군에서 각각 55.0%, 77.9%로 HBsAg 음성군의 81.8%, 90.6%에 비해 유의있게 낮았다( $p < 0.05$ ). 간조직 소견에 따라 carrier군과 CPH군으로 나누어 보았을 때, 이식신 생존율은 carrier군과 CPH군 모두에서 HBsAg 음성군에 비해 유의있게 낮았으나( $p < 0.05$ ), 환자 생존율은 CPH군에서만 유의있게 낮았다( $p < 0.05$ ).

이상의 결과로 HBsAg 양성인 신수혜자는 만성 간염, 간외 감염, 이식신 소실 및 간부전으로 인한 사망의 위험이 높기 때문에 신이식 전 간조직 검사 결과에 관계없이 좀 더 세밀한 신기능 및 간기능의 추적 관찰이 필요할 것으로 사료된다.

**Key Words:** HBsAg, Renal Transplantation, Graft and Patient Survival

The impact of hepatitis B surface antigen(HBsAg) on the clinical outcome of renal transplantation has been controversial. Several studies<sup>1-3)</sup> have revealed an increased mortality from hepatic failure and other diseases after renal transplantation in HBsAg(+) patients, whereas others<sup>4,5)</sup> have not shown such deleterious effects. However, most of these studies included cadaveric kidney transplants and lacked liver biopsy findings prior to transplantation.

In this study, we analyzed not only the effect of HBsAg on graft and patient survival after living-donor renal transplantation but also the differences in them according to the pre-operative liver pathology.

## PATIENTS AND METHODS

From April 1979 to December 1994, 1259 kidney transplantations were performed in our center. Among them, 1102 patients who received living-donor renal graft, were treated with cyclosporine A, and were not positive for anti-HCV, were the basis of this study. Thirty-four patients(3.1%), 26 males and 8 females, with a mean age of 32.5 years, were HBsAg(+) at the time of transplantation. Pre-transplant liver biopsy was done in 33 cases; no evidence of viral hepatitis in 14(42.4%), chronic persistent

hepatitis(CPH) in 18(54.5%), and mild chronic active hepatitis in 1(3.1%).

In addition to the usual monitoring for renal functions, liver function tests(LFT) including serum protein, albumin, aminotransferase(SGOT and SGPT), bilirubin, and alkaline phosphatase were also examined. Chronic hepatitis was defined as an elevation in aminotransferase level to twice the upper limit of normal for at least 6 months. Graft and patient survival rates were estimated with the Kaplan-Meier method.

## RESULTS

Of the 34 HBsAg(+) recipients, 6 patients have died; 3 died of hepatic failure and 3 of extrahepatic causes. Hepatic failure presented as the cause of death significantly more in the HBsAg(+) patients(50.0%) than in the HBsAg(-) recipients(5.4%)( $p<0.05$ ). Chronic hepatitis and extrahepatic infection occurred in 14(41.2%) and 7(20.6%) of these 34 cases, respectively. Compared to the HBsAg(-) recipients, chronic hepatitis and extrahepatic infection occurred significantly more in the HBsAg(+) patients(41.2% vs. 1.1%, 20.6% vs. 9.1%, respectively) ( $p<0.05$ ). However, there was no difference in the episode of acute rejection between the HBsAg(+) and HBsAg(-)

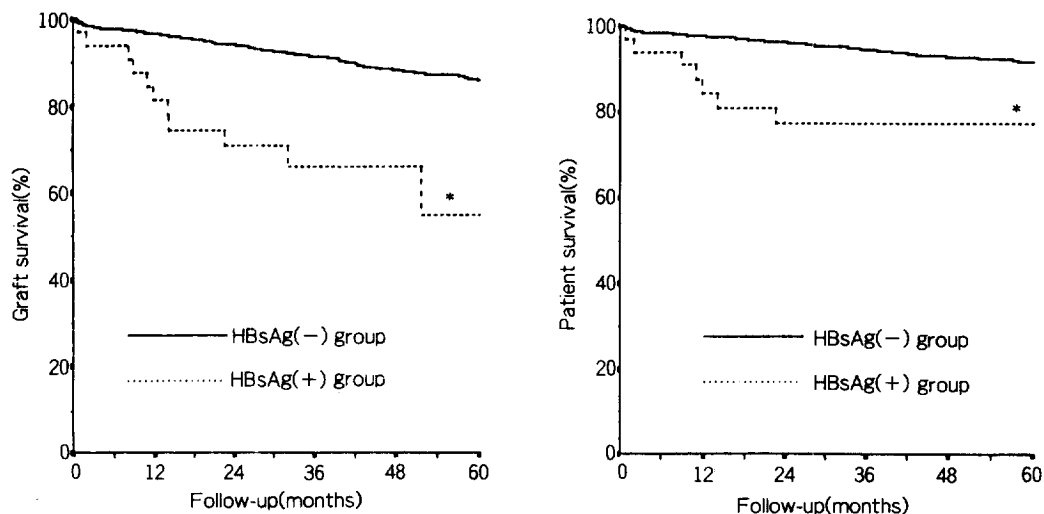


Fig. 1. Graft and patient survival according to the pre-operative HBsAg status \* $p<0.05$ , vs. HBsAg(-) group.

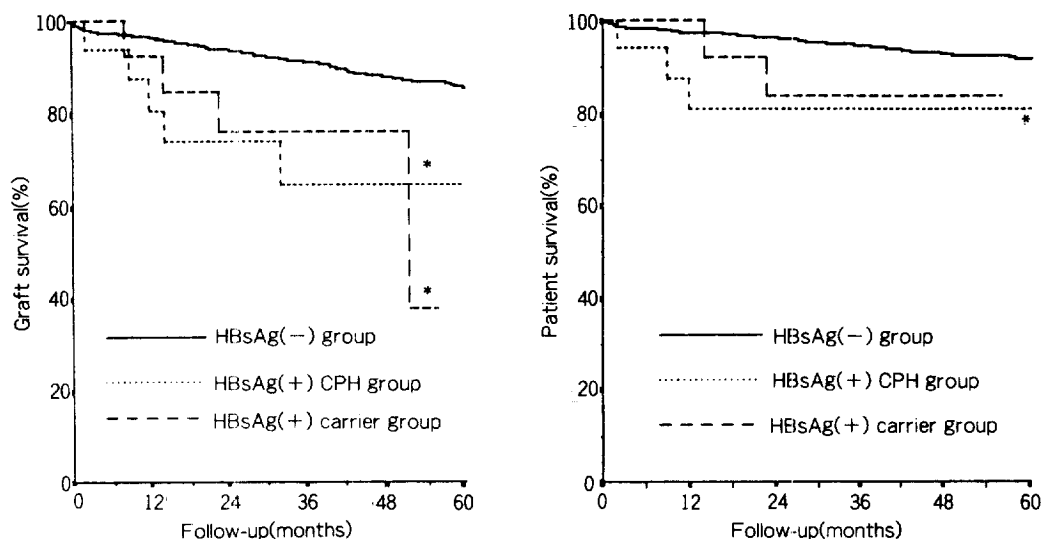


Fig. 2. Graft and patient survival according to the pre-operative liver pathology \* $p < 0.05$ , vs. HBsAg(-) group.

cases.

The graft and patient survival rates at 5 year in the HBsAg(+) patients were 55.0% and 77.9%, respectively. These results were significantly worse than those in the HBsAg(-) recipients (81.8% and 90.6%, respectively) ( $p < 0.05$ ) (Fig. 1). Considering the pre-operative liver pathology, the graft survival in both the carrier (77.4% at 3 year) and CPH (67.1% at 5 year) group were significantly worse than that in the HBsAg(-) recipients ( $p < 0.05$ ), whereas the patient survival was significantly lower only in the CPH group (77.9% at 5 year) ( $p < 0.05$ ) (Fig. 2).

## DISCUSSION

The impact of HBsAg on the clinical outcome of renal transplantation has been controversial and few of the reports included the pre-operative liver biopsy findings. Our results concerning the deleterious effect of HBsAg on the graft and patient survival are in agreement with the majority of recent studies<sup>1-3)</sup>. It seems that more chronic hepatitis and extrahepatic infection, probably due to immunosuppression, led to these results.

HBsAg(+) patients with CPH had worse graft and

patient survival as expected. And the graft survival in the carrier group was also inferior to that in the HBsAg(-) recipients. It raises the question of whether HBsAg(+) patient, even with no evidence of hepatitis on liver biopsy, should be a candidate for renal transplantation.

In summary, HBsAg(+) recipients are at increased risk for development of chronic hepatitis, extrahepatic infection, graft failure and death from hepatic failure after renal transplantation. Therefore, a careful follow-up for LFT as well as renal function tests in HBsAg(+) recipients will be necessary even though the pre-operative liver biopsy reveals no evidence of hepatitis.

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