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Original Research

Short-Term Outcomes of Total Hip Arthroplasty after Liver Transplantation

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ABSTRACT

Background: Idiopathic osteonecrosis of the femoral head (ONFH) frequently occurs after liver transplantation (LT) because of lifelong administration of corticosteroids or immunosuppressants and often requires total hip arthroplasty (THA). This study examines patient characteristics and short-term outcomes of THA after LT.

Methods: We observed 9 hips in 7 patients who underwent THA from August 2015 to December 2017 for ONFH after LT (group L). Cementless implants were inserted in all hips. Medical records were retrospectively reviewed to reveal reasons for LT, type of donor, and period from LT to THA. Preoperative laboratory data, operative time, intraoperative blood loss, complication rates, and Harris Hip Score were compared with a control group of 27 cementless THAs in 27 patients with ONFH.

Results: Causative diseases were liver cirrhosis (n = 4), type B fulminant hepatitis (n = 1), congenital biliary atresia (n = 1), and iatrogenic biliary tract injury (n = 1). Four livers were from living donors and 3 from cadavers. Mean time from LT to THA was 10.4 (1-20) years. Preoperative blood test showed a significant decrease in platelet count (178 vs 268 [$*10^3/\mu l$]) and rise in total bilirubin (1.1 vs 0.7 [mg/dL]) in group L. There was no significant difference in operative time (86 vs 100 [minutes]), but intraoperative blood loss (303 vs 163 [mL]) increased significantly in group L. There were no significant differences in complication incidence or Harris Hip Score between the 2 groups.

Conclusion: THA after LT requires caution because risks for bleeding increase. However, short-term outcomes appear to be equivalent to normal THA.

Introduction

The procedure of liver transplantation (LT) is becoming a widely used and safe approach for the treatment of end-stage liver disease. In order for LT to be successful, lifelong administration of corticosteroids or immunosuppressants is required to protect the transplanted liver and reduce the chance of rejection [1]. This often leads to idiopathic osteonecrosis of the femoral head (ONFH), which is typically treated with total hip arthroplasty (THA) [2–4]. However, few studies have been carried out involving patients undergoing THA after LT. Cadaveric LT from brain-dead donors is routinely performed worldwide; in Japan, living donors are the most common source of donor livers for LT. As strict immunosuppression is often necessary in such cases [5,6], the results of THA after LT may differ between Japan and other countries.

The purpose of this study was, therefore, to evaluate the short-term outcomes of THA which was performed after LT in a Japanese population.

Material and methods

Study population

This retrospective study was approved by the ethics committee of our institution (no. 20,170,241). We retrospectively recruited all patients who underwent THA after LT at our institution between

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August 2015 and December 2017. During the study period, THA was performed on 9 hips in 7 patients with ONFH which developed after LT (group L). Group L consisted of 4 males and 3 females with a mean age of 58.4 years. A control group was recruited from patients who underwent unilateral cementless THA for all other ONFH patients during the same period (group C). Group C consisted of 27 ONFH patients (14 males and 13 females), with a mean age of 55.8 years. Background and operative characteristics of group L are shown in Table 1.

Surgical procedure

Surgery was performed with patients in the supine position using a minimally invasive anterior or anterolateral approach and with cementless implants in all patients. The surgical approach used in group L is shown in Table 1.

Survey items

Intraoperative data were obtained for each patient from medical records and our hospital-based computer system. Evaluated items included background characteristics, underlying disease for LT, type of donor liver, and duration from LT to THA. Preoperative laboratory tests (complete blood count, renal function, liver enzyme), operative time, intraoperative blood loss, incidence of perioperative complications, and the Harris Hip Score (HHS) were recorded preoperatively and postoperatively.

Statistical analysis

The Student's *t*-test was used to compare parameters such as age, laboratory data, operation time, and intraoperative blood loss between the groups. The chi-square test was used to assess the incidence of perioperative complications. A P value of <.05 was considered statistically significant.

Results

The preoperative platelet count was significantly lower in group L (178,000/μL) than in group C (268,000/μL) ($P < .01$), and total bilirubin (T-Bil) level was significantly higher in group L (1.09 mg/dL) than in group C (0.73 mg/dL) ($P < .05$) (Table 2). The operative time was not significantly different between groups L (86 minutes) and C (100 minutes) ($P > .05$), but the blood loss was significantly greater in group L (303.6 mL) than in group C (163.4 mL) ($P < .01$) (Table 3). Concerning complications, deep venous thrombosis was observed in one patient from group L; in group C, intraoperative bone fracture was observed in one patient, deep venous thrombosis in 3, superficial infection in one, and cerebral infarction in one, but the incidence of complications did not differ between the 2 groups ($P > .05$) (Table 3). In both groups, implants were correctly placed, and no revision of THA was required. The mean HHS was 52.1 in group L and 56.7 in group C preoperatively and 82.9 in group L and 87.1 in group C at the time of final follow-up (mean 46.3 months). These were not significantly different at any time point ($P > .05$). When the operation was satisfactorily performed, both groups experienced favorable outcomes with no significant difference in improvement rate (Fig. 1).

Table 1
Patient characteristics and surgical approach of total hip arthroplasty after previous liver transplantation.

Case	Age (y)	Sex	Underlying disease	Donor type	Duration LT to THA (y)	Final follow-up period (mo)	Surgical approach
1	35	M	Congenital biliary atresia	Cadaver	13	36	DAA (bilateral)
2	69	F	Liver cirrhosis	Living	9	48	DAA
3	58	M	Liver cirrhosis	Living	9	60	DAA
4	42	M	Fulminant hepatitis	Cadaver	1	60	ALS
5	68	F	Liver cirrhosis	Living	8	60	DAA
6	66	M	Iatrogenic biliary injury	Cadaver	13	36	DAA
7	71	F	Primary biliary cirrhosis	Living	20	24	ALS (bilateral)
Mean	58.4				10.4	46.3	

ALS, antero-lateral supine approach; DAA, direct anterior approach; F, female; LT, liver transplant; M, male; THA, total hip arthroplasty.

Table 2
Preoperative laboratory data.

Blood test items	Group L (n = 7)	Group C (n = 27)	*P* value
WBC (/μL)	5810	7020	.09
Hb (g/dL)	13.04	13.34	.64
PLT ($\times 10^4$/μL)	17.80	26.79	<.01
AST (U/L)	42.86	24.19	.13
ALT (U/L)	26.29	20.04	.50
TP (g/L)	7.29	7.16	.59
T-Bil (mg/dL)	1.09	0.73	<.05
PT-INR	1.02	1.01	.89
BUN (mg/dL)	24.14	16.58	.07
Cre (mg/dL)	1.05	1.16	.88
APTT (sec)	30.63	27.43	.09

ALT alanine aminotransferase; APTT, partial thromboplastin time; AST, aspartate aminotransferase; BUN, blood urea nitrate; Cre, serum creatinine; Hb, hemoglobin; PLT, platelets; PT-INR, prothrombin time International Normalized Ratio; T-Bil, total bilirubin; TP, total protein; WBC, white blood cell count.
Group L, cases who underwent cementless total hip arthroplasty for osteonecrosis of the femoral head after previous liver transplantation. Group C, control group who underwent cementless total hip arthroplasty for osteonecrosis of the femoral head for all other reasons.

Discussion

Patients with end-stage liver disease often suffer from severe coagulopathy [7]. Among patients with severe liver disorders, THA should be performed with caution because the rate of perioperative complications is high and outcomes are often poor [8]. However, there are few reports on the outcomes of THA in patients who have previously undergone LT for severe liver disorders. Although there have been some studies on joint replacement after organ transplantation, the transplanted organs and joints which required

Table 3
Operative time, intraoperative blood loss and perioperative complications.

Survey items	Group L (n = 9)	Group C (n = 27)
Operation time (min)	86	100
Intraoperative blood loss (mL)	303.6	163.4
Intraoperative fracture	0	1
Infection	0	1
Dislocation	0	0
Reoperation	0	0
Pulmonary thromboembolism	0	1
Deep vein thrombosis	1	3

Group L, cases who underwent cementless total hip arthroplasty for osteonecrosis of the femoral head after previous liver transplantation. Group C, control group who underwent cementless total hip arthroplasty for osteonecrosis of the femoral head for all other reasons.

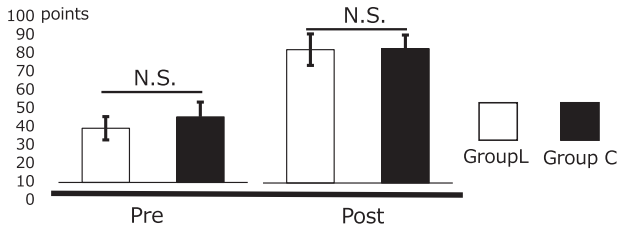

Figure 1. Bar graphs of preoperative and postoperative Harris Hip score. The mean Harris Hip score was 52.1 in group L and 56.7 in group C preoperatively and 82.9 and 87.1 in groups L and C, respectively, at the time of final observation. Definitions: Group C, control group who underwent cementless total hip arthroplasty for osteonecrosis of the femoral head; group L, cases who underwent cementless total hip arthroplasty for osteonecrosis of the femoral head after previous liver transplantation. N.S., not significant.

surgery often differed among the study cohorts [9-15]. Studies involving only LT or THA are limited (Table 4).

In the case of THA after LT, hepatic functional reserve is the primary concern for surgery, as a low reserve may mean that surgery under general anesthesia aggravates liver function, resulting in liver failure and consequent deterioration of the general condition [17]. Parameters of hepatic functional reserve include platelet count and T-Bil levels; thus, these parameters should be evaluated before any surgery on patients who have undergone LT.

The risk of bleeding tendency is another major concern for THA after LT. The liver produces platelets and coagulation factors. As such, when hepatic function is decreased, the production of platelets and coagulation factors decreases concomitantly, resulting in a tendency to bleed readily [7]. Preoperative blood analysis in this study revealed that group L had decreased platelet counts, which may indicate decreased platelet production in the liver and mild liver impairment. Of all elective orthopedic operative procedures, THA is associated with a higher risk of blood loss as there is no effective method for controlling bleeding from the acetabular cancellous bone and femoral medullary cavity, which are exposed by acetabular reaming and femoral broaching. Quick implant placement is necessary to minimize the blood loss. In the present study, intraoperative blood loss was significantly greater, although not life-threatening, in group L despite operative times tending to be shorter in group L than in group C. The third problem for THA after LT is decreased bone quality. The liver plays a key role in bone metabolism. Bile is produced in the liver, concentrated in the gallbladder, and finally secreted into the duodenum via the bile ducts, where it has functions in fat absorption. A decrease in bile secretion leads to reduced absorption of fat-soluble vitamins. Among these, vitamins D and K are important for bone formation [18,19]. Therefore, abnormalities in the pathways between the liver and bile ducts result in decreased bone quality. In addition, vitamin D is activated in the liver and kidney, which does not occur in the case of liver impairment. The liver also synthesizes proteins that form the bone matrix; reduced liver function leads to decreased protein synthesis and reduced bone quality [20,21]. A decrease in bone quality related to liver impairment is referred to as hepatic osteodystrophy [22]. When orthopedic surgery is performed, decreased bone quality and changes in bone metabolism affect the long-term outcomes. Therefore, changes in bone metabolism should be evaluated and considered in surgical planning.

The final concern for THA is the increased susceptibility to infection of patients who have undergone LT. Immunosuppressants suppresses humoral immunity, which increases the risk of postoperative complications [10,13,14]. In the present study, immunosuppressants such as tacrolimus were administered to all patients. Although no patient developed postoperative infection or wound troubles after THA, administration of immunosuppressants after organ transplantation must be continued throughout the patient's life. As delayed infection is a risk, efforts should be made to prevent delayed infection in the entire body, including the respiratory and urinary tract systems, and to carry out early treatment as much as possible.

Aminata et al. [16] reported a study on 33 patients who underwent THA after LT between 2005 and 2011 and described the following preoperative criteria for THA: 1) preoperative hemoglobin >10 g/dL, 2) white blood cell count >5000 mL^3 and neutrophils >3000/mL^3, 3) aspartate aminotransferase and alanine aminotransferase <20 IU and T-Bil <1 mg/dL, 4) serum creatinine <1.7 mg/dL, 5) over 8 months since LT, 6) no intravenous steroid administration, 7) more than 1 week between operations in bilateral cases, 8) the recipient is liver tolerant of general anesthesia, and 9) continuation of immunosuppression therapy [16]. In the present study, almost all patients of group L fulfilled these criteria, despite slightly high T-Bil levels. Although there were 2 patients who underwent simultaneous bilateral THA operations at our hospital and these required allogenic blood transfusion, they developed no complications during the perioperative period. Therefore, when the patient condition permits and indications are carefully determined, simultaneous bilateral operations may also be possible.

The limitation of this study is that the follow-up period is 2-5 years, so the long-term results are unknown.

Table 4
Reports of artificial joint surgery after organ transplantation.

Author	Transplanted organs	Surgeries	Clinical results
Lezitsky et al., 2003 [11]	Liver	8 TKA, 3 THA, 1 TAA	Uneventful
Orban et al., 2012 [9]	Liver, kidney	4 THA, 1TKA	Uneventful, cement implant is recommended
Aminata et al., 2012 [16]	Liver	33 THA	Blood loss increased
Ledford et al., 2014 [13]	Heart, lung, liver, kidney	55 THA, 21 TKA	Reoperation, renal failure, infection in TKA increased
Klement et al., 2016 [10]	Heart, lung, liver, kidney, pancreas	3334 TKA	Reoperation, fracture, infection increased
Chalmers et al., 2016 [14]	Heart, lung, liver, kidney, pancreas	136 THA	Mortality, reoperation, infection increased

TAA, total ankle arthroplasty; THA, total hip arthroplasty; TKA, total knee arthroplasty.

Conclusions

THA performed after LT requires careful attention because of a possible increased risk of intraoperative blood loss, although this blood loss is manageable by autologous or allogenic blood transfusion. The context of prior LT does not appear to increase the risk of perioperative complications such as intraoperative bone fractures or infections in THA. Concerning clinical results, the improvement in HHS does not appear to be affected by previous LT in patients with ONFH. Our results suggest that THA after LT must be carefully planned and managed but achieves similar outcomes to general THA if the patient's general condition permits surgery. Longer follow-up should be carried out for patients undergoing

THA after LT, and annual changes in bone responses and implant loosening should be carefully monitored.

Conflict of Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

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