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# Liver Transplantation from Brain-Dead Donors with Hepatitis B or C in South Korea: A 2014-2020 Korean Organ Transplantation Registry Data Analysis

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**Conflict of interest:** None declared

**Background:** According to the current guidelines for liver transplantation (LT) of brain-dead donors with hepatitis B or C virus (HBV or HCV) in Korea, grafts from hepatitis B surface antigen (HBsAg)(+) or HCV antibody (anti-HCV)(+) donors must be transplanted only to HBsAg(+) or anti-HCV(+) recipients, respectively. We aimed to determine the current status and outcomes of brain-dead donor LT with HBV or HCV in Korea.

**Material/Methods:** This retrospective observational study included all LTs from brain-dead donors in the Korean Organ Transplantation Registry between April 2014 and December 2020. According to donor hepatitis status, 24 HBV(+), 1 HCV(+), and 1010 HBV(-)/HCV(-) donors were included.

**Results:** Baseline/final model for end-stage liver disease score (MELD) for HBV(+), HCV(+), and HBV(-)/HCV(-) were 22.4±9.3/27.8±7.8, 16/11, and 33.0±15.4/35.5±7.1, respectively. MELD score of HBV (+) were lower than those of HBV(-)/HCV(-) ($P$<0.01). Five-year graft and patient survival rates of HBV(+) and HBV(-)/HCV(-) recipients were 81.7%/85.6%, and 76.6%/76.7%, respectively ($P$=0.73 and $P$=0.038). One-year graft and patient survival rates of HCV (+) graft recipients were both 100%.

**Conclusions:** No differences in graft and patient survival rates between HBV(+) and HBV(-)/HCV(-) groups were observed. Although accumulating the results of transplants from HBV (+) or HCV(+) grafts to HBV(-) or HCV(-) recipients is not possible owing to domestic regulations, Korea should conditionally permit transplantations from HBV(+) or HCV(+) grafts to HBV(-) or HCV(-) recipients by considering the risks and benefits based on foreign studies. Thereafter, we can accumulate the data from Korea and analyze the outcomes.

**Keywords:** Brain Death • Hepatitis B • Hepatitis C • Liver Transplantation • Tissue Donors

**Full-text PDF:** https://www.annalsoftransplantation.com/abstract/index/idArt/943588





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## Introduction

As of 2020, 6102 people were waiting for liver transplants in Korea, which accounts for 14% of all organ transplant waiting lists and has increased annually from 4422 in 2014 [1]. To resolve donor–recipient disparity due to the organ shortage, the concept of expanded criteria donors was introduced, and donors with hepatitis B and C virus (HBV and HCV) were included [2]. Under the current Center for Korean Network for Organ Sharing (KONOS) guideline, in cases of liver transplantation (LT) of a deceased brain-dead donor with HBV or HCV in Korea, grafts from hepatitis B surface antigen (HBsAg)(+) donors must be transplanted only to HBsAg(+) recipients, and the grafts from HCV antibody (anti-HCV)(+) donors must also be transplanted to anti-HCV(+) recipients [3]. Previous studies have shown that the transplantation of an antibody to hepatitis B core antigen (anti-HBc)(+) graft is safe, and peri-transplantation antiviral prophylaxis helps to obtain similar post-transplant outcomes [4-7]. Although the transplantation of HBsAg(+) grafts remains controversial, many studies have reported positive outcomes of transplantation using HBsAg(+) liver grafts [8-11]. We aimed to determine the current status and outcomes of brain-dead donor LT in patients with HBV or HCV in Korea.

## Material and Methods

This retrospective observational study used data from the Korean Organ Transplantation Registry (KOTRY) database between April 2014 and December 2020. Data included all LTs from brain-dead donors in the KOTRY database, which were divided into 3 groups according to their hepatitis status. A total of 1035 LTs were performed, including 24 from HBV(+) donors, 1 from HCV(+) donors, and 1010 from HBV(-)/HCV(-) donors. No patients were excluded owing to a lack of data or other reasons. All continuous data are presented as medians, standard deviations, and ranges. Categorical data are presented as numbers. All statistical analyses were performed using SPSS Statistics for Windows (version 26.0; IBM Corp., Armonk, NY). The chi-square, Fisher's exact, and *t* tests and Kaplan-Meier survival analysis were used. This study was approved by the Institutional Review Board of the Korea University Medical Center (2023AN0021). Owing to the retrospective nature of the study, the requirement of informed consent was waived.

## Results

**Table 1** presents the characteristics of the donors in the 3 groups. Because there was only 1 HCV(+) donor, statistical analysis was only performed between HBV(+) and HBV(-)/HCV(-) donors. No statistically significant differences were noted between the HBV(+) and HBV(-)/HCV(-) donor groups, except for the donor type. The causes of brain death in HBV(+) donors were disease progression (n=11, 45.8%), suicide (n=7, 29.2%), and trauma (n=6, 25%). In HCV(+) donors, underlying disease progression was the single cause of brain death (n=1, 100%). Among the HBV(-)/HCV(-) donors, underlying disease progression (n=422, 41.8%), trauma (n=336, 33.2%), suicide (n=146, 14.5%), and other or unknown causes (n=106, 10.5%) were the causes of brain death. The mechanisms of

**Table 1.** Donor characteristics.

| | HBV(+) donors (n=24) | HCV(+) donor (n=1) | HBV(-)/HCV(-) donors (n=1010) | p value[a)] |
|---|---|---|---|---|
| **Age (median)** | 49.1±13.1 | 61 | 47.4±16.4 | HBV(+)- HBV(-)/ HCV(-): p=0.55 |
| **Sex** | | | | HBV(+) - HBV(-)/ HCV(-): p=0.39 |
| Male | 18 (75%) | 1 (100%) | 658 (65.1%) | |
| Female | 6 (25%) | 0 | 352 (34.9%) | |
| **BMI (median)** | 23.9±3.6 | 29 | 23.1±3.6 | HBV(+)-HBV(-)/ HCV(-): p=0.32 |
| **Cause of brain death** | | | | HBV(+)-HBV(-)/ HCV(-): p=0.09 |
| Trauma | 6 (25%) | 0 | 336 (33.2%) | |
| Underlying disease progression | 11 (45.8%) | 1 (100%) | 422 (41.8%) | |
| Suicide | 7 (29.2%) | 0 | 146 (14.5%) | |
| Other/unknown | 0 | 0 | 106 (10.5%) | |





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**Table 1 continued.** Donor characteristics.

| | HBV(+) donors (n=24) | HCV(+) donor (n=1) | HBV(-)/HCV(-) donors (n=1010) | p value[a)] |
|---|---|---|---|---|
| **Mechanism of brain death** | | | | HBV(+)-HBV(-)/ HCV(-): p=0.74 |
| Subarachnoid hemorrhage | 9 (37.5%) | 0 | 319 (31.6%) | |
| Intracranial hemorrhage | 5 (20.8%) | 1 (100%) | 293 (29%) | |
| Cerebral infarction | 0 | 0 | 38 (3.7%) | |
| Hypoxic damage | 10 (41.7%) | 0 | 321 (31.8%) | |
| CNS malignancy | 0 | 0 | 4 (0.4%) | |
| Other/unknown | 0 | 0 | 35 (3.5%) | |
| **Donor type** | | | | HBV(+)-HBV(-)/ HCV(-): p=0.01 |
| Standard donor (by KONOS category) | 11 (45.8%) | 0 | 736 (72.9%) | |
| Marginal donor (by KONOS category)[b)] | 13 (54.2%) | 1 (100%) | 274 (27.1%) | |
| **Vasopressor or inotropics used (+)** | 19 (79.2%) | 1 (100%) | 768 (76%) | HBV(+)-HBV(-)/ HCV(-): p=1 |
| **Graft type** | | | | HBV(+)-HBV(-)/ HCV(-): p=1 |
| Whole liver | 24 (100%) | 0 | 937 (92.8%) | |
| Modified Rt. Lobectomy | 0 | 0 | 5 (0.5%) | |
| Extended Rt. Lobectomy (Rt. Lobe with MHV) | 0 | 0 | 18 (1.8%) | |
| Rt. Lobectomy | 0 | 0 | 15 (1.5%) | |
| Lt. Lobectomy | 0 | 0 | 6 (0.6%) | |
| Extended Lt. Lobectomy (Lt. lobe with MHV) | 0 | 0 | 1 (0.1%) | |
| Lt. Lateral segmentectomy | 0 | 0 | 26 (2.5%) | |
| Rt. Posterior sectionectomy | 0 | 0 | 0 | |
| Reduced left lateral or mono-segment | 0 | 0 | 1 (0.1%) | |
| Others | 0 | 1[c)] (100%) | 1 (0.1%) | |

BMI – body mass index; CNS – central nervous system; KONOS – Korean Network for Organ Sharing; Rt – right; Lt – left; MHV – middle hepatic vein.

**a) Only statistical analysis was implemented between patients with HBV(+) and HBV(-)/HCV(-) due to the single number of HCV(+).**

**b) ≥3 of the following conditions:**

(1) Blood pressure was measured, regardless of whether inotropic agents were used in the last 12 h; systolic blood pressure was <60 mmHg and the duration exceeded 1 h.
(2) In case the inotropic agents have been used for >6 h in the past 12 h, and dopamine dose is >15 μg/kg/min or amines dose is >0.2 μg/kg/min.
(3) Length of stay in the intensive care unit exceeding 7 d.
(4) The serum sodium level remained >160 mEq/L more than twice (>6 h) during the most recent test.
(5) Serum bilirubin level is >2.5 mg/dL more than twice (≥6 h) during the most recent test.
(6) Prothrombin time (PT) remained <40% more than twice (>6 h) during the most recent test.

**c) Reduced Lt. lat. or mono-segment.**





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**Table 2.** Recipient characteristics.

| | HBV(+) graft recipients (n=24) | HCV(+) graft recipient (n=1) | HBV(-)/HCV(-) graft recipients (n=1010) | p value |
|---|---|---|---|---|
| **Age (median)** | 57.3±8.8 | 53 | 49.8±13.7 | HBV(+)-HBV(-)/ HCV(-): p=0.01 |
| **Sex** | | | | HBV(+)-HBV(-)/ HCV(-): p=0.81 |
| Male | 17 (71%) | 1 (100%) | 993 (98.3%) | |
| Female | 7 (29%) | 0 | 347 (1.7%) | |
| **ABO iso/compatible** | | | | HBV(+)-HBV(-)/ HCV(-): p=1 |
| Iso | 24 (100%) | 1 (100%) | 1,010 (100%) | |
| Compatible | 0 | 0 | 0 | |
| **HCV(±)** | | | | HBV(+)-HBV(-)/ HCV(-): p=0.40 |
| HCV(+) | 1[a] (4.2%) | 1 (100%) | 66 (6.5%) | |
| HCV(-) | 23 (95.8%) | 0 | 944 (93.5%) | |
| **HBV(±)** | | | | HBV(+)-HBV(-)/ HCV(-): p<0.001 |
| HBV(+) | 24 (100%) | 1 (100%) | 313 (31%) | |
| HBV(-) | 0 | 0 | 697 (69%) | |
| **Primary liver disease** | | | | HBV(+)-HBV(-)/HCV(-): p<0.01 |
| Hepatitis A | 0 | 0 | 10 (1%) | |
| Hepatitis B | 22 (91.6%) | 1[b] (100%) | 323 (31.9%) | |
| Hepatitis C | 0 | 0 | 56 (5.5%) | |
| Hepatitis D | 0 | 0 | 0 | |
| Alcoholic liver disease | 1 (4.2%) | 0 | 421 (41.6%) | |
| Cryptogenic | 0 | 0 | 45 (4.5%) | |
| Autoimmune | 0 | 0 | 26 (2.6%) | |
| Primary biliary cirrhosis | 0 | 0 | 8 (0.8%) | |
| Biliary atresia | 0 | 0 | 30 (3%) | |
| Primary sclerosing cholangitis | 0 | 0 | 3 (0.3%) | |
| Secondary sclerosing cholangitis | 0 | 0 | 3 (0.3%) | |
| Drug reaction | 0 | 0 | 33 (3.3%) | |
| Other cholestatic liver disease | 0 | 0 | 5 (0.5%) | |
| Alagilles syndrome | 0 | 0 | 4 (0.4%) | |
| Glycogen storage disease | 0 | 0 | 1 (0.1%) | |
| Budd-Chiari syndrome | 0 | 0 | 2 (0.2%) | |
| GVH/chronic rejection | 0 | 0 | 7 (0.7%) | |





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**Table 2 continued.** Recipient characteristics.

| | HBV(+) graft recipients (n=24) | HCV(+) graft recipient (n=1) | HBV(-)/HCV(-) graft recipients (n=1010) | p value |
|---|---|---|---|---|
| Hepatic failure (re-LT) | 1 (4.2%) | 0 | 4 (0.4%) | |
| Others | 0 | 0 | 29 (2.9%) | |
| **MELD score (baseline, median)** | 22.4±9.3 | 16 | 33.0±15.4 | HBV(+)-HBV(-)/ HCV(-): p<0.01 |
| **MELD score (KONOS final, median)** | 27.8±7.8 | 11 | 35.5±7.1 | HBV(+)-HBV(-)/ HCV(-): p<0.01 |
| **Cold ischemic time (median, hours)** | 4.6±3.6 | 4 | 4.5±4.3 | HBV(+)-HBV(-)/ HCV(-): p=0.84 |
| **Warm ischemic time (median, mins)** | 34.0±11.3 | 30 | 35.8±13.9 | HBV(+)-HBV(-)/ HCV(-): p=0.58 |
| **Pre-transplant HCC status** | | | | |
| No viable tumor | 5 (20.8%) | 0 (0%) | 126 (12.5%) | HBV(+)-HBV(-)/ HCV(-): p=0.21 |
| Within Milan criteria | 1 (25%) | 1 (100%) | 59 (33%) | HBV(+)-HBV(-)/ HCV(-): p=1 |
| Beyond Milan criteria | 3[c] (75%) | 0 | 108 (60.3%) | |
| Incidental liver cancer | 0 | 0 | 12 (6.7%) | |

GVH – graft versus host; MELD – Model for End-stage Liver Disease; KONOS – Korean Network for Organ Sharing; HCC – hepatocellular carcinoma.

**a) Second liver transplantation due to hepatic failure.**

**b) Recipient who received HCV(+) graft was both HCV(+) and HBV(+).**

**c) They had been within the Milan criteria when diagnosed, but became nonviable tumor status after TACE.**

brain death in the HBV(+) donors included hypoxic damage (n=10, 41.7%), subarachnoid hemorrhage (n=9, 37.5%), and intracranial hemorrhage (n=5, 20.8%). Intracranial hemorrhage was the single mechanism of brain death in HCV(+) donors. In the HBV(-)/HCV(-) donors, hypoxic damage (n=321, 31.8%), subarachnoid hemorrhage (n=319, 31.6%), intracranial hemorrhage (n=293, 29%), cerebral infarction (3.7%), others/unknown (n=35, 3.5%), and central nervous system malignancy (n=4, 0.4%) were the mechanisms of brain death. Donor types in the HBV(+) group were 11 (45.8%) standard and 13 (54.2%) marginal donors. In the HCV(+) donors, only 1 marginal donor was observed. In the HBV(-)/HCV(-) donors, 736 (7.9%) standard and 274 (27.1%) marginal donors were observed. The ratio of standard donors was significantly higher in the HBV(-)/HCV(-) donors than that in the HBV(+) donors (72.9% vs 45.8%, HBV(+) and HBV(-)/HCV(-), p=0.01).

The characteristics of the recipients in the 3 groups are presented in **Table 2**. The median age of the HBV(+), HCV(+), and HBV(-)/HCV(-) donors were 57.3±8.8, 53, and 49.8±13.7, respectively (HBV[+]-HBV[-]/HCV[-], p=0.01). The median age of the HBV(-)/HCV(-) graft recipients was lower than that of the HBV(+) graft recipients. The ratio of males to females was higher in the HBV(+) graft recipients than that in the HBV(-)/HCV(-) graft recipients (male/female; 71%/29% and 98.3%/1.7%, p=0.81). All LTs in the 3 groups were ABO-ISO. Among the HBV(+) graft recipients, 24 were HBV(+) and 1 was HCV(+); the latter was both HBV(+) and HCV(+). Only 1 HCV(+) graft recipient was HBV(+) and HCV(+). In the HBV(-)/HCV(-) grafts, 66 (6.5%) and 313 (31%) were HCV(+) and HBV(+) recipients, respectively. Among HBV(+) graft recipients with primary liver diseases, 22 (91.6%) had HBV, 1 (4.2%) had alcoholic liver disease, and 1 (4.2%) had hepatic failure (re-LT). For the HCV(+) graft recipient, HBV was the primary liver disease. Among the HBV(-)/HCV(-) graft recipients, 421 (41.6%) had alcoholic liver disease; 323 (31.9%) had HBV, 45 (5.5%) had HCV; 45 (4.5%) were cryptogenic; 30 (3%) had biliary atresia, 33 (3.3%) had drug reactions, 26 (2.6%) had autoimmune diseases, 8 (0.8%) had primary biliary cirrhosis, 7 (0.7%) had graft-versus-host disease/chronic rejection, and 29 (2.9%) had other diseases. The ratio of HBV was higher in the HBV(+) graft recipient group than in the HBV(-)/HCV(-) graft recipient group (HBV[+]-HBV[-]/HCV[-], $P$<0.01). Baseline model for end-stage liver disease (MELD) scores for the HBV(+), HCV(+), and HBV(-)/HCV(-)





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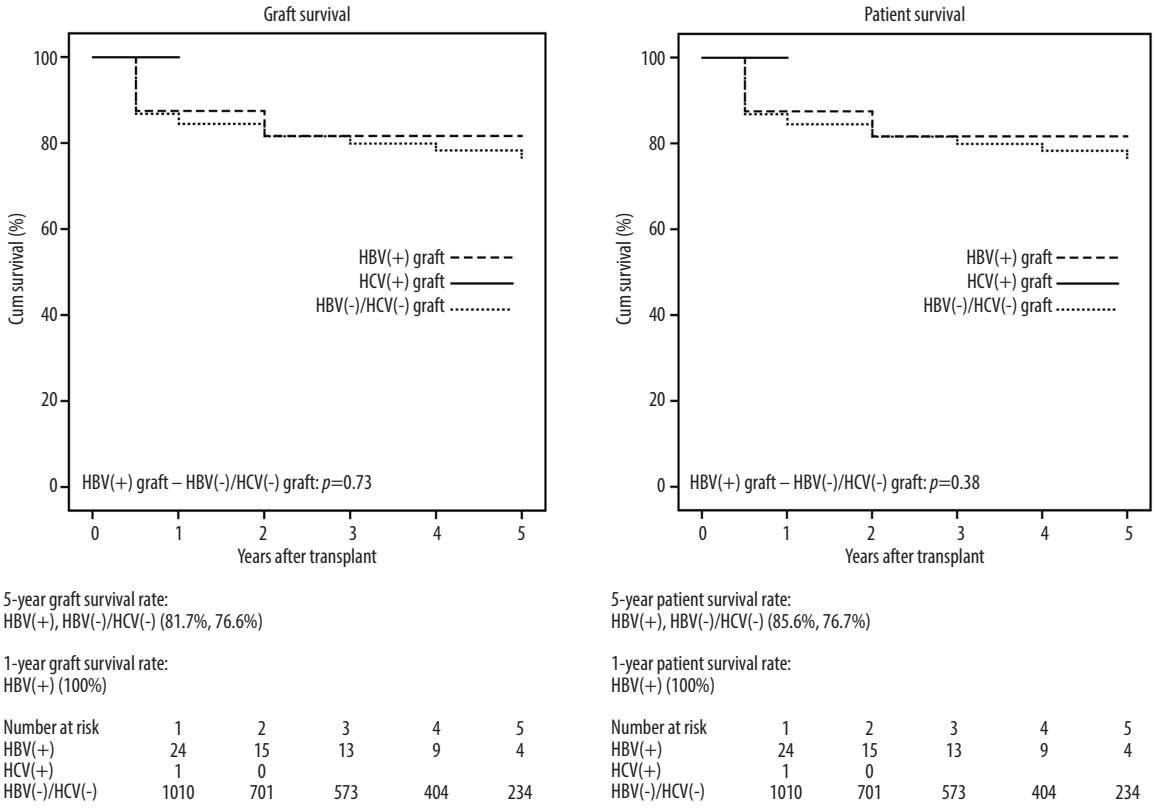


**Figure 1.** Kaplan-Meier graft and patient survival estimate according to the HBV/HCV(±) status.

recipients were 22.4±9.3, 16, and 33.0±15.4, respectively (HBV[+]-HBV[-]/HCV[-]: *P*<0.01). Final MELD scores for HBV(+), HCV(+), and HBV(-)/HCV(-) were 27.8±7.8, 11, and 35.5±7.1, respectively (HBV[+]-HBV[-]/HCV[-]: *P*<0.01). The baseline and final MELD scores of the HBV(+) graft recipients were significantly lower than those in the HBV(-)/HCV(-) graft recipients. Cold ischemic time, warm ischemic time, and pretransplant hepatocellular carcinoma (HCC) status were not significantly different between the HBV(+) and HBV(-)/HCV(-) graft recipients.

The outcomes of LTs are presented in **Table 3**. No statistically significant differences were observed in the follow-up period, number of LTs, postoperative hospital days, cause of death, cause of graft loss, complications, immunosuppressant use for induction therapy, HCV recurrence, or HCC recurrence between the HBV(+) and HBV(-)/HCV(-) graft recipients. The HBV recurrence rate was significantly higher in the HBV(+) graft recipients than in the HBV(-)/HCV(-) graft recipients (20.8% vs 2.9%, HBV[+]-HBV[-]/HCV[-], *P*<0.01). For post-transplant prophylaxis treatment for HBV, the ratio of those who did not receive the prophylaxis was higher in the HBV(-)/HCV(-) graft recipients than that in the HBV(+) graft recipients (4.2% vs 52.6%, HBV[+]-HBV[-]/HCV[-], *P*<0.001). Among the HBV(+) graft recipients who received prophylaxis treatment HBV, 18 (78.3%) received hepatitis B immunoglobulin (HBIG)+antiviral treatment, 4 (17.4%) received only antiviral treatment, and 1 (4.3%) received only HBIG. In the HBV(-)/HCV(-) graft recipients, 288 (60.1%) received HBIG + antiviral treatment, 184 (38.4%) received HBIG only, and 7 (1.5%) received antiviral treatment only. The rate of HBIG only was significantly higher in the HBV(-)/HCV(-) graft recipients than that in the HBV(+) group, and the rate of antiviral only treatment was significantly higher in the HBV(+) graft recipients than in the HBV(-)/HCV(-) graft recipients (HBV[+]-HBV[-]/HCV[-], *P*<0.001).

Graft and patient survival rates at 5 years after LT are shown in **Figure 1**. The 5-year graft survival rates of the HBV(+), HBV(-)/HCV(-) recipients were 81.7 and 76.6%, respectively (HBV[+]-HBV[-]/HCV[-], *P*=0.73). The 1-year graft survival rate of the HCV(-) graft recipients was 100%. No difference was observed between the 5-year graft survival rates of the HBV(+) and HBV(-)/HCV(-) graft recipients. The 5-year patient survival rates of the HBV(+) and HBV(-)/HCV(-) recipients were 85.6% and 76.7%, respectively (HBV[+]-HBV[-]/HCV[-], *P*=0.38). The 1-year graft survival rate of the HCV(+) recipients was 100%. No difference was observed between the 5-year patient survival rate of the HBV(+) and HBV(-)/HCV(-) graft recipients.





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**Table 3.** Outcomes of liver transplantation.

| | HBV(+) graft recipients (n=24) | HCV(+) graft recipient (n=1) | HBV(-)/HCV(-) graft recipients (n=1010) | p value |
|---|---|---|---|---|
| **Follow-up (median, months)** | 35.1±24.6 | 12 | 32.1±24.6 | HBV(+)-HBV(-)/ HCV(-): p=0.58 |
| **Number of liver transplantation** | | | | HBV(+)-HBV(-)/ HCV(-): p=1 |
| Once | 23 (95.8%) | 1 (100%) | 960 (95%) | |
| Twice | 1[a)] (4.2%) | 0 | 48 (4.8%) | |
| Thrice | 0 | 0 | 2 (0.2%) | |
| **Postoperative hospital stay (median)** | 24.0±18.8 | 48 | 37.1±37.6 | HBV(+)-HBV(-)/ HCV(-): p=0.09 |
| **Cause of death** | | | | HBV(+)-HBV(-)/ HCV(-): p=0.11 |
| Infection | 0 | 0 | 93 (44.8%) | |
| Cardiovascular disease | 1 (33.3%) | 0 | 7 (3.4%) | |
| Cerebrovascular disease | 0 | 0 | 14 (6.8%) | |
| Hepatic failure | 1 (33.3%) | 0 | 49 (23.7%) | |
| Recurred HCC | 0 | 0 | 11 (5.4%) | |
| Accident or trauma | 0 | 0 | 1 (0.5%) | |
| Suicide | 0 | 0 | 1 (0.5%) | |
| Other/unknown | 1 (33.3%) | 0 | 31 (14.9%) | |
| **Cause of graft loss** | | | | HBV(+)-HBV(-)/ HCV(-): p=0.8 |
| Patient death with functioning graft | 3 (75%) | 0 | 136 (66.6%) | |
| Primary non-function | 1 (25%) | 0 | 25 (12.3%) | |
| Hepatic artery complication | 0 | 0 | 6 (2.9%) | |
| Hepatic vein/IVC complication | 0 | 0 | 2 (1%) | |
| Portal vein complication | 0 | 0 | 2 (1%) | |
| Biliary complication | 0 | 0 | 5 (2.5%) | |
| Acute rejection | 0 | 0 | 8 (3.9%) | |
| Chronic rejection | 0 | 0 | 2 (1%) | |
| Drug related toxicity | 0 | 0 | 3 (1.5%) | |
| Recurred liver disease | 0 | 0 | 1 (0.5%) | |
| Recurred HCC | 0 | 0 | 6 (2.9%) | |
| Other/unknown | 0 | 0 | 8 (3.9%) | |





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**Table 3 continued.** Outcomes of liver transplantation.

| | HBV(+) donors (n=24) | HCV(+) donors (n=1) | HBV(-)/HCV(-) donors (n=1010) | p value |
|---|---|---|---|---|
| **Complication** | | | | HBV(+)-HBV(-)/ HCV(-): p=0.23 |
| Bleeding from operation site | 1 (25%) | 0 | 101 (19.8%) | |
| Intraperitoneal abscess | 1 (25%) | 0 | 30 (5.9%) | |
| Hepatic artery stenosis/thrombosis | 0 | 0 | 14 (2.8%) | |
| Hepatic artery aneurysm | 0 | 0 | 3 (0.6%) | |
| Portal vein stenosis/thrombosis | 1 (25%) | 0 | 17 (3.3%) | |
| Hepatic vein stenosis/thrombosis | 0 | 0 | 16 (3.1%) | |
| IVC stenosis/thrombosis | 0 | 0 | 13 (2.6%) | |
| Bile leakage | 0 | 0 | 36 (7.1%) | |
| Bile duct stenosis | 1 (25%) | 0 | 106 (20.8%) | |
| Biliary stone | 0 | 0 | 17 (3.3%) | |
| Others | 0 | 0 | 156 (30.7%) | |
| **Immunosuppressant used for induction therapy** | | | | HBV(+)-HBV(-)/ HCV(-): p=0.29 |
| Anti-T-lymphocyte-globulin | 0 | 0 | 0 | |
| Basiliximab | 17 | 1 | 816 | |
| **Immunosuppressant** | | | | |
| | | | | N/A |
| Tacrolimus | 18 | 1 | 941 | |
| Cyclosporin | 0 | 0 | 8 | |
| Everolimus | 3 | 0 | 38 | |
| | | | | HBV(+)-HBV(-)/ HCV(-): p=1 |
| Mycophenolate mofetil | 13 (100%) | 1 | 616 (98.7%) | |
| Mycophenolate sodium | 0 | 0 | 8 (1.3%) | |
| | | | | HBV(+)-HBV(-)/ HCV(-): p=1 |
| Deflazacort | 0 | 0 | 22 (2.6%) | |
| Prednisolone | 17 (100%) | 1 | 836 (97.4%) | |
| **HBV recurrence** | 5 (5/24, 20.8%) | 0 | 9 (9/313, 2.9%) | HBV(+)-HBV(-)/ HCV(-): p<0.01 |
| **HCV recurrence** | 0[b)] (0/1, 0%) | 0 | 32 (32/66, 48.5%) | HBV(+)-HBV(-)/ HCV(-): p=1 |
| **HCC recurrence** | 1 (1/4, 25%) | 0 (0/1, 0%) | 32 (32/179, 17.9%) | HBV(+)-HBV(-)/ HCV(-): p=0.55 |





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**Table 3 continued.** Outcomes of liver transplantation.

| | HBV(+) donors (n=24) | HCV(+) donors (n=1) | HBV(-)/HCV(-) donors (n=1010) | p value |
|---|---|---|---|---|
| **Post-transplant HBV prophylaxis** | | | | |
| None | 1 (4.2%) | 0 | 531 (52.6%) | HBV(+)-HBV(-)/ HCV(-): p<0.001 |
| Done | 23 (95.8%) | 0 | 479 (47.4%) | HBV(+)-HBV(-)/ HCV(-): p<0.001 |
| HBIG only | 1 (4.3%) | 0 | 184 (38.4%) | |
| Anti-viral only | 4 (17.4%) | 0 | 7 (1.5%) | |
| HBIG + anti-viral | 18 (78.3%) | 1[c)] | 288 (60.1%) | |

IVC – inferior vena cava; HCC – hepatocellular carcinoma; HBIG – hepatitis B immunoglobulin.
**a) Due to hepatic failure.**
**b) One HBV(+) graft recipient was both HBV(+) and HCV(+).**
**c) Recipient who received HCV(+) graft was both HCV(+) and HBV(+).**

## Discussion

### Liver Transplant Using HBV(+) Grafts

In Western countries, transplantation from anti-HBc(+) donors to anti-HBc(-) recipients is more common than transplantation from HBsAg(+) donors to HBsAg(-) recipients. In the case of transplantation from anti-HBc(+) donors to anti-HBc(-) recipients, the risk of HBV infection reactivation is very low, and the risk of de novo hepatitis is negligible, even without prophylaxis, regardless of the recipient's HBV immune status. Additionally, its safety has been demonstrated in several studies, not only in LT but also in organ transplantation, such as the kidney, lung, and heart [12-14].

Organs that are HBsAg(+) are not routinely utilized, but are utilized in urgent cases with sufficient informed consent [15]. In Korea, transplantation must be implemented from HBsAg(+) donors to HBsAg(+) recipients, and from anti-HCV(+) donors to anti-HCV(+) recipients. The KOTRY and KONOS databases do not collect data on donor anti-HBc titers. Therefore, in this study, HBV(+) refers to HBsAg(+), and HCV(+) refers to anti-HCV(+).

In HBV-endemic areas, such as East Asia (Korea, China, and Japan), activation of the transplants using HBsAg(+) grafts can be considered. Although the completeness of surgery is important, appropriate administration of antiviral agents and HBIG through appropriate prophylactic and maintenance therapies, according to the virological status of the donor/recipient, is also important. In this study, the rate of prophylaxis treatment for HBV was higher in the HBV(+) group than that in the HBV(-)/HCV(-) group (95.8% vs 47.4%), which is thought to be due to the virological characteristics of the grafts in both groups.

The baseline and final MELD scores were lower in the HBV(+) graft recipients than in the HBV(-)/HCV(-) recipients (**Table 2**). This may be due to the social atmosphere, in which many people on waiting lists are reluctant to receive hepatitis (+) grafts. Therefore, hepatitis (+) grafts have lower priority, are stable, and have lower MELD scores.

### Liver Transplant Using HCV(+) Grafts

In the United States, HCV(+) donors accounted for 3% of deceased cadaveric liver donor pool between 2007 and 2010. Grafts that are HCV(+) have been used for HCV-viremic recipients because of de novo HCV infection. However, with the advent of direct-acting antiviral (DAA) in 2013, the number of transplants has increased [2]. The incidence of HCV infection in the United States has been increasing because of the opioid crisis. According to the Centers for Disease Control and Prevention data, between 2004 and 2014, HCV infection increased by 4-fold among those aged 18-29 years, and 3.25-fold among those aged 30-39 years [16]. A study based on the Mid-America Transplant Services database reported that approximately 10% of HCV(+) livers in the United States were discarded because of HCV infection between 2014 and 2017 [17].

According to the 2013-2017 KONOS and Korea Organ Donation Agency databases, of a total of 87 cases of organ transplantation of brain-dead donors from HCV(+) donors, 11 were transplanted, and of the 76 cases in which the transplantation failed, 24 (27.5%) were due to recipient refusal and 24 (27.5%) were not suitable donors. This may reflect the reluctance of recipients who do not want to receive HCV(+) grafts [18].

One of the important factors for the activation of extended-criteria donors is a change in the perception of recipients and





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their families about the safety and benefits of grafts from extended-criteria donors.

Between 2013 and 2017, recipients' refusal of brain-dead donors liver transplants from HBV(+) or HCV(+) donors accounted for 27% of all the donation failures in South Korea [18]. This suggests that despite being HBV(+) or HCV(+), many individuals do not wish to receive organ transplants from HBV(+) or HCV(+) donors. Donors who were infected with HIV, HBV, or HCV were categorized as "increased-risk donors" (IRD) by the US Public Health Service in 2013 [19]. In several studies, the IRD organ rejection rate ranged from 24% to 98.5%, and the IRD organ rejection rate in pediatric kidney transplantation in the United States was 98.5% [20,21]. As recipients benefit from the use of IRD organs, it is important to convince patients that the advantages of using this organ exceeds the risks. Patients and their families must be informed of the advantages and safety of organ donation from HBV(+) and HCV(+) donors.

This study has some limitations. First, the effects of selection bias due to its retrospective nature and the effects of confounding factors due to its observational nature cannot be excluded. Second, it was impossible to implement a statistical analysis in the HCV(+) group because it consisted of only 1 case. Additionally, there were fewer HBV(+) patients than HBV(-)/HCV(-) patients and the number of HBV(+) patients was very low. Therefore, the statistical power may have been decreased.

## Conclusions

No differences were observed in graft and patient survivals between the HBV(+) and HBV(-)/HCV(-) groups. However, a statistical analysis was not possible in the HCV (+) group because of the small sample size. The number of transplants in the HBV(+) and HCV(+) groups was very small compared to that in the HBV(-)/HCV(-) group. However, the transplant outcomes of the HBV(+) group were comparable to that of the HBV(-)/HCV(-) group. Although accumulating the results of transplants from HBV(+) grafts to HBV(-) recipients and from HCV(+) grafts to HCV(-) recipients is not possible owing to domestic regulations, there should be conditional permission for transplantation from HBV(+) or HCV(+) grafts to HBV(-) or HCV(-) recipients in Korea by considering the risks and benefits based on foreign studies. Thereafter, we can accumulate data from Korea and analyze the outcomes. With the advent of DAA, HCV control has become possible and HBV prophylaxis is now common. Considering that the number of people waiting for a liver transplant is increasing daily, this can no longer be delayed. Therefore, we hope HBV(+) to HBV(-) and HCV(+) to HCV(-) transplantations will be implemented in Korea as soon as possible.

### Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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