Donor Safety and Recipient Liver Function After Right-Lobe Liver Transplantation From Living Donors With Gilbert Syndrome

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ABSTRACT

Background. Donor safety is the most important aspect in living-donor liver transplantation (LDLT). Gilbert syndrome is an autosomal recessive condition that is a common cause of isolated unconjugated hyperbilirubinemia, and its prevalence is not negligibly low in the general population. This study intended to assess donor safety and recipient liver function after LDLT with the use of right liver grafts from living donors with Gilbert syndrome.

Methods. Among 2,140 right liver transplantations performed from January 2002 to December 20113 at our institution, we identified 12 living donors (0.6%) who showed a preoperative serum total bilirubin level of $\geq$2 mg/dL. These donors were clinically diagnosed with Gilbert syndrome. The clinical outcomes of these donors and their recipients were analyzed retrospectively.

Results. The mean donor age was 24.6 $\pm$ 7.1 years, and 11 donors were male. All subjects met the preoperative evaluation conditions for right liver donation except for the level of unconjugated hyperbilirubinemia. The mean serum total bilirubin level of the donors was 2.23 $\pm$ 0.20 mg/dL before and 1.79 $\pm$ 0.61 mg/dL 1 year after right liver donation. The preoperative donor direct bilirubin level was 0.43 $\pm$ 0.19 mg/dL. The preoperative indocyanine green retention rate at 15 minutes was 8.2 $\pm$ 2.8%. All donors and recipients recovered uneventfully and were alive at the time of writing. The recipient serum total bilirubin level was 1.29 $\pm$ 0.47 mg/dL 1 year after LDLT.

Conclusions. We suggest that LDLT with living donors with Gilbert syndrome can be safely performed, but that a meticulous preoperative evaluation is vital to maximize donor safety.

LIVING-DONOR LIVER TRANSPLANTATION (LDLT) has become the mainstay of liver transplantation in many Asian countries, including Korea, owing to an intractable donor organ shortage. For adult recipients, a right liver graft has been more frequently used to meet the metabolic demand. Thus, greater emphasis is now placed on donor safety than in the era of the left liver graft [1].

Gilbert syndrome is a common autosomal recessive hereditary condition with incomplete penetrance, mainly characterized by intermittent unconjugated hyperbilirubinemia, in the absence of hepatocellular disease or hemolysis [2]. In the general population, Gilbert syndrome is not uncommon, with a reported incidence of 3%–12%. In individuals with Gilbert syndrome, the episodes of unconjugated hyperbilirubinemia occur intermittently when the affected individuals are exposed to physical stress, such as surgical intervention, fatigue, and/or fasting. An absolute increase of total serum bilirubin >1.9 mg/dL while fasting for 12–24 hours is considered to be diagnostic for Gilbert syndrome, with other liver function tests being within normal limits.

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Table 1. Demographic Data for the Living Donors With Gilbert Syndrome Analyzed in This Study

Case No	Age (y)	Sex	Weight (kg)	Height (cm)	BMI	Fatty Change (%)*	ICG R_{15} (%)	FRL (%)	GRWR
1	26	M	68	175	22.2	0	8.5	33.5	1.22
2	25	F	52	160	20.3	10	6.0	33.6	1.23
3	17	M	60	171	20.5	5	7.7	38.4	1.34
4	44	M	89	177	28.4	15	10.9	39.8	2.43
5	24	M	73	178	23.0	0	9.7	35.8	1.15
6	23	M	72	180	22.2	2	11.6	34.1	0.97
7	27	M	59	163	22.2	0	15.6	38.7	1.26
8	19	M	73	177	23.3	0	5.2	34.4	1.15
9	25	M	56	174	18.5	5	8.2	34.9	1.46
10	23	M	70	180	21.6	0	8.5	36.7	1.23
11	26	M	53	168	18.8	5	6.7	33.8	1.20
12	16	M	55	173	18.4	10	0.3	32.4	0.69

Abbreviations: M, male; F, female; BMI, body mass index; ICG R15, indocyanine green retention test at 15 minutes; FRL, future remnant liver; GRWR, graft volume–recipient weight ratio.
*Hepatic steatosis measured by means of preoperative percutaneous biopsy.

Normally, >90% of bilirubin present in the bile is in the form of glucuronide derivatives. This glucuronidation process is governed by uridine diphosphate–glucuronyl transferase. The activity of this enzyme is reduced to 30% of the normal value in individuals with Gilbert syndrome [3].

In the present study, we assessed donor safety and recipient liver function after LDLT with the use of right liver grafts from living donors with Gilbert syndrome.

PATIENTS AND METHODS

Among 2,140 living donors who donated right liver grafts from January 2002 to December 2013 at our institution, we identified 12 donors (0.6%) who showed a preoperative serum total bilirubin level ≥2.0 mg/dL. These donors were clinically diagnosed with Gilbert syndrome, but further genetic mutation studies were not performed. The routine preoperative donor evaluation at our institution includes serologic and biochemical analyses, complete blood count, computerized tomography (CT), magnetic resonance cholangiography (MRC), and ultrasonography-guided liver biopsy. The detailed evaluation process has been described elsewhere [4]. We retrospectively reviewed the medical records of these 12 donors and their recipients regarding their clinical course and preoperative and postoperative laboratory data. All donors displayed normal liver function tests except for an elevated level of total bilirubin and unconjugated bilirubin. Hepatic parenchymal or vascular abnormalities were excluded through image studies, including abdominal CT, ultrasonography, MRC, and a preoperative percutaneous liver biopsy. Detailed surgical procedures for right liver graft resection and implantation have been described elsewhere [4–8].

This study protocol was approved by the Institutional Review Board at our institution. Numeric data are reported as mean ± SD. Continuous variables were compared with the use of a paired Student *t* test. A *P* value of <.05 was considered to be statistically significant. Statistical analyses were performed with the use of SPSS (version 20; IBM Corp, Armonk, New York).

RESULTS

The mean donor age was 24.6 ± 7.1 years, and 11 donors were male. Their mean body mass index was 21.6 ± 2.7. Fatty changes in the donor livers were confirmed by means of percutaneous liver biopsy, which showed a mean fatty change of 4.3 ± 4.3%. The preoperative indocyanine green retention rate at 15 minutes was 8.2 ± 2.8%. Detailed data from individual donors are presented in Table 1.

All donors met the preoperative evaluation conditions for right liver graft donation except for having isolated unconjugated hyperbilirubinemia. The serum total bilirubin level of donors was 2.23 ± 0.20 mg/dL before surgery and 1.79 ± 0.61 mg/dL 1 year after surgery. Preoperative direct bilirubin level was 0.43 ± 0.19 mg/dL. All donors recovered uneventfully after the surgery for right liver graft donation. All recipients also recovered successfully and were alive at the time of writing with a mean serum total bilirubin level of 1.29 ± 0.47 mg/dL at 1 year. None of the recipients showed any vascular, biliary, or immunologic problems at the end of follow-up at 1 year. The preoperative and postoperative laboratory profiles of the donors and recipients are summarized in Table 2. The variations in total bilirubin level in donors and recipients are collectively depicted in Fig 1.

DISCUSSION

LDLT is currently widely accepted as the main therapeutic option for adult patients with acute or chronic end-stage liver disease. Donor safety is given primary emphasis at all transplantation centers performing LDLT, and the evaluation of living donor candidates is the most important process for this procedure. At our institution, 3 sequential phases in the living donor selection process have been performed as follows: phase 1, screening consisting of clinical examination and serologic tests; phase 2, screening consisting of dynamic liver CT with volumetry and abdominal Doppler ultrasonography; and phase 3, screening consisting of percutaneous liver biopsy and indocyanine green retention test [4]. Assessment of the serum bilirubin level is an essential factor in the first step for evaluating living liver donor candidates. Donor candidates showing unconjugated hyperbilirubinemia should undergo repeated liver function tests as well as strict further assessment regarding their liver function.

For living donor safety, the remnant liver volume after donation, degree of hepatic steatosis, and donor age are the