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Long-term outcomes of primary total knee arthroplasty in patients with hepatitis B virus infection

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Aims

The purpose of this study was to compare the clinical outcomes, mortalities, implant survival rates, and complications of total knee arthroplasty (TKA) in patients with or without hepatitis B virus (HBV) infection over at least ten years of follow-up.

Methods

From January 2008 to December 2010, 266 TKAs were performed in 169 patients with HBV (HBV group). A total of 169 propensity score-matched patients without HBV were chosen for the control group in a one-to-one ratio. Then, the clinical outcomes, mortalities, implant survival rates, and complications of TKA in the two groups were compared. The mean follow-up periods were 11.7 years (10.5 to 13.4) in the HBV group and 11.8 years (11.5 to 12.4) in the control group.

Results

The mean Knee Society scores in the HBV and control groups improved from 37.1 (SD 5.6) and 38.4 (SD 5.4) points preoperatively to 78.1 (SD 10.8) and 81.7 (SD 10.2) points at final follow-up ($p = 0.314$), while the mean function scores in the HBV and control groups improved from 36.2 and 37.3 points preoperatively to 77.8 and 83.2 points at final follow-up ($p = 0.137$). Nine knees in the HBV group required revision surgery, including seven due to septic loosening and two due to aseptic loosening. Four knees in the control group required revision surgery, including three due to septic loosening and one due to aseptic loosening. Kaplan-Meier survivorship analysis with the revision of either component as an endpoint in the HBV and control groups estimated 96.6% and 98.5% chances of survival for ten years, respectively ($p = 0.160$).

Conclusion

TKA in patients with HBV infection resulted in good clinical outcomes and survivorship. However, there was a higher revision rate over a minimum ten-year follow-up period compared to TKA in patients without HBV infection.

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Introduction

Hepatitis B virus (HBV) infection is an intermediate endemicity and important public health problem in Korea;¹ the estimated prevalence is approximately 3% of the population, according to the 2016 Korea National Health and Nutrition Examination Survey (KNHANES).² Since a HBV vaccination programme was implemented three decades ago, the prevalence of HBV infection in younger age groups has markedly declined

(0.3% in 2016).³ However, the rate of chronic HBV infection is still high, ranging from 1.7% to 4.8% in adult groups.³

HBV infection results in a broad range of clinical manifestations, ranging from asymptomatic HBV carriers to progressive liver failure, and it can develop into liver cirrhosis or hepatocellular carcinoma.⁴ Recently, the advent of oral antiviral therapy in the treatment of hepatitis B has substantially increased the life expectancy of patients

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with the disease.³ Therefore, we are often confronted in clinical practice with situations where considerable chronically infected patients, with normal aspartate transaminase (AST) and alanine aminotransferase (ALT) levels following liver function testing, have to undergo total knee arthroplasty (TKA) for degenerative knee joint arthritis, osteonecrosis, and other causes. There are some studies reporting high complication rates in patients with liver cirrhosis after undergoing joint arthroplasty.^{5,6} Pour et al⁷ reported that patients with hepatitis C undergoing joint arthroplasty had a higher rate of surgical complications and longer hospital stays. However, the literature examining the long-term outcomes of TKA in patients with HBV infection is scarce.

Therefore, the purpose of this retrospective case-control study was to compare the clinical outcomes, mortality, implant survival rates, and complications of TKA in patients with or without HBV infection over at least ten years of follow-up.

Methods

The design and protocol of this retrospective study were approved by the institutional review board of our hospital, and the requirement for informed consent was waived due to the retrospective nature of the study. Between January 2008 and December 2010, 188 patients (292 knees) with HBV surface antigen (HBsAg) positivity underwent primary TKA at Himchan Hospital (Seoul, South Korea). By reviewing our medical records, we chose patients with seropositive HBsAg and normal AST and ALT levels on liver function tests who underwent primary TKA for inclusion. The exclusion criteria for this study were liver cirrhosis, hepatocellular carcinoma, acute hepatitis, abnormal AST and ALT levels, known co-infection with hepatitis C, and bleeding disorders. We excluded 11 patients (14 knees) from enrolment due to two patients having liver cirrhosis, five patients (seven knees) having abnormal AST and ALT levels, three patients (four knees) having a history of co-infection with hepatitis C, and one patient having a bleeding disorder. Of the remaining 177 patients (278 knees), eight (12 knees) were further excluded from the study due to follow-up loss. The final cohort consisted of 156 females (249 knees) and 13 males (17 knees) (HBV group). A total of 97 patients (57.4%) underwent staged bilateral procedures, and the second surgery was performed one week after the first. The HBV group was matched with a control group in a one-to-one ratio using the propensity score method. The control group was created according to the following matching criteria: sex, age, BMI, and initial diagnosis. A total of 169 sex-, age-, BMI-, and diagnosis-matched patients without HBV infection who had undergone primary TKA between January 2009 and December 2009 at our hospital were used as the control group. In total, 266 TKAs were included in 169 patients (13 males and

Table 1. Demographic data of patients.

Variable	HBV group	Control group	p-value*
Number of patients	169	169	
Number of TKA	266	266	
Male: female, n	13:156	13:156	1.000
Mean age, yrs (SD)	66.6 (6.5)	66.8 (5.3)	0.798
Mean BMI, kg/m ² (SD)	26.7 (3.8)	26.7 (3.3)	0.893
Diagnosis, n			
Osteoarthritis	165	165	
Rheumatoid arthritis	2	2	
Osteonecrosis	2	2	
Mean preoperative Knee Society scores (SD)			
Knee	37.1 (5.6)	38.4 (5.4)	
Function	36.2 (4.8)	37.3 (7.4)	

*Independent-samples *t*-test.

HBV, hepatitis B virus; SD, standard deviation; TKA, total knee arthroplasty.

156 females) (control group). Demographic data of age, sex, BMI, initial diagnosis, and preoperative Knee Society Score⁸ were obtained by reviewing medical records (Table 1). The mean follow-up period was 11.7 years (10.5 to 13.4) in the HBV group and 11.8 years (11.5 to 12.4) in the control group, respectively.

All surgical procedures were performed by three senior surgeons (SCL, CHN, see Acknowledgements) using the standard medial parapatellar approach, with sacrifice of the anterior and posterior cruciate ligaments in all patients. None of the patella was replaced, and only osteophytes were excised. All patients were treated using the posterior-stabilized Scorpio nonrestrictive geometry (NRG) total knee prosthesis (Stryker Orthopaedics, USA) or the posterior-stabilized Vanguard total knee prosthesis (Zimmer Biomet, USA). All implants were inserted with cement. Patients were mobilized with immediate weight-bearing as tolerated, and active exercise was initiated under supervision of a physiotherapist. Patients underwent clinical and radiological follow-up after surgery at two and six weeks, three, six, nine, and 12 months, and annually thereafter. During follow-up evaluations, patients who did not return for scheduled visits were contacted by telephone. Two nurses and one private doctor (see Acknowledgements) found and visited non-responders.^{9,10}

Clinical evaluations were performed using the Knee Society rating system.⁸ Results were classified as excellent (80 to 100 points), good (70 to 79 points), fair (60 to 69 points), or poor (< 60 points). Changes in patient activity were compared within a period of at least ten years of follow-up between the two groups. Radiological analysis included long-leg standing radiography from the pelvis to the ankle joint for evaluating the axis, weightbearing anteroposterior (AP) view, non-weightbearing AP view, lateral view at 30° flexion, and skyline view of the patella.

Table II. Comparison of mortality and Knee Society scores between hepatitis B virus and control groups.

Variable	HBV group	Control group	p-value
Mortality, n (%)			
3 yrs	0/169 (0)	0/169 (0)	
6 yrs	1/169 (0.6)	3/169 (1.8)	
10 yrs	9/169 (5.3)	8/169 (4.7)	
Mortality at most recent follow-up	9/169 (5.3)	8/169 (4.7)	0.807*
Mean postoperative Knee Society knee score (SD)	78.1 (10.8)	81.7 (10.2)	0.314*
Excellent or good, n	145	148	
Fair, n	15	13	
Poor, n	9	8	
Mean postoperative Knee Society function score (SD)	77.8 (11.6)	83.2 (11.2)	0.137*
Excellent or good, n	144	149	
Fair, n	16	13	
Poor, n	9	7	

*Chi-squared test.

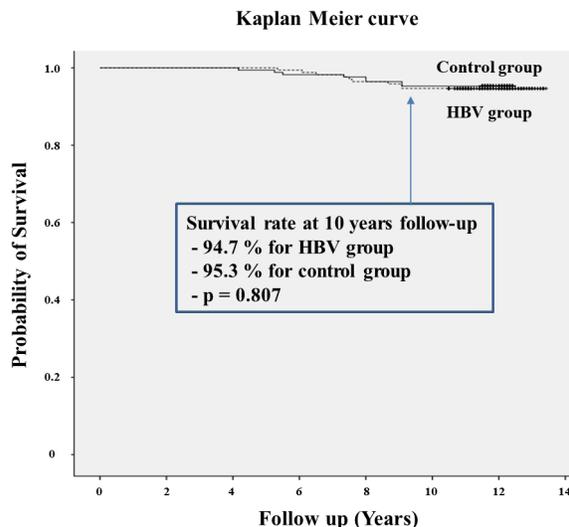
HBV, hepatitis B virus; SD, standard deviation.

Each radiograph was assessed for any radiolucent lines using the Knee Society Roentgenographic Evaluation and Scoring System.¹¹ Analyses of mortality status and implant survival were conducted using hospital records and/or via interviews with family members. Patients unable to attend follow-up evaluations were interviewed by telephone. During the follow-up evaluations, the same caregiver previously interviewed during the patient's hospitalization was questioned.

Statistical analysis. To balance the differences in basic clinical characteristics between the HBV and control groups, the propensity score-matching method was used. Propensity scores were calculated for age, sex, BMI, and diagnosis. HBV and control groups were matched 1:1 based on propensity scores, for which the matching tolerance was 0.01%. The cumulative crude mortality rate was calculated at three, six, and ten years, and compared between the two groups. Kaplan-Meier survival analysis was performed for both groups for a minimum ten-year follow-up period, using mortality as the primary endpoint. Additionally, Kaplan-Meier survival analysis was performed for all knees for a minimum ten-year follow-up period, with revision of either component as an endpoint. The correlation of survival rates in the groups was tested using the log-rank test. The independent-samples *t*-test was used to analyze age and BMI, and the chi-squared test was used to analyze sex, Knee Society knee and function scores, and cumulative mortality. The analyses were carried out using SPSS version 18.0 (IBM, USA). All reported p-values were two-sided, and $p < 0.05$ was considered statistically significant.

Results

The mean Knee Society knee scores in the HBV and control groups improved from 37.1 and 38.4 points

**Fig. 1**

Kaplan-Meier survival analysis of mortality, comparing the hepatitis B virus (HBV) group (dotted line) (95% confidence interval (CI) 93.0% to 96.4%) and control group (full line) (95% CI 93.7% to 96.9%).

preoperatively to 78.1 and 81.7 points at final follow-up, respectively ($p = 0.314$, independent-samples *t*-test). Clinical outcomes were classified as excellent or good for 145 patients (145/169; 85.8%), fair for 15 patients, and poor for nine patients in the HBV group, and excellent or good for 148 patients (148/169; 87.6%), fair for 13 patients, and poor for eight patients in the control group, respectively. Mean preoperative function scores in the HBV and control groups improved from 36.2 and 37.3 points to 77.8 and 83.2 points at final follow-up, respectively ($p = 0.137$, independent-samples *t*-test). Functional outcomes were classified as excellent or good for 144 patients (144/169; 85.2%), fair for 16 patients, and poor for nine patients in the HBV group, and excellent or good for 149 patients (149/169; 88.2%), fair for 13 patients, and poor for seven patients in the control group (Table II). The cumulative mortality rates in the HBV and control groups were 5.3% (9/169) and 4.7% (8/169) at the final follow-up, respectively ($p = 0.807$, independent-samples *t*-test) (Figure 1 and Table II).

In the HBV group, nine knees (nine patients) underwent revision procedures, including seven due to septic loosening and two due to aseptic loosening of the tibial component. Seven knees with septic loosening were treated by two-stage revision arthroplasty. Two cases of aseptic tibial loosening necessitated arthroplasty of only the tibial component. The mean timing of revision surgery was 5.9 years (2.8 to 9.1) after the index procedure. In the control group, four knees (four patients) underwent revision procedures, including three due to septic loosening and one due to aseptic loosening of the tibial component. The three knees with septic loosening were treated by two-stage revision arthroplasty. One case

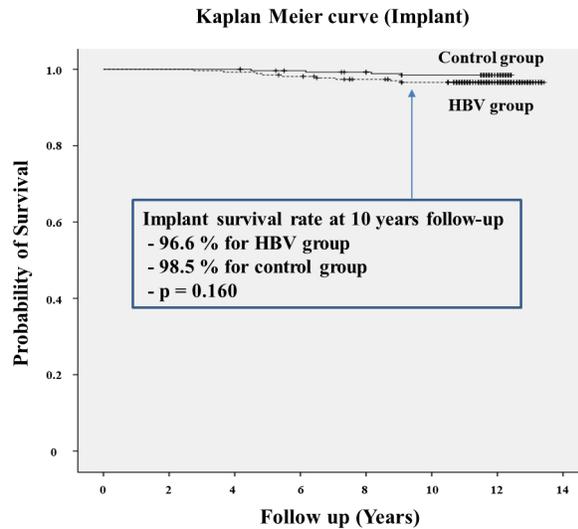


Fig. 2

Kaplan-Meier survival analysis of implant, comparing the hepatitis B virus (HBV) group (dotted line) (95% confidence interval (CI) 95.5% to 97.7%) and control group (full line) (95% CI 97.8% to 99.3%).

of aseptic tibial loosening was treated by replacing only the tibial component. The mean time of revision surgery was 7.0 years (4.6 to 9.2) after the index procedure. No revision surgery was needed for any other reason, such as component malalignment, liner wear, instability, or stiffness in the two groups. Kaplan-Meier survivorship analysis with revision of either component as an endpoint in the HBV and control groups estimated 96.6% (95% confidence interval (CI) 95.5% to 97.7%) and 98.5% (95% CI 97.8% to 99.3%) chances of ten-year survival, respectively ($p = 0.160$) (Figure 2).

Two knees (two patients) suffered early complications secondary to arthroplasty. Two knees in the HBV group experienced a superficial wound infection which was successfully treated with oral antibiotics. None of the knees required revision surgery. Periprosthetic fracture of the femoral shaft was observed in two patients in each group. All patients were treated with plate and screw fixation.

Discussion

This case-control study determined clinical outcomes, mortality, implant survival rates, and complications of TKA in patients with HBV infection in comparison with those without HBV infection, with a minimum follow-up period of ten years. The most important finding of this study was that TKA in patients with HBV infection led to good clinical outcomes and survivorship. However, there was a higher revision rate at a minimum of ten years of follow-up owing to periprosthetic infections.

Although HBV infection may be considered a modifiable risk factor of perioperative complications after joint arthroplasty, the lack of awareness of individual HBV

status and medical treatment in elective TKA patients is a major concern. The prediction of clinical outcome after TKA in patients with HBV might provide insights to better manage patient expectations. In our review of the literature, we identified only three studies that described outcomes of patients with HBV infection treated with arthroplasty.¹²⁻¹⁴ Kuo et al¹² reported that HBV infection was a risk factor for periprosthetic joint infection (PJI) following TKAs among men, and Wang et al¹³ demonstrated that HBV infection is an independent risk factor for complications of the arthroplasty operation. Kildow et al¹⁴ demonstrated that patients with HBV had increased risk of pneumonia, sepsis, joint infection, and revision surgery at 90 days and two years following arthroplasty. However, these studies might have limitations in predicting clinical outcomes because their investigation was limited to perioperative complications following arthroplasty. In this study, a significant difference was not observed between the two groups for postoperative Knee Society knee score (3.6 points) or function score (5.4 points) at a minimum of ten years of follow-up, and TKA in patients with HBV infection showed good clinical outcomes over long-term follow-up.

The present study showed that the revision rate due to infection was higher in patients with HBV infection, but there were no significant differences between the two groups in rates of revision due to noninfectious causes such as aseptic loosening. Previous studies have demonstrated that patients with HBV infection are at a significantly greater risk of infection following arthroplasty compared to patients without HBV infection.^{6,12} The increased risk of complications in HBV patients can be attributed to the change in immune functions due to HBV infection, and the strong associations between HBsAg positivity and thrombocytopenia.⁶ The current study revealed a comparative increase in the risk of revision for PJI in patients with HBV infection.

In our study, the mortality rates between patients with HBV infection and those without HBV infection were not statistically different over a minimum ten-year follow-up period. PJI is a challenging complication that can affect patients undergoing TKA, and can also result in a higher incidence of mortality.^{15,16} Shih et al⁶ reported higher rates of complications and mortality among cirrhotic patients undergoing TKA compared to controls. However, the impact of HBV infection on the incidence of cirrhosis was not apparent in our study. In addition, the relatively small number of patients with HBV infection undergoing TKA surgeries in our study may be too limited to perform a pertinent mortality analysis.

The current study did not find an increase in intraoperative complications in the HBV infection group compared to the control group. It might be that most patients with HBV positivity were "inactive HBV carriers" with low viral activity.¹⁷ Another reason for this result is that

a small cohort of patients might not have been large enough to have statistical power for the intraoperative complications.

This study has several limitations. First, it was retrospectively designed, and neither disease activity of HBV carriers nor the status of modern treatments were routinely documented. Therefore, disease severity could not be correlated with clinical outcomes following TKA. Second, the limited number of patients with HBV infection and normal liver function test results in our cohort might not have been enough to have pertinent statistical analyses. Third, the high discrepancy in the male to female ratio might have impacted our results. However, the strength of this study is that it is the first with a follow-up of more than ten years comparing the outcomes obtained after TKA in patients with and without HBV infection.

In conclusion, TKA in patients with HBV infection showed good clinical outcomes and survivorship. However, there was a higher revision rate at a minimum of ten years of follow-up owing to periprosthetic infections. Therefore, the surgeon should accurately explain to patients with HBV infection who are planning to undergo TKA that they are more likely to experience PJI post-surgery.



Take home message

- Total knee arthroplasty (TKA) patients with hepatitis B virus (HBV) infection showed good clinical outcomes and survivorship over long-term follow-up.

- There was a higher revision rate in TKA patients with HBV infection at a minimum of ten years of follow-up owing to periprosthetic infections.

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