

Changes in quality of life after hepatectomy and living donor liver transplantation.

Running title: Quality of life after hepatic surgery

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Abbreviation: Short Form 36 (SF-36); living donor liver transplantation (LDLT); quality of

life (QOL); hepatocellular carcinoma (HCC); hepatitis B virus (HBV); hepatitis C virus (HCV);

physical functioning (PF); role physical (RP); bodily pain (BP); general health (GH); vitality (VT); social functioning (SF); role emotional (RE); mental health (MH).

Abstract

Background/Aim: Quality of life has become important as an outcome in addition to conventional outcomes such as disease-free and overall survival. In this study, we compared the fluctuations of quality of life after hepatectomy and living donor liver transplantation.

Methodology: Thirteen adult patients undergoing hepatectomy and 7 with living donor liver transplantation were enrolled. The SF-36, which can objectively measure health-related generic physical and mental quality of life, was completed before surgery and at 3, 6, 9, and 12 months after surgery.

Results: Before surgery, the scores of 7 out of 8 domains in SF36 were significantly lower in the transplantation group than in the hepatectomy group. After hepatectomy, quality of life dropped temporarily and subsequently gradually recovered toward the baseline, while after transplantation, quality of life, especially mental function, tended to be improved beyond the baseline. Consequently, the quality of life of the transplantation patients became comparable to that of the hepatectomy patients 12 months after surgery.

Conclusions: living donor liver transplantation was demonstrated to be a sensible therapeutic

intervention for liver failure and malignancies from the point of view of improvement in physical and mental quality of life.

Introduction

Hepatectomy has been established as a therapeutic intervention for hepatic malignancies. Furthermore, living donor liver transplantation (LDLT) has been carried out for liver failure as well as hepatic malignancies (1). Although both modalities have been demonstrated to be sensible medicinally, in terms of curability and safety, some problems exist. Both are generally invasive procedures; for instance, they require a big incision, long operative and anesthetic durations, blood loss, hospitalization, and sometimes blood transfusion, and they may cause post-operative complications. Even after discharge, patients have to visit an out-patient clinic for follow-up examinations and medication for long periods. Furthermore, some patients may suffer from recurrent diseases. Because these requirements can impair the patient's physical and mental health, quality of life (QOL) has been deemed to be an important outcome in addition to traditional medical outcomes such as disease-free and overall survival (2, 3). The effects of liver diseases on QOL have been reported to some extent, such as in the case of resection for hepatic malignancy (2-4), liver transplantation (5, 6), hepatic fibrosis (7, 8), hepatitis C virus-related liver diseases (7, 9), and so on using various instruments.

The Short Form 36 (SF-36) was used to assess generic physical and mental health-related QOL by means of 36 questionnaires, which measures eight areas of functioning and well-being. Each subscale consists of 2 to 10 items with 2-point to 10-point scales. Higher scores represent higher functioning (10). In this study, we compared the fluctuations of QOL using SF-36 after hepatectomy and LDLT and analyzed their characteristics.

Methodology

Thirteen adult patients who underwent hepatectomy and 7 who underwent LDLT from November, 2006 through May, 2008, were enrolled in the clinical study. The underlying diseases were as follows: in the hepatectomy group, hepatocellular carcinoma (HCC) with hepatitis B virus (HBV) infection (4 patients, 30.8%), HCC with hepatitis C virus (HCV) infection (3, 23.1%), HCC with neither HBV nor HCV infection (5, 48.5%), and metachronous hepatic metastases from colon cancer (1, 7.7%); in the LDLT group, HBV-related liver cirrhosis (LC) with HCC (2, 28.6%), HCV-related LC with HCC (3, 42.9%), alcoholic LC (1, 14.3%), and Calori disease (1, 14.3%). The study protocol was approved by the Institutional Review Board, and all enrolled patients provided written informed consent.

Instrument for QOL assessment

The SF-36 questionnaire is a validated survey that measures general health-related QOL (10), and a Japanese-validated version of the SF-36 was used in this study. It consists of eight subscales of physical and mental functions: the physical functions include physical functioning (PF), role physical (RP), bodily pain (BP), and general health (GH); the mental functions include vitality (VT), social functioning (SF), role emotional (RE), and mental health (MH). The scores in each domain range from 0 to 100, with a higher score indicating a better health state. We transformed SF-36 scores (0-100) to norms for the Japanese population with the mean=50 and standard deviation=10 by using SF-36 Norm-Based Scoring software.

Study protocol

This was an observational study, and no treatments were provided to the patients. Patients were approached at the time of admission. After providing written consent, the patients were asked to complete the SF-36, and the completed form was collected the next day. The patients were sent the same questionnaire by mail at 3, 6, 9, and 12 months after being discharged.

Statistical analyses

Data were presented as median (range). We used a paired t-test for continuous variables at 2 time points and Student's t test for independent samples between the 2 groups. A comparison of categorical variables was performed using the χ^2 test. A p value of <0.05 was considered statistically significant.

Results

Table 1 shows the demographics and clinical data of the patients in both groups. The extent of hepatectomy was defined as major if 3 or more segments were resected, and minor if 2 or fewer segments were resected. The age of the patients in the LDLT group was significantly younger than that of the patients in the hepatectomy group ($p<0.01$). The proportion of the patients with Child–Pugh C was higher in the LDLT group than in the hepatectomy group ($p<0.05$). The length of hospitalization after surgery of the patients in the LDLT group tended to be longer, but not to a statistically significant degree ($p=0.07$). The proportion of the patients who needed to be re-hospitalized within 1 year was statistically higher in the LDLT group ($p<0.05$).

Changes of SF-36 scores beyond the operation

Changes of scores in the hepatectomy group

In the hepatectomy group, in the physical functions, the PF and GH scores did not change significantly after the operation (Figures 1a, d). The RP score dropped significantly at 3 months with a recovery after 6 months (Figure 1b). There was a significant decrease in BP scores through 12 months after surgery (Figure 1c). In the mental functions, there were significantly worse VT, SF, and RE scores at 3 months after the operation (Figures 1e, f, g). The VT score returned to its preoperative value at 6 months after surgery and remained there until 12 months after surgery. Although the SF and RE scores recovered at 6 months, they dropped again significantly compared with those before the operation. The MH score did not change significantly throughout the follow-up period (Figure 1h).

Changes of scores in the LDLT group

In the LDLT group, the PF score dropped significantly at 3 months compared with that before the operation, with a recovery after 6 months (Figure 1e). Although the scores of the remaining 7 subscales did not change significantly after the operation, they all had a tendency to get better over time after surgery (Figure 1).

Comparison of SF-36 scores between the 2 groups

Before the operation, the scores of all the subscales except PF were significantly lower in the LDLT group compared with those in the hepatectomy group (Figure 2a). Twelve months after surgery, however, there were no significant differences in the scores of any subscale between the 2 groups (Figure 2b). The scores of no subscales did not reach norms for the Japanese population (mean=50 and standard deviation=10) 12 months after surgery.

Discussion

Martin et al. (4) analyzed the QOL of 32 patients who underwent hepatectomy for malignancies. Although they used different QOL instruments from ours, the QOL scores of most domains, including function, symptom, global health, mood, emotion, liver disease-specific items, and so on, deteriorated after surgery and returned to baseline at 3 months, even after major hepatectomy, and throughout the experimental period (until 6 months). In the present study, after hepatectomy for malignant diseases, the scores of 5 of the subscales of SF-36 dropped significantly at 3 months, and 4 of these subscales recovered at 6 months. The scores of SF and RE deteriorated again thereafter. The BP score remained lower than before surgery without returning to baseline. One reason that delayed recovery and re-deterioration of QOL occurred in our study is likely the larger proportion of patients with HCC compared with the

previous report (92.3% vs. 12.5%) (4). Most cases of HCC would derive from a diseased liver, and the liver spare function is usually impaired in such cases. It was reported that LC and severe liver fibrosis were correlated with poor QOL in patients with nonalcoholic steatohepatitis (8) or HCV-related fibrosis (7, 9). In the present study, none of the patients in the hepatectomy group had cirrhotic liver as determined by pathological examination (data not shown) and all were Child-Pugh A or B. Furthermore, as shown in Figure 2a, the scores of most subscales of the SF-36 in the hepatectomy group before surgery were comparable to the norms for the Japanese population (mean=50 and standard deviation=10). The present results suggest that even a mild to moderate degree of poor liver function, which allowed the patients to undergo hepatectomy, can impair recovery of QOL after surgery. Because it was reported that the oral administration of branched-chain amino acid to patients with LC improved QOL as well as serum albumin concentration and event-free survival (11), this supplement could have a favorable influence on the fluctuation of QOL after hepatectomy.

In the LDLT group, only the PF score dropped significantly at 3 months after surgery, with a return to baseline after 6 months. The remaining 7 scores changed slightly at 3 months and tended to increase after 6 months. In particular, all 4 mental function scores after 6 months were above those obtained before surgery, although statistical significance was not shown. Compared to the hepatectomy group, scores in 7 out of 8 subscales in the SF-36 were

significantly lower in the LDLT group before surgery. At 12 months after surgery, however, there was no significant difference in any subscale in the SF-36 between the 2 groups. Generally speaking, LDLT would be more invasive, i.e., would require a longer operative time and a longer period of hospitalization and would cause a larger amount of bleeding. After being discharged, patients who have undergone LDLT need to visit the out-patient clinic frequently for follow-up examinations and medication including immunosuppression. Furthermore, in this study, the proportion of patients who needed re-hospitalization was larger in the LDLT group. Why did QOL after LDLT improve even in such adverse conditions? As shown in Table 2, the liver spare function represented by Child-Pugh improved after LDLT, and this may be one of the reasons for the improvement in physical and mental QOL. Moreover, recurrent disease has been reported to impair QOL after hepatectomy for HCC (2) or hepatobiliary malignancies (3). While 4 patients in the hepatectomy group suffered from recurrent disease in the study period, no patients in the LDLT group did.

In our institute, one of the exclusion criteria for LDLT is >65 years old, though there have been some exceptional cases. We have not defined an age criterion for hepatectomy, and elderly patients can undergo the surgery. Thus, a limitation of this study was that the patients in the LDLT group were younger than those in the hepatectomy group. The QOL of elderly patients is considered to recover more slowly after invasive interventions.

In summary, fluctuations of QOL were different after hepatectomy and LDLT as follows. After hepatectomy, QOL dropped temporarily and then recovered gradually toward the baseline, and after LDLT, both physical and mental QOL tended to be improved beyond the baseline. Consequently, the QOL of the LDLT patients, whose baselines in most domains were lower than those of the hepatectomy patients before surgery, became comparable to that of the hepatectomy patients 12 months after surgery. Even though LDLT is generally an invasive and complex therapeutic intervention with a greater amount of bleeding, longer operative time, and longer period of hospital stay compared with hepatectomy, and even though patients need to continue to take immunosuppressive agents after LDLT, our results demonstrated that LDLT is a reasonable therapeutic option in terms of the subsequent recovery of QOL as well as conventional medical outcomes.

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3:705-713.

Table 1. Demographic and clinical data of the patients

	Hepatectomy (n=13)	LDLT (n=7)	p
Sex ratio (F:M)	3:10	1:6	ns
Age (years) *	70.9±5.2 (58-80)	48.3±17.0 (25-68)	<0.01
Child-Pugh			
Before surgery			
A/B/C	12/1/0	4/1/2	ns
A+B/C	13/0	5/2	0.04
After 12 months			
A/B/C	11/2/0	6/1/0	ns
Extent of hepatectomy			
Major (%)	7 (53.8)	na	na
Minor (%)	6 (46.2)	na	na
Postoperative complications			
No/Yes	7/6	3/4	ns
Length of hospital stay after surgery (days) *	25.0±20.6 (9-85)	42.4±17.1 (26-79)	0.07
Patients with re-hospitalization (%)	7 (53.8)	7 (100)	ns
Patients with recurrence of malignancy (%)	4 (30.8)	0 (0)	ns

LDLT, living donor liver transplantation; ns, not significant; na, not applicable.

* values are median (range)

Figure legends

Figure 1: Fluctuations of SF-36 scores after surgery in patients with hepatectomy and living donor liver transplantation (LDLT). a. physical function (PF), b. role physical (RP), c. bodily pain (BP), d. general health (GH), e. vitality (VT), f. social functioning (SF), g. role emotional (RE), h. mental health (MH). * $p < 0.05$, ** $p < 0.01$ versus preoperative value of the hepatectomy group. # $p < 0.05$ versus preoperative value of the living donor liver transplantation (LDLT) group.

Figure 2: Comparison of SF-36 scores of patients with hepatectomy and living donor liver transplantation (LDLT). a. before surgery, b. 12 months after surgery. * $p < 0.05$, ** $p < 0.01$.

Figure 1

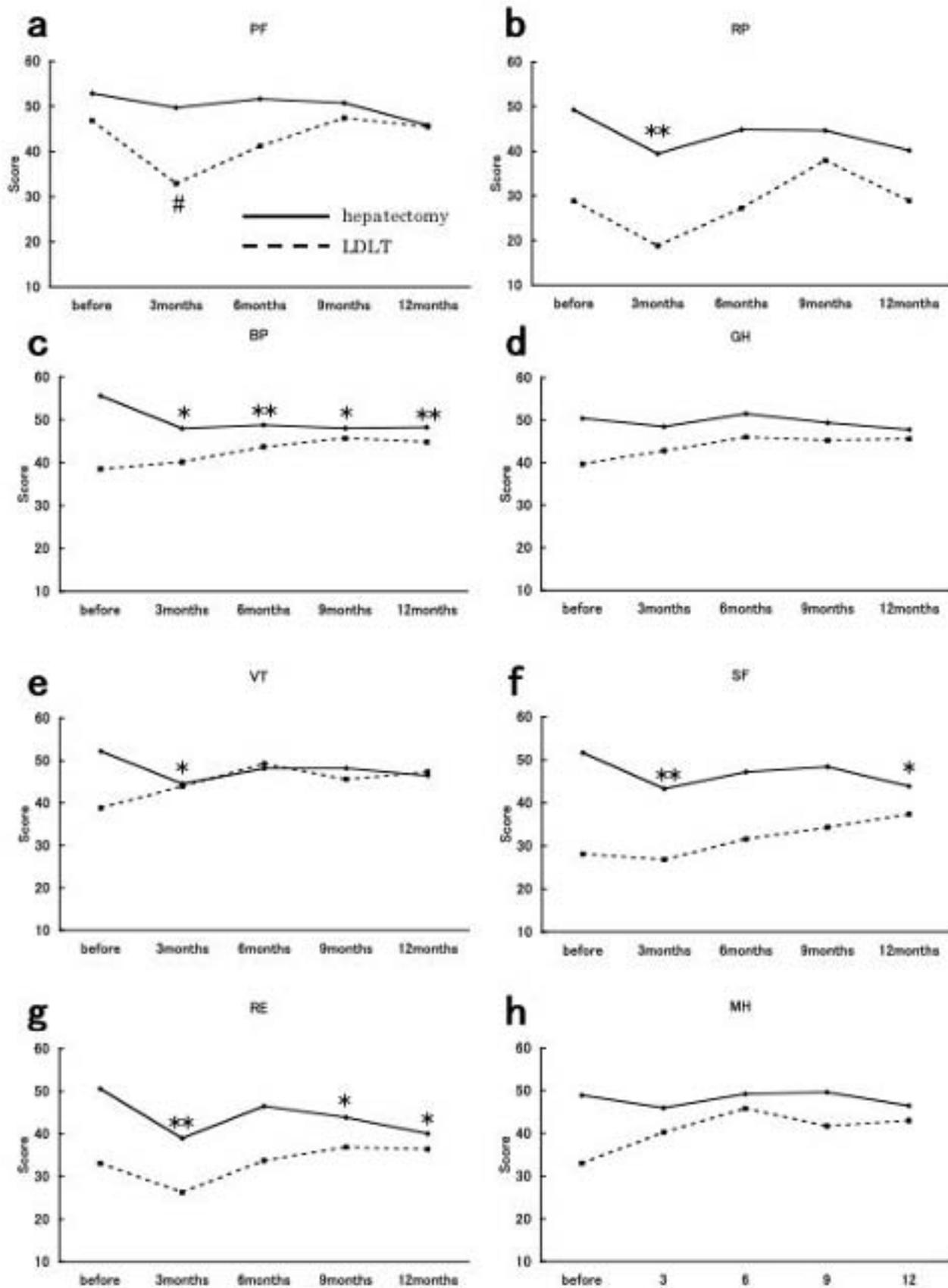


Figure 2

