Liver transplantation (LT) is an effective treatment for patients with end-stage liver disease because of improved results and broadening of indications. For pediatric patients, LT with size-matched whole liver allografts from pediatric donors is considered as ideal due to lower complication rates and better survival compared with other variant types of LT [1]. However, the number of liver allografts recovered from pediatric donors is very limited in Korea. Further-
more, the body size of pediatric patients is widely variable from infant to adolescent, thus donor-recipient body size matching is much more complex compared with adult-to-adult deceased donor liver transplantation (DDLT).

Because of low incidence of pediatric deceased donors and complex donor-recipient body size matching, split LT and living donor LT have been more frequently performed for pediatric patients than LT with whole liver grafts [2]. Small-sized whole liver grafts from young pediatric donors have usually been allocated to young pediatric recipients, and liver grafts from adolescent donors have been allocated to both adolescent and adult recipients, and those from adult donors have also been reciprocally allocated to adolescent recipients [2-6]. There exists only limited detailed information on pediatric DDLT in Korea, thus, there is an essential need to analyze the status of pediatric DDLT using whole liver grafts [2,6]. We herein investigated the incidence and outcomes of pediatric DDLT using whole liver grafts in a high-volume LT center.

### METHODS

The study protocol was approved by the Institutional Review Board of Asan Medical Center (IRB No. 2020-0857), which waived the requirement for informed consent due to the retrospective nature of this study. This study was performed in accordance with the ethical guidelines of the World Medical Association Declaration of Helsinki 2013.

**Study Design**

The study was a retrospective single-center analysis of DDLT in pediatric recipients. The study period was set as 20 years between January 2000 and December 2019. We defined pediatric recipients and pediatric donors to be aged ≤18 years. There were 348 cases of pediatric LTs including living donor LT in 250 and DDLT in 98 (split LT in 64 and whole liver graft LT in 34). The recipients of whole...
liver grafts were followed up until June 2020. The immunosuppressive regimens for pediatric recipients were similar to those for adult recipients [7,8].

Surgical Technique for Whole LT
The standard techniques for whole LT have been used for pediatric recipients in principle. There are four technical points unique for pediatric DDLT. For recipients with body weight less than 40 kg, a modified piggyback technique involving a large cavocaval anastomosis was primarily used to secure graft outflow vein reconstruction. This method effectively prevents graft hepatic outflow obstruction under the situation of extrinsic compression of the inferior vena cava due to large-for-size graft implantation (Fig. 1). For recipients with body weight less than 20 kg and portal vein hypoplasia, the side-to-side unification venoplasty technique was used for portal vein reconstruction as it enables accomplishment of the effective size of the anastomotic cross-sectional area and a streamlined configuration without axial rotation (Fig. 2) [9]. For congenital portal vein hypoplasia or agenesis, portal vein interposition with deceased donor femoral vein or external iliac vein was used. Surgical microscopy was used for hepatic artery reconstruction regardless of the diameter of the artery.

Statistical Analysis
The numerical data are presented as mean±standard deviation. The continuous variables were compared using Student t-test. The incidence variables were compared using the chi-square test and Fisher’s exact test. The survival rates were estimated using the Kaplan-Meier method and compared using a log-rank test. A P-value of <0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS ver. 22.0 (IBM Corp., New York, NY, USA).

RESULTS
Donor and Recipient Profiles
During the 20-year study period, there were a total of 1056 cases of DDLT. Of them, 98 cases (9.2%) involved pediatric patients. The number of pediatric whole LT was 34 out of 98 (34.7%). The correlation in the age of the 34 deceased donors (range, 3 months–56 years) and 34 pediatric recipients (range, 7 months–17 years) is presented in Fig. 3. Male to female ratio was 20:14 in donors and 16:18 in recipients. Detailed recipient and donor profiles are summarized in Table 1.

The primary diseases for LT in 34 pediatric recipients were biliary atresia in 13, acute liver failure in four, Wilson disease in four, congenital portal vein agenesis with congenital portosystemic venous shunt in three, genetic metabolic diseases in three (each one case of Alagille syndrome, glycogen storage disease, and ornithine transcarbamylase deficiency), Caroli disease in one, progressive familial intrahepatic cholestasis in one, hepatoblastoma in one, and retransplantation after LDLT in four cases. One patient with glycogen storage disease had undergone hepatocyte transplantation 3 years before

Fig. 3. Scatter plots showing the age distribution of recipients and donors. Distribution of all the 34 recipients (A) and younger subgroups with recipient age ≤6 years (B). A dotted line denotes correlation.
Eight deceased donors were managed at our institution and the remaining 26 donors were managed at other institutions.

Donor and Recipient Matchings Regarding Age, Body Weight and Graft Size
The age distribution of the deceased donors and pediatric recipients is depicted in Fig. 3A. The recipients were categorized into subgroups depending on the age: between 7 months and 6 years and between 10 years and 17 years. In the younger subgroup, the age of the donors and recipients exhibited good correlation (donor age=0.86×recipient age, \(r^2=0.83\), \(P<0.001\)) (Fig. 3B), and all the donors were pediatric donors. On the contrary, in the older subgroup, out of 15, only three were pediatric donors and the remaining 12 donors were adult donors. Thus, pediatric-to-pediatric and adult-to-pediatric whole LTs were 22 (64.7%) and 12 (35.3%), respectively (Table 1).

The body weight distribution of the deceased donors and pediatric recipients is depicted in Fig. 4. The body weight of donors and recipients exhibited good correlation (donor body weight=0.93×recipient body weight, \(r^2=0.92\), \(P<0.001\)). The Korean Network for Organ Sharing (KONOS) regulation regarding donor-recipient body weight ratio of 1:2–2:1 was met in 33 of 34 cases. The distribution of the recipient's body weight and liver allograft's weight is depicted in Fig. 5. A good correlation was observed between the recipient's body weight and allograft's weight (liver graft weight (g)=21.8×recipient body weight (kg), \(r^2=0.89\), \(P<0.001\)). The distribution of the recipient's body weight and graft-recipient weight ratio (GRWR) is depicted in Fig. 6. The recipient's body weight and GRWR demonstrated coarse correlation (GRWR=8.92×recipient body weight (kg)^{-0.35}, \(r^2=0.53\), \(P<0.001\)). The correlation curve was close to the theoretical upper limit of GRWR (4 for infants and 2.5 for adolescents or adults) according to the recipient’s age or body weight.

Operation Profiles
For pediatric recipients with a body weight of less than 40 kg, the abovementioned modified piggyback techniques were primarily used for graft outflow vein reconstruction. For older adolescent patients, the standard technique of DDLT with interposition of the graft inferior vena cava was used. The mean warm, cold, and total ischemic times were 275.8±153.4 minutes (range, 71–839 minutes), 46.1±9.9 minutes (range, 30–74 minutes), and 335.3±221.8 minutes (range, 101–1,397 minutes), respectively. There was no incidence of major vascular complications, except for portal vein stenosis in infant-to-infant whole LT in three cases [7].

Survival Outcomes
During a mean follow-up period of 73.1±51.5 months, four patients passed away. In-hospital mortality within 2 months occurred in two cases due to portal vein complication-associated graft failure. One patient who had DDLT as retransplantation died at 6 months due to progressive

| Table 1. Comparison of recipient and donor profiles |
|-----------------------------------------------|
| Variable                        | Pediatric-to-pediatric transplantation | Adult-to-pediatric transplantation | P-value |
| No. of patients                | 22                                      | 12                                     | -       |
| Recipient sex (male:female)    | 8:14                                     | 8:4                                      | 0.09    |
| Recipient age (yr)             | 4.2±4.4                                  | 13.8±2.1                                 | <0.001  |
| Primary disease                | NA                                      |                                         |         |
| Biliary atresia                | 12                                      | 1                                      |         |
| Acute liver failure            | 0                                       | 4                                      |         |
| Wilson disease                 | 0                                       | 4                                      |         |
| Metabolic disease              | 3                                       | 0                                      |         |
| Congenital portal vein agenesis| 3                                       | 0                                      |         |
| Retransplantation              | 2                                       | 2                                      |         |
| Others                         | 2                                       | 1                                      |         |
| Recipient ABO blood group      | NA                                      |                                         |         |
| A                              | 8                                       | 4                                      |         |
| B                              | 2                                       | 2                                      |         |
| O                              | 6                                       | 5                                      |         |
| AB                             | 6                                       | 1                                      |         |
| Preoperative laboratory finding|                                         |                                         |         |
| Total bilirubin (mg/dL)        | 11.3±11.1                                | 20.6±13.6                               | 0.05    |
| Albumin (g/dL)                 | 2.9±0.6                                  | 3.1±0.7                                 | 0.51    |
| Serum creatinine (mg/dL)       | 0.34±0.21                                | 0.83±0.46                               | <0.001  |
| Prothrombin time (INR)         | 1.24±0.34                                | 2.77±1.22                               | <0.001  |
| PELD/MELD score                | 10.5±7.3                                 | 27.0±8.6                                | <0.001  |
| Donor sex (male:female)        | 14.8                                     | 6.6                                     | 0.44    |
| Donor age (yr)                 | 3.4±3.9                                  | 42.3±10.1                               | <0.001  |
| Graft weight (g)               | 576.1±315.2                              | 1,222.3±492.9                           | <0.001  |
| Graft-recipient weight ratio   | 3.69±1.66                                | 2.68±0.91                               | 0.03    |
| Ischemic time                  |                                         |                                         |         |
| Cold                           | 297.8±262.6                              | 286.1±131.9                             | 0.88    |
| Warm                           | 46.2±9.2                                 | 45.7±11.7                               | 0.84    |

Values are presented as mean±standard deviation.
NA, not available; INR, international normalization ratio; PELD, pediatric end-stage liver disease; MELD, model for end-stage liver disease.
One patient died at 23 months due to progressive graft failure after repeated episodes of acute cellular rejection. Graft and overall patient survival rates were 91.2% and 91.2% at 1 year, 88.0% and 88.0% at 3 years, and 88.0% and 88.0% at 5 years, respectively (Fig. 7).

**DISCUSSION**

The present study included 22 cases of pediatric-to-pediatric and 12 cases of adult-to-pediatric DDLT using whole liver grafts. During the 20-year study period, there were 348 cases of pediatric LTs including living donor LT in 250 and DDLT in 98 with inclusion of split LT in 64 and whole liver graft LT in 34. Thus, the proportion of whole liver graft LT was 9.8% in pediatric LT cases. There were also a total of 1,056 cases of DDLT, thus pediatric whole liver graft LT occupied 3.2% of all DDLTs. These proportions indicate that whole liver graft LT is the least common form of pediatric LT. The body weight of the deceased donors and pediatric recipients were well matched, thus high correlation between the recipient’s body weight and allograft’s weight and reasonable GRWR were observed.

We previously demonstrated that, of the 31 pediatric
graft failure. One patient died at 23 months due to progressive graft failure after repeated episodes of acute cellular rejection. Graft and overall patient survival rates were 91.2% and 91.2% at 1 year, 88.0% and 88.0% at 3 years, and 88.0% and 88.0% at 5 years, respectively (Fig. 7).
donor liver allografts, nine whole liver grafts were implanted in pediatric recipients, 16 whole liver grafts in adult recipients, and 10 split liver grafts in four pediatric and six adult patients [6]. In our previous study, more than half of the pediatric donor liver grafts were allocated to adult patients. Considering that adult-to-pediatric DDLT occupied one-third of pediatric whole LT and more than half of the pediatric donor liver grafts were used as pediatric-to-adult DDLT, pediatric liver grafts from older children were more frequently used for adult patients than pediatric patients, probably due to donor-recipient body weight matching and lack of pediatric patients with high-priority on the pediatric waiting list. Our previous study and the present study demonstrate the real-world status of DDLT for pediatric donors and recipients in Korea.

According to the Korean standardized growth patterns of children, the 50th percentiles of body weight at 5 years, 10 years, and 15 years are 19.0 kg, 35.5 kg, and 60.1 kg, respectively. Thus, pediatric donors over 10 years of age have comparable body weight to that of adult patients. According to the KONOS regulations of donor-recipient body weight match ratio of 1:2—1:2, the liver graft from adolescent donors can be allocated to adult recipients as whole or split liver grafts. To the best of our knowledge, there is still no KONOS regulation for the priority allocation of pediatric liver allografts to pediatric recipients.

In the present study, for pediatric patients aged ≤6 years of age, a high correlation was observed between donor and recipient age, which resulted in the reasonable matching of donor and recipient body weight and GRWR values. On the contrary, pediatric patients aged more than 10 years received liver grafts more frequently from adult donors than pediatric donors, primarily because the incidence of deceased donors of that age is lowest, as shown in our previous analysis of the KONOS database [6].

Graft-recipient size matching to avoid large-for-size graft implantation is one of the main concerns for young pediatric recipients and avoidance of small-for-size graft implantation is important for adolescent and adult recipients [10,11]. The results of this study revealed that the KONOS regulations on donor-recipient body weight ratio appeared to be too wide for accurate size matching, but it was reasonably acceptable for real-world liver organ allocation because severe size mismatching was selectively precluded by the transplant teams.

The incidence of vascular complications reported in the pediatric LT literature is variable and can be up to 25%–33% [12–14]. Hepatic artery thrombosis is the most serious complication after LT, and early hepatic artery thrombosis is the main cause of graft loss in pediatric LT. A similar incidence of early vascular complication in the pediatric-to-pediatric LT group and the pediatric-to-adult LT group has been reported, and the low body weight of the recipient was identified as an independent risk factor for vascular complications in pediatric LT [4]. A meta-analysis compared the survival rates and incidence of surgical complications between pediatric whole LT and other types of LT, in which the graft and patient survival rates were higher in the whole LT group; the incidence of portal vein thrombosis and biliary complications were lower in the whole LT group and the incidence of hepatic artery thrombosis was comparable between the two groups [1].

Vascular complications frequently occur following the implantation of a whole liver graft in an infant recipient because of the small vessel size per se although the graft size is well-matched to the recipient body size. We previously demonstrated the occurrence of portal vein complications in four of seven cases with infant-to-infant whole LT, and successful prevention through customized surgical techniques with side-to-side unification venoplasty [9].

The pediatric end-stage liver disease (PELD) scores used in pediatric patients are usually lower than the model for end-stage liver disease (MELD) scores used in adult patients. Considering the characteristics of liver diseases in childhood, pediatric patients with PELD scores cannot directly compete with adult patients with MELD scores. Many grave conditions that require LT in children do not show abnormal liver function [2]. In this study with a study period of 20 years, 12 cases of pediatric whole LT were performed in the form of adult-to-pediatric DDLT, but there were only three cases of adult-to-pediatric whole LT after the adoption of MELD score for organ allocation in 2016. The results of this study and our previous study on pediatric deceased donors reveal that pediatric patients are more disadvantageous concerning organ allocation under the current MELD/PELD score-based KONOS allocation system compared to the previous situation [6].

The Organ Procurement and Transplantation Network (OPTN) of North America prioritizes pediatric potential transplant recipients while allocating livers from pediatric deceased donors [15]. The ethical principles behind their pediatric organ allocation policy are elucidated by the OPTN/United Network for Organ Sharing Pediatric Transplantation and Ethics Committees [16], which states that the National Organ Transplant Act charges the OPTN to recognize the differences in health and organ transplan-
tation issues between children and adults throughout the system and adopt criteria, policies, and procedures that address the unique health care needs of children.

We contemplate that it is reasonable to add a PELD score exception for patients with inborn errors of metabolism, hepatoblastoma, and some unusual diseases to the current MELD/PELD score-based allocation system. Considering the relatively small number of such patients at the pediatric DDLT waiting list, we hypothesize that a policy of “pediatric donor liver grafts to pediatric recipients with priority” will be effective to shorten the pediatric waiting list [2].

This study had a notable limitation. This was a retrospective, single-center study with a relatively small number of study patients. Further high-volume multicenter studies are necessary to validate the results of this study.

In conclusion, the results of this study revealed that KONOS regulations with the matching of donor-recipient body weight worked well and older pediatric patients also received whole liver grafts from adult donors. Considering the adult-favoring reciprocal trades of liver organs among pediatric and adult donors and recipients, it is necessary to establish a policy for pediatric donor liver grafts to pediatric recipients on a priority basis.

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Conflict of Interest
Shin Hwang is an editorial board member of the journal but did not involve in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

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REFERENCES
1. Ye H, Zhao Q, Wang Y, Wang D, Zheng Z, Schroder PM, et al. Outcomes of technical variant liver transplantation versus whole liver transplantation for pediatric patients: a meta-analysis. PLoS One 2015;10:e0138202.
2. Lee S, Lee SK. Pediatric liver transplantation in Korea: long-term outcomes and allocations. J Korean Soc Transplant 2019;33:1-5.
3. Feng AC, Liao CY, Fan HL, Chen TW, Hsieh CB. A successful child-to-adult deceased donor liver transplantation: a case report and literature review. Ann Transplant 2015;20:21-4.
4. Zhang R, Zhu ZJ, Sun LY, Wei L, Qu W. Outcomes of liver transplantation using pediatric deceased donor livers: a single-center analysis of 102 donors. Chin Med J (Engl) 2018;131:677-83.
5. Emre S, Soejima Y, Altaca G, Facciuto M, Fishbein TM, Sheiner PA, et al. Safety and risk of using pediatric donor livers in adult liver transplantation. Liver Transpl 2001;7:41-7.
6. Namgung JM, Hwang S, Ahn CS, Kim KH, Moon DB, Ha TY, et al. Korea-nationwide incidence of pediatric deceased donors and single-institutional status of liver transplantation using pediatric donor liver grafts. Korean J Transplant 2020;34:178-84.
7. Kang SH, Hwang S, Ha TY, Song GW, Jung DH, Ahn CS, et al. Cross-sectional analysis of immunosuppressive regimens focused on everolimus after liver transplantation in a Korean high-volume transplantation center. Korean J Transplant 2019;33:98-105.
8. Hwang S, Namgoong JM, Oh SH, Kim KM, Ahn CS, Kwon H, et al. Effect of everolimus rescue therapy for acute cellular rejection following pediatric living donor liver transplantation: report of one case. Ann Hepatobiliary Pancreat Surg 2020;24:216-20.
9. Namgoong JM, Hwang S, Ahn CS, Jung DH, Park...
GC. Side-to-side portal vein reconstruction for infant-to-infant deceased donor whole liver transplantation: report of 2 cases with video. Ann Hepatobiliary Pancreat Surg 2020;24:301-4.

10. Kiuchi T, Kasahara M, Uryuhara K, Inomata Y, Uemoto S, Asonuma K, et al. Impact of graft size mismatching on graft prognosis in liver transplantation from living donors. Transplantation 1999;67:321-7.

11. Vanatta JM, Esquivel CO. Status of liver transplantation in infants <5 kg. Pediatr Transplant 2007;11:5-9.

12. Heffron TG, Welch D, Pillen T, Fasola C, Redd D, Smallwood GA, et al. Low incidence of hepatic artery thrombosis after pediatric liver transplantation without the use of intraoperative microscope or parenteral anticoagulation. Pediatr Transplant 2005;9:486-90.

13. Shackleton CR, Goss JA, Swenson K, Colquhoun SD, Seu P, Kinkhabwala MM, et al. The impact of microsurgical hepatic arterial reconstruction on the outcome of liver transplantation for congenital biliary atresia. Am J Surg 1997;173:431-5.

14. Ooi CY, Brandão LR, Zolpys L, De Angelis M, Drew W, Jones N, et al. Thrombotic events after pediatric liver transplantation. Pediatr Transplant 2010;14:476-82.

15. United Network for Organ Sharing (UNOS). Organ distribution: allocation of livers [Internet]. Richmond, VA: UNOS; 2011 [cited 2020 Oct 30]. Available from: https://optn.transplant.hrsa.gov.

16. United Network for Organ Sharing (UNOS). Ethical principles of pediatric organ allocation [Internet]. Richmond, VA: UNOS; 2011 [cited 2020 Oct 30]. Available from: https://optn.transplant.hrsa.gov.