Days alive and out of hospital and graft survival after living donor liver transplantation

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Background: Days alive and out of hospital (DAOH) is a simple metric representing the number of days not in hospital within a defined postoperative period. In a case of mortality within the defined period, the DAOH is considered zero. DAOH has been validated in various surgical procedures, but not in living donor liver transplantation (LDLT). This study aimed to demonstrate correlation between DAOH and graft failure after LDLT.

Methods: In this cohort study, we identified 1,335 adult-to-adult LDLT performed from June 1997 to April 2019 in our institution. We calculated DAOH at 30, 60, and 90 days among survivors and divided the recipients according to the estimated threshold of each defined period.

Results: The median duration of hospital stay after LDLT in the entire population was 25 (interquartile 22–41) days. Mean DAOH of survivors at 30, 60, and 90 days were 3.3 (±3.9), 19.7 (±15.9), and 40.3 (±26.3) days, respectively. We estimated the thresholds associated with three-year graft failure for DAOH at 30, 60, and 90 days and they were 1, 12, and 42 days, respectively. The incidence of graft failure was higher in recipients with short DAOH than long DAOH (10.9% *vs.* 23.6%, 10.3% *vs.* 24.3%, and 9.3% *vs.* 22.2% for DAOH at 30, 60, and 90 days, respectively). Among survivors at 60 days, recipients with short DAOH showed significantly higher incidence of three-year graft failure [hazard ratio (HR), 2.49; 95% confidence interval (CI): 1.86–3.34; P<0.001].

Conclusions: Considering clinical situations after LDLT, DAOH at 60 days may be a valid outcome measure.

Keywords: Outcome; living donor liver transplantation (LDLT); graft failure

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Introduction

Liver transplantation is a well-established therapy for individuals who have advanced liver disease or inoperable hepatocellular carcinoma, with or without cirrhotic changes. Meanwhile, living donor liver transplantation (LDLT) offers a comparable survival advantage while also reducing the waiting time for potential recipients (1). There remains a considerable burden for organ donors so a reliable measure for LDLT outcome is highly required for clinicians to select recommended patients for LDLT. As postoperative mortality is declining in LDLT recipients, outcome measures that can adequately reflect long-term graft survival are needed.

Days alive and out of hospital (DAOH) is a recently introduced outcome measure that can be easily calculated (2). The concept of DAOH arose among patients with chronic diseases (3) and has been validated in various surgical procedures (2,4,5). The Standardized Endpoints in Perioperative Medicine (StEP) initiative recommended DAOH at 30 days after surgery as a reliable outcome measure in the general surgical population (6). However, LDLT has a different aspect as a surgical procedure with higher mortality, longer period of in-hospital treatment, and higher readmission rate. Therefore, in this study, we aimed to investigate the association between graft failure and DAOH at 30, 60, and 90 days after LDLT to identify a reliable outcome measure. Additionally, we evaluated factors that were associated with shortened DAOH using machine learning technique. We present this article in accordance with the STROBE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-6595/rc).

Highlight box

Key findings

- Days alive and out of hospital (DAOH) at 60 days after living donor liver transplantation (LDLT) was shown to be associated with long-term incidence of graft failure.

What is known and what is new?

- DAOH is a recent concept for outcome assessment, and it has been validated in various clinical setting. DAOH has not been validated in patients undergoing LDLT, and an adequate amount of follow-up duration for DAOH in LDLT has not been specified. This study showed that DAOH at 60 days after LDLT was shown as a valid outcome measure.

What is the implication, and what should change now?

- DAOH is a simple outcome measure, and it could be sued in LDLT recipients at postoperative 60 days.

Methods

Study population, data collection, and study endpoints

This study used a retrospective observational cohort and was approved by the institutional review board of Samsung Medical Center (No. 2022-03-141). We conducted this study following the Declaration of Helsinki (as revised in 2013). Due to the retrospective nature of the study and minimal risk to the participants, the institutional review board has waived the requirement for written informed consent.

We reviewed the entire cohort of liver transplantation at our institution between June 1997 and April 2019 to identify adult-to-adult LDLT recipients. In recipients with multiple liver transplantations, only the first transplantation was included in analysis. Clinical, laboratory, and outcome data were organized by the study coordinator, who was not otherwise involved in this study and was blinded to clinical outcomes. Our electronic hospital record system used mortality data from the National Population Registry of the Korea for patients outside the institution.

The primary endpoint of this study was to evaluate the association between graft failure during three-year follow-up and DAOH at 30, 60, and 90 days. Graft failure during one-year follow-up was also evaluated. Graft failure was defined as either the recipient's death or the need for re-transplantation. In cases where a recipient underwent re-transplantation before their death, they were counted as both a death and a re-transplantation.

Donor selection, surgical procedures, and anesthetic care

Donor selection criteria and surgical procedures followed the institution protocol, which has been previously described (7). Briefly, our donor selection criteria included adults younger than 65 years old with a body mass index lower than 35, biochemistry within normal range, and adequate size of graft and expected remnant liver of more than 30%. Any conditions related to increased surgical risk excluded the patient from donor selection.

The right side of the liver consisting of 5 to 8 segments according to the Couinaud's classification system was the primary graft choice. The surgical margin of the graft was determined based on anatomical characteristics.

After implanting harvested graft liver, the right hepatic vein was initially anastomosed, and if necessary, the anastomosis of the inferior hepatic vein followed. After portal vein anastomosis, the hepatic vein and portal vein were unclamped for reperfusion of the graft liver, and after reperfusion, the hepatic artery and biliary tract were anastomosed.

Anesthetic care was standardized for all recipients. During the surgical procedure, the patient's vital signs were monitored through peripheral capillary oxygen saturation, 5-lead electrocardiography, and non-invasive arterial blood pressure. General anesthesia was induced using thiopental sodium and maintained with isoflurane adjusted to a bispectral index of 40 to 60. Mechanical ventilation was adjusted to a tidal volume of 8 to 10 mL/kg based on the ideal body weight, using a mixture of medical air and oxygen at a fresh gas flow rate of 2 L/min. The respiratory rate was continually adjusted to maintain normocapnia. If the patient's blood hemoglobin levels dropped below 8.0 g/dL, intraoperative transfusion of packed red blood cells was considered.

The criteria for discharge after LDLT recipients included hemodynamic stability, stabilization of liver enzyme tests, and no active intraoperative infection. Recipients with minor infection were discharged when the infection was well controlled with oral antibiotics. Recipients with minimal leakage were also discharged when it was well controlled with successful drainage.

Calculation of DAOH

DAOH was calculated according as previously described (2). We obtained the number of days spent out of hospital by subtracting the total duration of initial or subsequent in-hospital days from the total defined time periods (30, 60, and 90 days). In a case of mortality within the defined period, the DAOH was 0; thus, DAOH ranged from 0 to the defined length of period with a smaller number indicating an adverse outcome.

Statistical analysis

In this study, we analyzed descriptive data of the entire population and the association with graft failure among survivors at the defined periods of DAOH. In the descriptive analysis, differences of continuous data were presented as mean ± standard deviation, and categorical variables were presented numerically with incidence. Receiver operating curve (ROC) plots were constructed to estimate thresholds of DAOH at each follow-up day; the survivors of at each follow-up period were divided according to these thresholds. We also compared the incidence of graft failure during three-year follow-up according to the estimated threshold of DAOH at 60 days and provided it as a hazard ratio (HR) with 95% confidence interval (CI). As an added investigation, we utilized a machine learning technique with an extreme gradient boosting (XGB) algorithm to examine the factors linked to short duration of hospitalization after surgery. The impact of each variable was assessed using SHapley Additive exPlanations (SHAP) values, which were determined by comparing the model's prediction with and without each variable (8). SHAP summary plot explains the intensity and direction of impact on the outcome of interest. All statistical analyses were performed with R 4.1 (Vienna, Austria; http://www.R-project.org/). All tests were 2-tailed, and P<0.05 was considered statistically significant.

Results

From June 1997 to April 2019, a total of 1,335 cases of adult-to-adult LDLT were performed in our institution. The results of descriptive analysis on the entire study patients are summarized in *Table 1*. The incidence of graft failure during the three-year follow-up was 20.1% (269/1,335). The median duration of hospital stay after LDLT was 25 (interquartile 22–41) days. The mean days of DAOH at 30, 60, and 90 days in the entire population were 3.2 (±3.9), 18.7 (±15.9), and 37.9 (±27.2), respectively (*Table 2*).

Because this study aimed to investigate whether DAOH at each period is associated with future outcomes, we enrolled survivors at each follow-up period of DAOH. There were 1,295, 1,266, and 1,254 survivors at 30, 60, and 90 days, respectively (*Table 2*). Mean DAOH for survivors at 30, 60, and 90 days were 3.3 (±3.9), 19.7 (±15.9), and 40.3 (±26.3), respectively, and readmission rates were 4.1% (53/1,295), 23.6% (299/1,266), and 31.7% (398/1,254), respectively.

The ROCs for the association between DAOH and graft failure during the three-year and one-year follow-ups are shown in *Figure 1*. The thresholds associated with graft failure during the three-year follow-up for DAOH at 30, 60, and 90 days were 1, 12, and 42 days, respectively. The areas under ROC curves were 0.621, 0.644, and 0.654, respectively (*Figure 1*). The sensitivities and specificities of these thresholds are presented in *Figure 1*. The baseline

Table 1 Baseline characteristics and outcomes of the entire population of 1,335 recipients

Variables	Values (N=1,335)
Recipient variables	
Age, years	52.1 (±8.9)
Male	1,038 (77.8)
Smoking	217 (16.3)
Alcohol use	217 (16.3)
Hepatorenal syndrome	67 (5.0)
Encephalopathy	286 (21.4)
Varix	248 (18.6)
Ascites	777 (58.2)
Bacterial peritonitis	145 (10.9)
Hypertension	153 (11.5)
Diabetes	263 (19.7)
Stroke	17 (1.3)
Tuberculosis	59 (4.4)
MELD score	18.1 (±10.4)
Albumin	3.2 (±0.6)
Preoperative intensive care	109 (8.2)
Pathology	
Alcohol related	135 (10.1)
Viral	996 (74.6)
Acute	141 (10.6)
Cirrhosis	1,192 (89.3)
Hepatocellular carcinoma	736 (55.1)
Donor variables	
Age, years	32.9 (±11.4)
Male	862 (64.6)
Body mass index, kg/m^2	23.3 (±3.1)
Macrosteatosis, %	7.0 (±6.3)
GRWR	1.1 (±0.2)
Operative variables	
Right graft	1,309 (98.1)
Operative duration, minutes	557.1 (±123.1)
Graft failure during 3 years	269 (20.1)
Retransplantation	41 (3.1)
Death	253 (19.0)
Graft failure during one year	162 (12.1)
Retransplantation	26 (1.9)
Death	150 (11.2)

Values are n (%) or mean (± SD). MELD, model for end-stage liver disease; GRWR, graft-to-recipient body weight ratio; SD, standard deviation.

characteristics and incidences of graft failure according to the estimated thresholds are summarized in *Table 3*. According to the estimated thresholds, the incidences of graft failure during three-year and one-year follow-ups were consistently higher in recipients with short DAOH compared with long DAOH (10.9% *vs.* 23.6% for three-year graft failure and 4.1% and 14.0% for one-year graft failure in DAOH at 30 days, 10.3% *vs.* 24.3% for three-year graft failure and 3.3% and 13.7% for one-year graft failure in DAOH at 60 days, and 9.3% *vs.* 22.2% for three-year graft failure and 2.4% and 11.6% for one-year graft failure in DAOH at 90 days). Among survivors at 60 days after LDLT, recipients with lower DAOH at 60 days showed significantly higher incidence of graft failure during the three-year follow-up (10.3% *vs.* 24.4%; HR, 2.64; 95% CI: 1.99–3.51; P<0.001). After an adjustment with relevant variables, the result was similar (HR, 2.49; 95% CI: 1.86–3.34; P<0.001).

In the SHAP summary plot, the effects of each variable on short DAOH 60, DAOH 30, and DAOH 90 was presented in descending order (*Figure 2*). The variables that were highly associated with short DAOH 60 included operation duration, preoperative albumin level, international normalized ratio, graft-to-recipient weight ratio, model for end-stage liver disease, and macrosteatosis for DAOH 60. Additionally, operation duration and the components of model for end-stage liver disease score tended to show large effects on DAOH regardless of follow-up duration.

Discussion

This study demonstrated that DAOH correlated well with postoperative outcomes in a large cohort of LDLT patients. In recipients who survived for 30, 60, and 90 days after LDLT, DAOH was associated with the incidence graft failure for both one-year and three-year follow-up periods. In ROC analysis, the area under the curve tended to be larger for DAOH at longer follow-up periods.

An objective and standardized measure to grade postoperative outcome for clinical trials and quality improvement has long been investigated (6). The length of hospital stay reflects clinical outcomes in an isolated form but has a major pitfall in representing early mortality. DAOH on the other hand provides a single summary that extends into the postoperative recovery period (2,6). DAOH was first introduced as a perioperative outcome measure in 2017 (2) and has been further validated in broader settings of a surgical patient cohort in Sweden (9), an elective

Table 2 Summary of DAOH relevant measures in the entire population and survivors at 30, 60, and 90 days after transplantation

Variables	DAOH	Readmission	Mortality
Entire population (N=1,335)			
At 30-day follow-up	3.2 (±3.9)	53 (4.0)	40 (3.0)
At 60-day follow-up	18.7 (±15.9)	302 (22.6)	69 (5.2)
At 90-day follow-up	37.9 (±27.2)	403 (30.2)	81 (6.1)
Survivors			
At 30-day follow-up (N=1,295)	3.3 (±3.9)	53 (4.1)	–
At 60-day follow-up (N=1,266)	19.7 (±15.9)	299 (23.6)	–
At 90-day follow-up (N=1,254)	40.3 (±26.3)	398 (31.7)	–

Values are n (%) or mean (± SD). DAOH, days alive and out of hospital; SD, standard deviation.

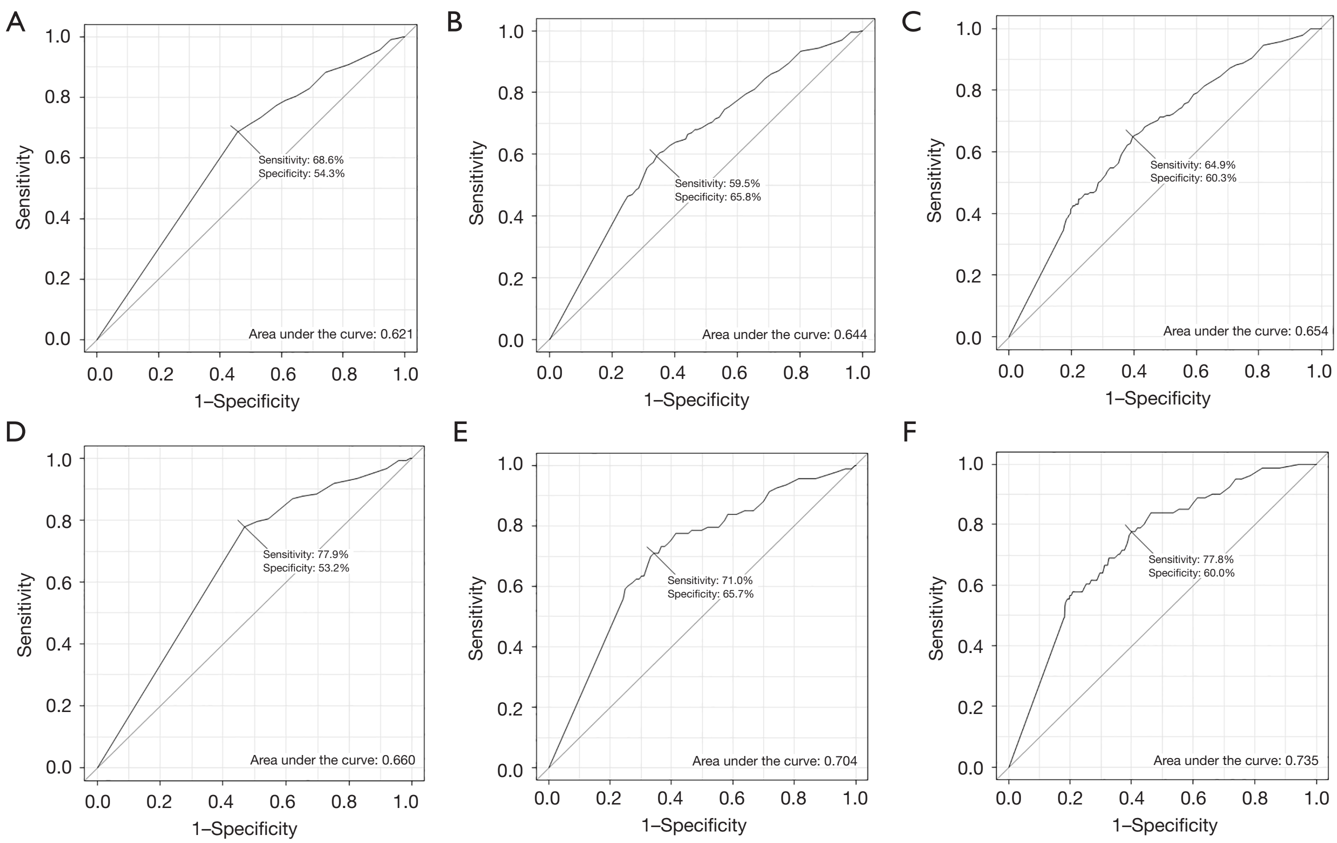

Figure 1 Receiver operating curves showing the association between (A) DAOH 30 and three-year graft failure, (B) DAOH 60 and three-year graft failure, (C) DAOH 90 and three-year graft failure, (D) DAOH 30 and one-year graft failure, (E) DAOH 60 and one-year graft failure, and (F) DAOH 90 and one-year graft failure. DAOH, days alive and out of hospital.

Table 3 Baseline characteristics and outcomes of survivors at 30, 60, and 90 days after transplantation according to estimated cut-off points of DAOH 30, 60, and 90

Variables	DAOH 30 (N=1,295)		DAOH 60 (N=1,266)		DAOH 90 (N=1,254)	
	Long >1 (N=603)	Short ≤1 (N=692)	Long >12 (N=769)	Short ≤12 (N=497)	Long >42 (N=700)	Short ≤42 (N=554)
Recipient variables						
Age, years	52.6 (±8.5)	51.7 (±9.0)	52.0 (±8.5)	52.2 (±9.3)	51.9 (±8.4)	52.3 (±9.3)
Male	493 (81.8)	514 (74.3)	610 (79.3)	376 (75.7)	558 (79.7)	419 (75.6)
Smoking	97 (16.1)	110 (15.9)	116 (15.1)	88 (17.7)	109 (15.6)	93 (16.8)
Alcohol use	85 (14.1)	119 (17.2)	114 (14.8)	86 (17.3)	105 (15.0)	92 (16.6)
Hepatorenal syndrome	12 (2.0)	50 (7.2)	24 (3.1)	35 (7.0)	23 (3.3)	34 (6.1)
Encephalopathy	105 (17.4)	163 (23.6)	159 (20.7)	99 (19.9)	149 (21.3)	107 (19.3)
Varix	109 (18.1)	132 (19.1)	155 (20.2)	81 (16.3)	144 (20.6)	89 (16.1)
Ascites	318 (52.7)	440 (63.6)	461 (59.9)	281 (56.5)	423 (60.4)	310 (56.0)
Bacterial peritonitis	44 (7.3)	94 (13.6)	88 (11.4)	46 (9.3)	79 (11.3)	54 (9.7)
Hypertension	67 (11.1)	78 (11.3)	86 (11.2)	55 (11.1)	76 (10.9)	63 (11.4)
Diabetes	114 (18.9)	138 (19.9)	140 (18.2)	106 (21.3)	129 (18.4)	114 (20.6)
Stroke	8 (1.3)	8 (1.2)	9 (1.2)	6 (1.2)	7 (1.0)	8 (1.4)
Tuberculosis	20 (3.3)	38 (5.5)	31 (4.0)	26 (5.2)	28 (4.0)	29 (5.2)
MELD score	15.7 (±8.8)	19.7 (±11.0)	17.5 (±9.9)	18.2 (±10.5)	17.7 (±10.1)	17.8 (±10.2)
Albumin	3.2 (±0.7)	3.1 (±0.6)	3.2 (±0.7)	3.2 (±0.6)	3.2 (±0.7)	3.2 (±0.6)
Preoperative intensive care	23 (3.8)	73 (10.5)	38 (4.9)	52 (10.5)	36 (5.1)	50 (9.0)
Pathology						
Alcohol related	63 (10.4)	65 (9.4)	72 (9.4)	54 (10.9)	66 (9.4)	58 (10.5)
Viral	471 (78.1)	504 (72.8)	601 (78.2)	355 (71.4)	549 (78.4)	401 (72.4)
Acute	41 (6.8)	91 (13.2)	68 (8.8)	56 (11.3)	63 (9.0)	57 (10.3)
Cirrhosis	562 (93.2)	599 (86.6)	700 (91.0)	440 (88.5)	636 (90.9)	496 (89.5)
Hepatocellular carcinoma	379 (62.9)	347 (50.1)	445 (57.9)	268 (53.9)	506 (72.3)	301 (54.3)
Donor variables						
Age	32.6 (±11.4)	33.1 (±11.4)	33.7 (±11.5)	32.2 (±11.3)	32.2 (±11.4)	33.4 (±11.4)
Male	399 (66.2)	443 (64.0)	512 (66.6)	311 (62.6)	471 (67.3)	344 (62.1)
Macrosteatosis, %	6.8 (±6.2)	7.0 (±6.4)	6.9 (±6.0)	7.1 (±6.7)	6.8 (±6.0)	7.1 (±6.6)
GRWR	1.1 (±0.2)	1.1 (±0.2)	1.1 (±0.2)	1.1 (±0.3)	1.1 (±0.2)	1.1 (±0.2)
Operative variables						
Right graft	596 (98.8)	675 (97.5)	761 (99.0)	483 (97.2)	692 (98.9)	540 (97.5)
Operative duration, minutes	538.4 (±113.5)	569.3 (±124.9)	543.6 (±114.4)	565.8 (±121.4)	543.5 (±109.8)	562.5 (±124.7)
Graft failure during 3 years	66 (10.9)	163 (23.6)	79 (10.3)	121 (24.3)	65 (9.3)	123 (22.2)
Retransplantation	5 (0.8)	31 (4.5)	5 (0.7)	29 (5.8)	4 (0.6)	29 (5.2)
Death	64 (10.6)	149 (21.5)	77 (10.0)	107 (21.5)	63 (9.0)	109 (19.7)
Graft failure during 1 year	25 (4.1)	97 (14.0)	25 (3.3)	68 (13.7)	17 (2.4)	64 (11.6)
Retransplantation	1 (0.2)	20 (2.9)	2 (0.3)	17 (3.4)	2 (0.3)	16 (2.9)
Death	24 (4.0)	86 (12.4)	24 (3.1)	57 (11.5)	16 (2.3)	53 (9.6)

Values are n (%) or mean (± SD). DAOH, days alive and out of hospital; MELD, model for end-stage liver disease; GRWR, graft-to-recipient body weight ratio; SD, standard deviation.

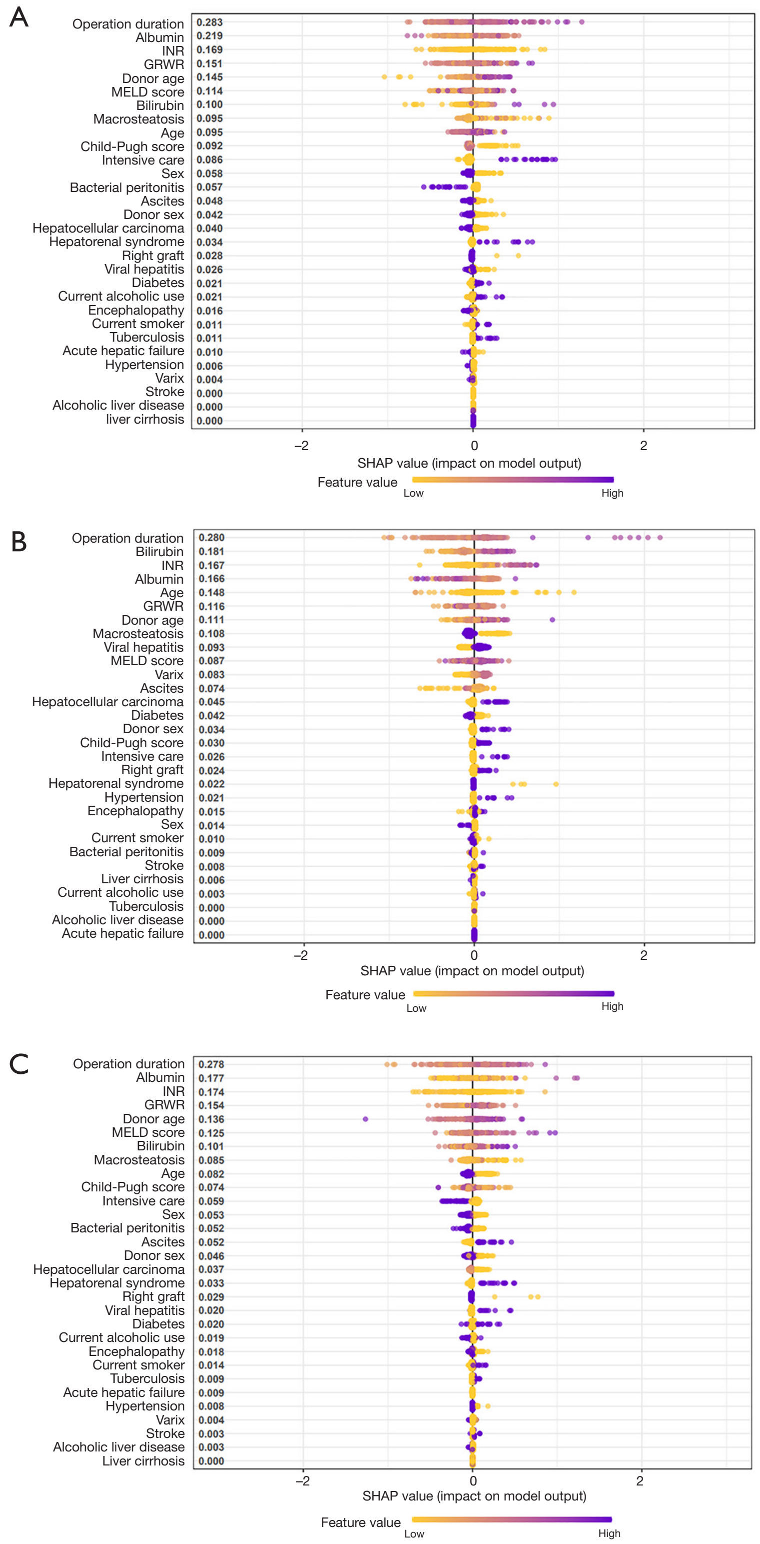

Figure 2 SHAP summary plot representing the results of the XGB algorithm of machine learning techniques on effect of each variable on shortened (A) DAOH 60, (B) DAOH 30, and (C) DAOH 90. INR, international normalized ratio; GRWR, graft-to-recipient body weight ratio; MELD, model for end-stage liver disease; SHAP, SHapley Additive exPlanations; XGB, extreme gradient boosting; DAOH, days alive and out of hospital.

surgery cohort in Canada (5), a hip and knee arthroplasty cohort in Denmark (10), and an emergency laparotomy cohort in England (4). DAOH is now accepted as a well-defined measure that indirectly but adequately reflects perioperative risk and complications. Moreover, it is simple to calculate and easily applied in daily practice.

One considerable issue in applying DAOH is to choose the duration of the follow-up period. The correlation outcome is predictably associated with improvement as the follow-up period of DAOH becomes longer. However, DAOH can be used for more patients if it is more rapidly obtainable. Additionally, a previous study warned that a mortality over 10% may significantly affect DAOH (2), because in this situation, DAOH =0 may represent mortality rather than longer duration of hospital stay. In this regard, DAOH at 30 days has been commonly recommended by previous studies (4,5,10) and the StEP initiative (6).

The liver transplant procedure usually requires a long duration of initial hospital stay with considerably high rate of early mortality and readmission for treatment of complications (7,11,12). Our recipients were often hospitalized for more than 30 days after LDLT. In addition, the mean value of DAOH of survivors at 30 days was 3.3 with an estimated threshold of 1, indicating that DAOH at 30 days in LDLT recipients shows a bimodal distribution and could not reflect postoperative outcome as a continuous variable. In fact, an issue regarding the bimodal distribution of DAOH has been mentioned in previous studies (4), but our case of DAOH at 30 days was extreme, and we do not recommend DAOH 30 days as an outcome measurement. As a result, we conducted analysis for longer periods in a consideration of not exceeding the period where mortality becomes too high. Although DAOH at 90 days was shown to correlate better with graft failure than DAOH at 60 days, the difference was not significant. Considering that 60 days is more rapidly obtainable for more recipients, the DAOH at 60 days seemed reasonable for an outcome measurement for LDLT recipients.

In an additional analysis, variables that were shown to be associated with short DAOH were in line with those that are known to affect LDLT outcomes. An intriguing finding was that the top variables associated with short DAOH tended to be donor-related. Moreover, the age difference between the recipients of short and long DAOH was not clinically significant. In fact, DAOH was largely dependent on patient age in previous studies with other surgical procedure (4,5,10). This seemed to be related to the nature of the LDLT procedure that recipients of LDLT are relatively young compared with patients of other surgical procedures and may have obscured the relationship between older age and short DAOH. In addition, the complexity of patients due to immunosuppressive state and accompanying complications would have affected the readmission and death beyond the effects of old age (13,14). On the other hand, the operative duration was consistently longer in recipients with short DAOH, indicating that the prognosis of LDLT is more dependent on surgical outcome than on the underlying condition of the recipients because it is mostly performed for selected candidates. In fact, operation duration was the variable that had the largest effect on DAOH regardless of follow-up period. So, minimizing operation duration may be helpful in improving outcomes and extending DAOH after LDLT. Additionally, the model for end-stage liver disease along with its components and albumin level were commonly associated with shortened DAOH. These blood laboratory tests are also well-known factors of LDLT (15,16). Further studies are needed on whether modifying preoperative blood laboratory tests could extend DAOH after LDLT.

This study should be interpreted with caution considering the following limitations. First, it is a single-center, retrospective study, which may have been affected by unrevealed confounding factors. Owing to the differences in clinical protocols between institutions, our results may not be generalizable, especially for the estimated thresholds of DAOH. The results should be interpreted as showing an inverse trend between DAOH and graft failure of LDLT. In addition, surgical techniques and postoperative management have advanced over the long study period, which also may have affected the results. A well-designed, future study with multi-center data is needed to confirm our findings. Although there were limitations to the study, our study presented noteworthy results that demonstrated the correlation between DAOH and postoperative outcomes in LDLT recipients.

Conclusions

DAOH is a simple measure that is readily available. In LDLT recipients, DAOH at 60 days may be a valid outcome measure with respect to graft failure. An effort to extend DAOH may be helpful for improving outcome of LDLT recipients.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-6595/rc

Data Sharing Statement: Available at https://atm.amegroups.com/article/view/10.21037/atm-22-6595/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-6595/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study used a retrospective observational cohort and was approved by the institutional review board of Samsung Medical Center (No. 2022-03-141). We conducted this study following the Declaration of Helsinki (as revised in 2013). The need for written informed consent was waived by the institutional review board considering the minimal risk for the participants and retrospective nature of the study.

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