Liver transplantation for HBV-related cirrhosis in Europe: An ELTR study on evolution and outcomes

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Introduction

Chronic hepatitis B remains the leading cause of liver-related mortality globally, accounting for almost 1 million deaths per year. HBV-related liver disease is one of the indications for liver transplantation (LT) in Europe and in the US, and LT is the treatment of choice for selected patients with end-stage liver disease or acute liver failure with a 5-year survival, which is currently 70–80% [1,2].

In HBsAg positive recipients, with either acute or chronic liver failure, LT offers a life-saving alternative for cases who progress despite viral suppression, and for those who develop hepatocellular carcinoma (HCC) within well-defined criteria [3,4].

The main issue in HBsAg positive recipients is the risk of HBV recurrence after LT. Before the advent of effective prophylaxis,
Materials and methods

The methods and details used to obtain the data have been described previously [8]. The quality of ELTR data is controlled regularly by audit visits to the contributing centres [9]. We present analyses based on data from first transplants performed in adults (aged >16 years) for HBV-related liver disease between January 1988 and December 2010.

Procedures and statistical analysis

Patients transplanted for HBV-related liver disease were grouped and analysed separately according to the indication for LT: decompensated cirrhosis (HBVdec) or hepatocellular carcinoma (HBV/HCC).

Each group was compared with co-infected patients: HBV and HDV (HBDV), HBV and HCV (HBVC), and HBV, HDV, HCV (HBDCV), and with patients transplanted for HCV-related liver disease. These groups of patients were again stratified according to the indication for LT (Supplementary Fig. 1 – Supplementary material).

Patients transplanted for associated viral disease and alcoholic liver disease were included only if the primary indication was the viral disease. If this was the case, they were grouped with the main category (HBV or HCV), otherwise they were excluded.

Patients transplanted for alcoholic liver disease alone, cholestatic liver disease, autoimmune liver diseases, cryptogenic cirrhosis and for any chronic liver disease other than HBV or HCV were excluded. All patients with acute liver failure and patients with HIV co-infection were also excluded from the analysis.

Patients were stratified according to different time periods (1988–1995, 1996–2000, 2001–2005, and 2006–2010) to evaluate the evolution of recipient, donor and surgical characteristics, as well as changes in patient and graft survival after LT.

As cut-off value of HBV-DNA has changed during the last 20 years, HBV-DNA was considered negative or positive according to the cut-off used at the corresponding period. No information on post-transplant antiviral prophylaxis and ethnicity of the recipients was available in the ELTR database.

The causes of death or graft failure after the first liver transplant were analysed in all groups: primary–non-function (PNF) or delayed function, intra-operative failure, technical problems, infection, acute or chronic rejection (which are combined in the analysis), renal disease, cardiovascular disease, pulmonary disease, cerebrovascular disease, gastrointestinal disease, multiorgan failure, recurrence of primary liver disease, recurrence of tumours, de novo solid tumours, lymphoproliferative disorders, social problems (including non-adherence with immunosuppressive therapy, suicide or trauma).

Patient and graft survival according to the entire patient group was evaluated using the life-table method. Comparison between different groups was performed with the log-rank test. Discrete variables were shown as percentages and parametric variables as mean values ± SD. We used the Chi-square test for the comparison of discrete variables and Student’s t test for parametric variables and ANOVA analyses when more than two groups were compared. Differences were considered statistically significant when the p-value was less than or equal to 0.05.

The effect of patient and donor variables on graft survival was evaluated by univariate Cox analysis. Variables corresponding to the statistically significant risk-ratio (p < 0.1) were used for the subsequent multivariate analysis.

Results

88,229 liver transplants were reported in the ELTR database between January 1988 and June 2010. We excluded data for the following: 8458 paediatric transplants (age <16 years), 1889 combined organ transplants, and 504 transplants with missing information on recipient sex (n = 56), and recipient age (n = 448). A further 52,350 patients were excluded because transplanted for non-viral-related liver disease, leaving 25,028 patients for the analysis. Among them, 5912 patients were transplanted for HBV-related liver disease, out of which 4623 (78%) for HBVdec and 1289 (22%) for HBV/HCC.

Study cohort

Male donors were 59.1% with a mean age of 45 ± 17 years (range 2–97).

Donor age was significantly lower in HBVdec (43 ± 18 years) compared to HCVdec (45 ± 17; p < 0.001) and to HBCVdec patients (44 ± 16; p = 0.03) (Table 1).

Among patients transplanted for HCC on viral cirrhosis, donor age was significantly higher in HBV/HCC (49 ± 18) compared to HBCV/HCC (44 ± 17; p = 0.02) (Table 1).

An incompatible donor/recipient ABO matching was used between 0% and 2.7% of the cases across different groups. Non-heart-beating donors were used in 92 patients, ranging between 0% and 0.7% across the different groups (Table 1).

Male recipients were 75.2% with a mean age of 52 ± 9 years (range 16–78).

Patients transplanted for HBVdec were significantly younger compared to HCVdec (50 ± 10 vs. 53 ± 9 years; p = 0.001). Conversely, they were significantly older than HBDVdec and HBDCVdec patients (44 ± 10 and 43 ± 8 years respectively; each p < 0.001) (Table 1).

HBV/HCC patients were significantly older compared to HBDV/HCC (54 ± 9 vs. 57 ± 7 years; p = 0.001) and to HBDCV/HCC patients (47 ± 6 years; p < 0.001), whereas they were significantly younger compared to HCV/HCC patients (52 ± 7 years; p < 0.001) (Table 1).

Mean MELD score at LT was 19.2 ± 8 (range: 6–40), with no significant difference across groups (Table 1).

HBV-DNA at LT was negative in 71.5% of patients, being significantly lower in HBVdec (67.6%), HBV/HCC (70.9%) and HBCV/HCC (71.2%) compared to other groups (p < 0.001) (Table 1).

Full size grafts were used in 91.3% of the cases. Living donors were used between 0% and 15.6% of the cases, with a significantly higher percentage in HBDVdec and HBVdec patients (15.6%, 12.5% respectively) compared to other groups (each p < 0.001). Emergency transplantation was performed in 1.5–4.5% of the cases, in significant higher percentage in HBVdec recipients compared to other aetiologies (p < 0.001) (Table 1).

Evolution of liver transplantation for HBV-related liver disease over time


Donor age significantly increased in the last 20 years both in HBVdec (from 33.5 ± 13.8 to 45.5 ± 18.7 years; p < 0.001) and in HBV/HCC patients (from 35.8 ± 14.9 to 33.9 ± 18.1 years; p < 0.001), with donors ±40 years of age reduced by 50% and donors >60 years increasing nearly 6-fold (p < 0.001). The percentage of female donors increased significantly in the last five years com-
Table 1. Recipient, donor, transplant characteristics and causes of death or graft loss according to the aetiology of liver disease. Each group of patients was stratified according to the indication for liver transplantation (decompensated cirrhosis or hepatocellular carcinoma).

<table>
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<tr>
<th></th>
<th>Decompensated cirrhosis</th>
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<th>Hepatocellular carcinoma</th>
<th>p value</th>
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All data are expressed as % except where indicated.

*Data available for 8439 patients.
pared to 1988–1994: from 28.7% to 41.7% in HBVdec (p < 0.001) and from 28.2% to 43.2% (p < 0.001) in HBV/HCC (Table 2).

Recipient age increased both in HBVdec (from 45 ± 10.1 to 50.7 ± 9.4 years; p < 0.001), and in HBV/HCC patients (from 51.7 ± 9.7 to 56 ± 8.4 years; p < 0.001), this effect being due to a significant increase in the number of recipients >50 years, and a concomitant decrease in those ≤40 years (Table 2).

The proportion of recipients with HBV-DNA negative at LT progressively decreased in the last 20 years in both the HBVdec and HBV/HCC group (from 81.2% to 51% and from 82% to 57.4% respectively; each p < 0.001) (Table 2).

Considering the whole cohort of patients transplanted for virus-related liver disease, HBV-related cirrhosis dropped from 24.4% in 1988–1995 to 16.3% in 2006–2010 (p < 0.001) (Fig. 1A). Among the patients transplanted for HBV-related liver disease, decompensated cirrhosis as indication for LT decreased from 84.2% in 1988–1995 to 70.4% in 2006–2010, whereas HBV/HCC nearly doubled, moving from 15.8% to 29.6% (p < 0.001) in the same period (Fig. 1B). The same trend was found in patients transplanted for HCV-related liver disease: HCVdec decreased from 84% in 1988–1995 to 67.5% in 2006–2010, and HCV/HCC from 16% to 32.5% (p < 0.001) (data not shown).

Living donor LT and LT using split liver significantly increased (p < 0.001) in HBV/HCC patients (84%, 67.5%, 53.9%, 32.5%), compared to HBV/HCC patients (84%, 57.4%, 53.9%, 32.5%) (Table 2). The same trend was found in patients transplanted for HCV-related liver disease: HCVdec decreased from 84% in 1988–1995 to 67.5% in 2006–2010, and HCV/HCC from 16% to 32.5% (p < 0.001) (data not shown).

Living donor LT and LT using split liver significantly increased in both HBVdec and HBV/HCC patients (p < 0.001), whereas no modifications were seen with auxiliary liver transplants (Table 2).

Survival after liver transplantation for HBV

Overall, patients and graft survival rates at 1, 3, 5, and 10 years after LT for HBV were 83%, 77%, 74%, 67%, and 80%, 73%, 70%, 63%.

When HBV-transplanted patients were compared according to the liver transplant indication (HBVdec vs. HBV/HCC), HBVdec patients had a significantly better patient and graft survival at the liver transplant indication (HBVdec vs. HBV/HCC), HBVdec patients had a significantly better patient and graft survival at the liver transplant indication (p < 0.001) (Fig. 1A). The same trend was found in patients transplanted for HCV-related liver disease: HCVdec decreased from 84% in 1988–1995 to 67.5% in 2006–2010, and HCV/HCC from 16% to 32.5% (p < 0.001) (data not shown).
Among the patients transplanted for decompensated cirrhosis, HBVdec patients had a significantly better patient and graft survival at 1, 3, 5, and 10 years compared to HCVdec patients (81%, 71%, 65%, 52%, and 77%, 67%, 60%, 48%; each \( p < 0.001 \)) and to HBCVdec patients (81%, 75%, 70%, 61%; \( p = 0.005 \) and 75%, 68%, 63%, 57%; \( p < 0.001 \)). Conversely, they had a lower patient and graft survival compared to HBVDVdec patients (92%, 90%, 89%, 86%, and 89%, 86%, 85%, 80%; each \( p < 0.001 \))(Fig. 2A and B).

HBV/HCC patients had a significantly better patient and graft survival at 1, 3, 5, and 10 years compared to HCV/HCC (81%, 75%, 70%, 61%; \( p = 0.005 \) and 75%, 68%, 63%, 57%; \( p < 0.001 \)). No survival differences were found comparing patients transplanted for HBV/HCC and HBV/DV/HCC patients (Fig. 2C and D).

In HBVdec patients, no statistical difference was found in terms of patient and graft survival between patients who were HBV-DNA positive or negative at time of LT (Fig. 3A and B). When HBV/HCC patients were considered, patients with HBV-DNA negative at time of LT had a significantly better patient and graft survival at 1, 3, 5, and 10 years (85%, 76%, 72%, 64%, and 83%, 74%, 70%, 62%) compared to HBV-DNA positive patients (81%, 65%, 60%, 55%, and 77%, 60%, 58%, 55%; \( p = 0.002 \) and \( p < 0.001 \) respectively)(Fig. 3C and D).

The variation over time of patient and graft survival after LT for HBVdec and HBV/HCC was also evaluated.

Considering HBVdec patients, patient and graft survival at 1 and 3 years before 1995 was significantly lower (73%, 65% and 69%, 60%) compared to 1996–2000 (86%, 81% and 83%, 75%; each \( p < 0.001 \)), 2001–2005 (88%, 83% and 84%, 79%; each \( p < 0.001 \)), and 2006–2010 (86%, 81% and 83%, 77%; each \( p < 0.001 \)). No statistical difference in terms of graft survival was found comparing patients transplanted between 2006–2010 and 2001–2005 or 1996–2000 (Fig. 4A and B).

Considering HBV/HCC patients, patient and graft survival at 1 and 3 years before 1995 were significantly lower (65%, 48% and 61%, 45%) compared to 1996–2000 (82%, 73% and 80%, 71%; each \( p < 0.001 \)), 2001–2005 (87%, 78% and 84%, 74%; each \( p < 0.001 \)), and 2006–2010 (89%, 78% and 87%, 75%; each \( p < 0.001 \)). No survival differences were found comparing patients transplanted between 2006–2010 and 2001–2005 or 1996–2000 (Fig. 4C and D).

![Fig. 1. Evolution of liver transplantation for virus-related chronic liver disease in Europe according to different time periods. (A) Evolution of liver transplantation for HBV-related liver disease considering the whole cohort of study. (B) Evolution of liver transplantation for HBV-related liver disease according to the indication for liver transplantation (HBVdec and HBV/HCC).](image_url)
**Research Article**

**Decompensated cirrhosis**

A

- **n = 19,335 patients, global log-rank p < 0.001**
- **Patient survival (%)**
  - **Years**: 1 2 3 4 5 6 7 8 9 10
  - **HBV**: 83 80 78 76 75 74 72 71 70 68
  - **HCV**: 81 75 71 68 65 62 60 57 55 52
  - **HBDV**: 92 91 90 89 88 87 86 85 84 83
  - **HBCV**: 81 77 75 73 70 69 67 66 64 61
  - **HBDCV**: 89 88 85 82 82 80 77 74 67

B

- **n = 19,335 patients, global log-rank p < 0.001**
- **Graft survival (%)**
  - **Years**: 1 2 3 4 5 6 7 8 9 10
  - **HBV**: 80 77 74 72 71 69 68 66 65 64
  - **HCV**: 77 71 67 63 60 58 55 53 50 48
  - **HBDV**: 81 87 86 85 84 83 82 81 80 78
  - **HBCV**: 75 70 68 66 63 62 61 60 68 57
  - **HBDCV**: 87 86 83 80 77 74 67 62 62 62

**Hepatocellular carcinoma**

C

- **n = 5626 patients, global log-rank p < 0.001**
- **Patient survival (%)**
  - **Years**: 1 2 3 4 5 6 7 8 9 10
  - **HBV/HCC**: 84 76 73 70 68 66 65 63 62 61
  - **HCV/HCC**: 83 75 70 64 61 58 55 52 48 45
  - **HBDV/HCC**: 84 78 76 73 72 70 70 68 66 64
  - **HBCV/HCC**: 78 72 69 65 63 56 55 51 51 47
  - **HBDCV/HCC**: 100 80 69 69 69 - - - - -

D

- **n = 5626 patients, global log-rank p < 0.001**
- **Graft survival (%)**
  - **Years**: 1 2 3 4 5 6 7 8 9 10
  - **HBV/HCC**: 81 73 70 67 65 63 62 61 59 58
  - **HCV/HCC**: 80 72 66 61 57 54 51 48 45 42
  - **HBDV/HCC**: 82 75 73 70 69 69 68 66 64 65
  - **HBCV/HCC**: 75 69 67 62 59 53 53 49 49 44
  - **HBDCV/HCC**: 95 76 65 65 65 65 - - - - -

- **Patients at risk (n)**
  - **Years**: 1 2 3 4 5 6 7 8 9 10
  - **HBV/HCC**: 923 720 598 497 417 351 282 223 168 135
  - **HCV/HCC**: 2818 2199 1782 1444 1162 934 728 586 455 346
  - **HBDV/HCC**: 131 108 92 72 60 49 33 28 24 18
  - **HBCV/HCC**: 93 74 61 52 48 40 33 23 19 14
  - **HBDCV/HCC**: 17 13 8 4 3 1 - - - - -

- **Patients at risk (n)**
  - **Years**: 1 2 3 4 5 6 7 8 9 10
  - **HBV/HCC**: 888 692 574 474 395 334 268 209 157 127
  - **HCV/HCC**: 2719 2112 1702 1368 1092 879 681 543 413 321
  - **HBDV/HCC**: 128 105 89 70 58 48 31 26 22 17
  - **HBCV/HCC**: 94 73 60 51 45 38 32 22 18 13
  - **HBDCV/HCC**: 17 13 7 4 3 1 - - - - -

**n = 19,335 patients, global log-rank p < 0.001**

**n = 5626 patients, global log-rank p < 0.001**

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Research Article

292 Journal of Hepatology 2013 vol. 58 | 287–296
Fig. 2. Patient and graft survival after liver transplantation for virus-related chronic liver disease according to the indication for liver transplantation. (A and B) Patient and graft survival after liver transplantation for virus-related decompensated cirrhosis. (C and D) Patient and graft survival after liver transplantation for hepatocellular carcinoma.

Fig. 3. Patient and graft survival after liver transplantation for HBV-related chronic liver disease according to the HBV-DNA status at the time of transplantation. (A and B) Patient and graft survival after liver transplantation in HBVdec patients. (C and D) Patient and graft survival after liver transplantation in HBV/HCC patients.
Fig. 4. Patient and graft survival after liver transplantation for HBV-related chronic liver disease according to years of transplantation. (A and B) Patient and graft survival after liver transplantation in HBVdec patients. (C and D) Patient and graft survival after liver transplantation in HBV/HCC patients.
liver disease, decompensated cirrhosis was still the major indication, reaching 70.6% compared to 29.6% of HBV/HCC. The same trend was seen for HCV and HCV/HCC, where a massive reduction of HBV-related liver disease, decompensated cirrhosis was still the major indication for LT was reported [10–12].

More recently, Ott et al. [13] have shown that the decreasing number of patients transplanted for HBV seems to be related to the decreased prevalence of chronic HBV infection in most regions, including Europe, and to the effective antiviral therapy that may reverse acute HBV reactivation and therefore control hepatic decompensation. Conversely, in line with data reported from European and American studies, HCC in either HBV or HCV positive recipients has nearly doubled in the period 2006–2010, when compared to 1988–1994.

This phenomenon might be explained considering that the expansion of HCC criteria for liver transplantation has allowed a greater number of patients to be transplanted for HCC in the recent years. Moreover, we can speculate that the medium-term nucleos(t)ide analogue therapy, despite being able to dramatically reduce HBV viremia and progression of liver disease or cirrhosis decompensation, is not able to completely control the risk to develop HCC, as already reported in patients with pre-existing cirrhosis [14].

Three-year patient survival in HBVdec and HBV/HCC before 1995 was 63% and 48% respectively, and it increased to 81% and 73% between 1996 and 2000, remaining stable thereafter. Graft survival showed a similar trend. The initial improvement of patient and graft survival might be due to the introduction of more effective antiviral drugs, together with the use of post-transplant immunoprophylaxis [HBIG + lamivudine], whereas the following stabilisation could be explained by the constant increase in recipient age, which has been found to be a risk factor for death or graft loss in our cohort of study, and by the use of older donors, which is a well-documented risk factor for decreased survival after LT [15].

Donor age increased significantly in the last 20 years, with donors younger than 40 years who nearly halved (64% to 30%), and donors older than 60 years who increased from 5% to nearly 30%. Recipient age did not change as much as donor age, however, a significant increase occurred for recipients older than 60 years who increased from nearly 11% in 1988–1995 to 22% in 2006–2010. Conversely, patients younger than 40 years decreased from 20% to 7%. Despite historically the transplant community has been reluctant to offer LT to patients older than 60–65 years, this demand continues to grow as the population continues to live longer with better health [16].

When patients were stratified according to the indication for LT, HBVdec patients had a better patient and graft survival compared to HBV/HCC patients, although this difference was evident only between 1988 and 1995 (each p < 0.001) and between 1996 and 2000 (p = 0.029 and p = 0.046). This could be explained by the introduction of Milan criteria in 1996 [17], which significantly improved survival rates in patients transplanted for HCC.

Since the multicentre analysis on the impact of the HBV-DNA status at transplantation by Samuel et al. [18], the majority of liver transplant centres have first adopted the policy to select candidates with low viremia, and later on to treat candidates with high viremia, before listing and transplanting them [19]. This policy, together with long-term antiviral prophylaxis, resulted in a massive reduction of HBsAg recurrence rate, which is now <10%, at least in Western countries [7]. In the present analysis, the proportion of recipients who was HBV-DNA negative at transplantation progressively decreased over the last 20 years (from 85% to 55%). When patient and graft survival was evaluated according to HBV-DNA status at LT, no difference was observed between HBVdec patients with either positive or negative HBV-DNA. This result could be related to the availability, in most recent years, of more potent and more effective anti-HBV drugs to be used in prophylaxis after transplant. Thus, patients with residual viremia, and those who developed antiviral treatment failure, might have been allowed to be transplanted with the prospective to start a double or triple prophylaxis post-transplantation (association with immunoglobulins and nucleotide and/or nucleoside analogues).

Conversely, HBV/HCC patients showed a significantly better patient and graft survival when transplanted with HBV-DNA negative compared to HBV-DNA positive. This could be due to a viral replication in HCC cells, which would then act as a viral reservoir [20].

The sensitivity of commercial assays for the assessment of HBV viral load has improved dramatically over the time course of this analysis. Therefore, the lack of information on the HBV-DNA status, which is classified in the ELTR database only as “positive vs. negative”, can represent a limitation of the above reported results.

HBV recurrence was reported in this study only when it caused death or graft loss. In HBVdec recipients, disease recurrence, as cause of death or graft failure, significantly decreased over time (from 21.5% to 1.1%). Conversely, it was the major cause of death or graft loss in HCV recipients, either alone or associated with HBV or HCC.

According to the HBV-DNA status at the time of transplant, the incidence of disease recurrence, as cause of death or graft loss, was nearly 12% in HBV-DNA negative and nearly 15% in

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**Table 3. Multivariate Cox regression analysis of independent risk factor for death or graft loss after liver transplantation for HBV-related liver disease.**

<table>
<thead>
<tr>
<th>Factor</th>
<th>RR 95% CI for RR</th>
<th>p value Lower Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recipient age (yr)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>31-40</td>
<td>1.16 0.77 1.74</td>
<td>0.47</td>
</tr>
<tr>
<td>41-50</td>
<td>1.35 0.92 1.96</td>
<td>0.12</td>
</tr>
<tr>
<td>51-60</td>
<td>1.29 0.88 1.98</td>
<td>0.19</td>
</tr>
<tr>
<td>&gt;60</td>
<td>1.62 1.09 2.43</td>
<td>0.018</td>
</tr>
<tr>
<td>HBV-DNA (positive)</td>
<td>1.21 1.04 1.39</td>
<td>0.011</td>
</tr>
<tr>
<td>HBV/HCC (yes)</td>
<td>1.27 1.1 1.46</td>
<td>0.001</td>
</tr>
<tr>
<td>Donor age (yr)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40-60</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>&lt;40</td>
<td>0.83 0.72 0.96</td>
<td>0.010</td>
</tr>
<tr>
<td>&gt;60</td>
<td>1.13 0.95 1.36</td>
<td>0.18</td>
</tr>
<tr>
<td>ABO group matching</td>
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<td></td>
</tr>
<tr>
<td>Identical</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Compatible</td>
<td>1.15 0.91 1.35</td>
<td>0.29</td>
</tr>
<tr>
<td>Incompatible</td>
<td>1.28 1.04 1.59</td>
<td>0.018</td>
</tr>
<tr>
<td>Year of transplantation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2006-2010</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>2001-2005</td>
<td>1.11 0.91 1.35</td>
<td>0.29</td>
</tr>
<tr>
<td>1996-2000</td>
<td>1.28 1.04 1.59</td>
<td>0.018</td>
</tr>
<tr>
<td>1988-1995</td>
<td>2.82 2.25 3.54</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Type of graft (Split/living/reduced)</td>
<td>1.27 1.01 1.59</td>
<td>0.043</td>
</tr>
</tbody>
</table>

*Including HBVdec and HBV/HCC.*
HBV-DNA positive cases, with no difference between the two groups.

Ten-year patient survival after LT was significantly higher in HBV (68%) compared to HCV recipients (53%), as well as graft survival (64% vs. 49%). These results are in line with previous studies showing that in patients undergoing LT for viral hepatitis (HBV or HCV or HBV/HCV), HBV recipients had the best survival rate, followed by HBV/HCV and HCV [21]. The reason for a better survival rate in HBV mono-infected patients is the effectiveness of new antiviral drugs to recurrent hepatitis [12], together with the combined post-transplant immunoprophylaxis using HBIG and lamivudine. The negative influence of HCV status was also confirmed in co-infected HBV/HCV recipients in whom 10-year patient survival was 62% significantly lower compared to HBV/HCV recipients, in whom the survival was excellent. The same negative impact of HCV infection was seen in patients transplanted for HCC.

Finally, as previously reported, HDV co-infection was associated with better outcome. The better survival is presumably resulting from some inhibitory interaction of HDV on the HBV replicative cycle, causing the abrogation of the expression of nucleocapsid HBV antigens [22]. This positive influence of HDV was not confirmed in HBV/HDV/HCC patients. This could be due to the persistence of HDV-RNA as cause of HCC and liver failure [23]. However, HDV-RNA data are not available from the registry.

In conclusion, LT is the best treatment option for advanced HBV-related chronic liver disease. The number of patients transplanted for HBV decompensated liver disease dropped down during the most recent years, while the number of patients transplanted for HCC increased. It seems that HBV DNA at transplant does not influence the survival after transplantation in HBVdec patients, while it seems to remain a risk factor in HBV/HCC patients. This observation could induce to expand LT eligibility in viremic patients with HBV-related decompensated cirrhosis and to treat them with an effective prophylaxis after surgery. However, the virologic background and high rate of tumour recurrence in patients with HBV/HCC suggest the need to maintain a complete suppression of viremia in this group of patients.

Conflict of interest

The authors who have taken part in this study declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jhep.2012.10.016.

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296 Journal of Hepatology 2013 vol. 58 | 287–296